

**UNITED STATES
 SECURITIES AND EXCHANGE COMMISSION**
 Washington, D.C. 20549

**FORM S-1
 REGISTRATION STATEMENT**

*Under
 The Securities Act of 1933*

ORIC PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its charter)

Delaware
 (State or other jurisdiction of
 incorporation or organization)

2834
 (Primary Standard Industrial
 Classification Code Number)

47-1787157
 (I.R.S. Employer
 Identification Number)

240 E. Grand Ave, 2nd Floor
 South San Francisco, CA 94080
 (650) 388-5600

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act

Large accelerated filer
 Non-accelerated filer

Accelerated filer
 Smaller reporting company
 Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)(2)	Amount of Registration Fee
Common Stock \$0.0001 par value	\$	\$

(1) Includes offering price of any additional shares of common stock that the underwriters have the option to purchase.
 (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

Explanatory note

Pursuant to the applicable provisions of the Fixing America's Surface Transportation Act, we are omitting our unaudited financial statements as of and for the nine months ended September 30, 2018 and 2019 because they relate to historical periods that we believe will not be required to be included in the prospectus at the time of the contemplated offering. We intend to amend the registration statement to include all financial information required by Regulation S-X at the date of such amendment before distributing a preliminary prospectus to investors.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state or other jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated _____, 2020

Preliminary prospectus



Common stock

This is an initial public offering of shares of common stock by ORIC Pharmaceuticals, Inc. We are offering _____ shares of our common stock to be sold in the offering. The initial public offering price is expected to be between \$ _____ and \$ _____ per share.

Prior to this offering, there has been no public market for our common stock. We intend to apply to list our common stock on the _____ under the symbol "ORIC."

We are an "emerging growth company" as defined under the federal securities laws and, as such, have elected to comply with certain reduced reporting requirements.

	Per share	Total
Initial public offering price	\$ _____	\$ _____
Underwriting discounts and commissions(1)	\$ _____	\$ _____
Proceeds to ORIC Pharmaceuticals, Inc., before expenses	\$ _____	\$ _____

(1) See "Underwriting" for a description of the compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to _____ additional shares of common stock.

Investing in our common stock involves a high degree of risk. See "[Risk factors](#)" beginning on page 12.

Neither the Securities and Exchange Commission nor any other state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on or about _____, 2020.

J.P. Morgan

Citigroup

Jefferies

Guggenheim Securities

, 2020

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Through and including _____, 2020 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

Neither we nor the underwriters have authorized anyone to provide you any information or make any representations other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

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For investors outside of the United States: we have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

Prospectus summary

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the section in this prospectus titled "Risk factors" and our financial statements and the related notes appearing elsewhere in this prospectus, before making an investment decision. As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our," "our company," and "ORIC" refer to ORIC Pharmaceuticals, Inc.

Overview

ORIC Pharmaceuticals is a clinical-stage biopharmaceutical company dedicated to improving patients' lives by *Overcoming Resistance In Cancer*.

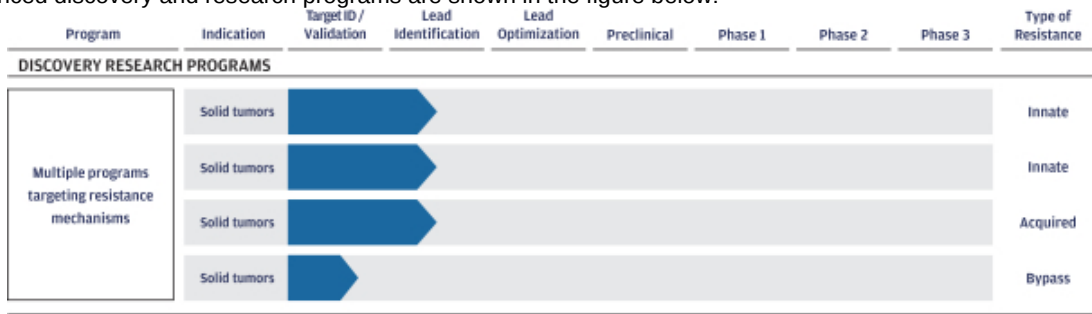
Profound advancements in oncology drug development have expanded the treatment options available to patients, yet therapeutic resistance and relapse continue to limit the efficacy and duration of clinical benefit of such treatments. Collectively, our founders and management team have a decades-long heritage of identifying and characterizing resistance mechanisms in oncology, having discovered and developed groundbreaking medicines at companies such as Ignyta, Medivation, Aragon and Genentech.

At ORIC, our fully integrated discovery and development team is advancing a diverse pipeline of innovative therapies designed to counter resistance mechanisms in cancer by leveraging our expertise within three specific areas: hormone-dependent cancers, precision oncology and key tumor dependencies. Our lead product candidate, ORIC-101, builds upon a legacy of successful drug development by our founders in the field of nuclear hormone receptors and their efforts to elucidate the cause of resistance to the groundbreaking prostate cancer therapies that they had developed. ORIC-101 is a potent and selective small molecule antagonist of the glucocorticoid receptor (GR), which has been linked to resistance to multiple classes of cancer therapeutics across a variety of solid tumors. In 2019, we initiated two separate Phase 1b trials of ORIC-101 in combination with (1) Xtandi (enzalutamide) in metastatic prostate cancer and (2) Abraxane (nab-paclitaxel) in advanced or metastatic solid tumors, and we expect to report interim data for one of these trials in the first half of 2021. Our second product candidate, ORIC-533, is an orally bioavailable small molecule inhibitor of CD73, a key node in the adenosine pathway believed to play a central role in resistance to chemotherapy- and immunotherapy-based treatment regimens. We expect to file an IND for ORIC-533 in 2021. Beyond these two product candidates, we are developing multiple precision medicines targeting other hallmark cancer resistance mechanisms. We believe our team and capabilities uniquely position us to be a leader in developing novel therapies to overcome resistance in cancer.

We own full worldwide development and commercialization rights to each of our programs. Our product candidates are shown in the figure below:



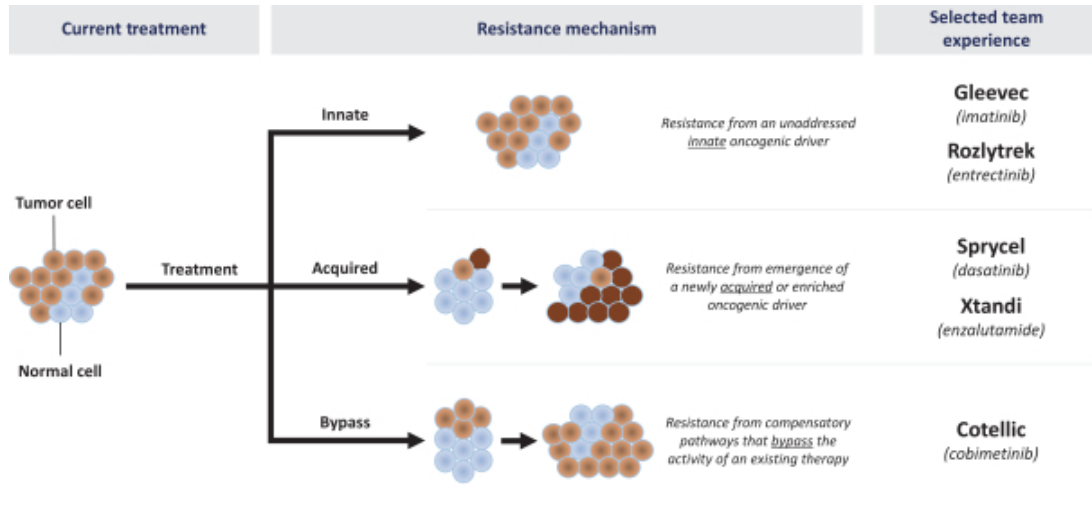
Our most advanced discovery and research programs are shown in the figure below:



Our areas of focus within cancer resistance

Cancer resistance continues to be one of the most daunting challenges facing patients, clinicians and researchers in oncology today. A multitude of biological factors and pathways have been linked to resistance, which enables tumors to restore cell growth and survival by circumventing a treatment’s intended mechanism of action. Within resistance, we focus on three areas: (1) innate resistance, which derives from an unaddressed oncogenic driver that promotes tumorigenesis; (2) acquired resistance, the result of an induced or enriched oncogenic driver that arises in response to treatment; and (3) bypass resistance, the activation of a compensatory signaling pathway in response to treatment.

Overview of key resistance mechanisms and ORIC team’s prior relevant experience



We are building a portfolio of novel agents targeting multiple resistance mechanisms by leveraging our specialized expertise in hormone-dependent cancers, precision oncology and key tumor dependencies:

- **Hormone-dependent cancers:** Two of our founders, Drs. Charles Sawyers and Richard Heyman, are leading experts in nuclear hormone receptors and hormone-dependent cancers. They previously co-founded two oncology companies, Aragon (acquired by Johnson & Johnson in 2013) and Seragon (acquired by Roche in

2014), that developed therapeutics targeting two nuclear hormone receptors, the androgen receptor (AR) and estrogen receptor (ER), respectively, the former effort leading to the approved drug Erleada (apalutamide). Our lead product candidate, ORIC-101, while independently developed by ORIC, builds on academic work from Dr. Sawyers' laboratory at Memorial Sloan Kettering Cancer Center (MSKCC) implicating GR as a potential mechanism of resistance to Xtandi (discovered by Dr. Sawyers and developed by Medivation, which was acquired by Pfizer in 2016) in prostate cancer. Given the breadth of solid tumor indications in which hormone signaling pathways have been implicated in driving disease, or in the development of resistance, we believe our differentiated insight into this biology is a crucial component of our future success.

- **Precision oncology:** Our precision medicine approach of utilizing biomarkers for demonstration of target and pathway engagement and ultimately for patient selection is rooted in our management team's prior experience at Ignyta (acquired by Roche in 2018) in successfully developing Rozlytrek (entrectinib), which was approved by the U.S. Food and Drug Administration (FDA) for the treatment of ROS1-positive metastatic non-small cell lung cancer (NSCLC) and neurotrophic tyrosine receptor kinase (NTRK)-positive solid tumors in 2019. Our team's experience in precision oncology dates back decades, including Dr. Sawyers' pivotal role in the development of Gleevec (imatinib) and Sprycel (dasatinib). We believe our team's expertise and experience in precision oncology will allow us to develop drugs with a higher probability of clinical success within biomarker-defined patient populations, while also potentially reducing the time and cost of development.
- **Key tumor dependencies:** Key tumor dependencies are abnormal alterations that promote cancer cell growth and survival and also confer specific vulnerabilities that normal cells lack; these cancer-specific dependencies are compelling therapeutic targets. Our scientific team—led by our Chief Scientific Officer, Head of Biology and Head of Translational Medicine—has amassed deep knowledge of key oncogenic drivers and pathways in order to identify and validate oncology targets. They most recently worked together at Genentech, where they progressed more than 20 oncology discovery programs into clinical development, with three approvals to date, including Cotellic (cobimetinib), Zelboraf (vemurafenib) and Polivy (polatuzumab vedotin). Our knowledge of innate, acquired and bypass resistance mechanisms, as well as our in-depth experience in forward and reverse translation, underpins our discovery efforts to identify key drivers of cancer resistance that can be exploited for therapeutic gain. For example, our understanding of innate resistance has led to the discovery of ORIC-533, an orally bioavailable small molecule inhibitor of CD73.

We are leveraging these three areas of expertise to develop innovative therapies targeting the critical cancer resistance mechanisms that we believe will bring the largest benefit to patients, including by making existing therapies more effective for a longer period of time.

Our pipeline to treat cancer resistance

GR antagonist program: ORIC-101

GR is a nuclear hormone receptor that mediates responses to glucocorticoid hormones involved in regulating a range of cellular functions, such as metabolism, cell growth and differentiation. The original hypothesis for our lead program targeting GR was borne out of work conducted in the laboratory of Dr. Sawyers at MSKCC in search of explanatory factors underlying resistance to anti-androgen prostate cancer therapies, including Xtandi and Erleada. His work demonstrated that GR signaling is a bypass mechanism to anti-androgen therapy, and that increased expression of GR in prostate cancer is correlated with resistance to Xtandi. We and others have shown that, in addition to prostate cancer, GR is also overexpressed across over 20 advanced solid tumors

including pancreatic, triple negative breast (TNBC) and ovarian cancers, and that GR overexpression is associated with worse survival outcomes.

Our lead product candidate, ORIC-101, is a potent and selective small molecule GR antagonist designed to inhibit GR transcriptional activity and block pro-survival signals downstream of its activation that confer resistance to anti-androgen therapies and chemotherapies. Since its initial discovery at ORIC, we have rapidly advanced ORIC-101 through preclinical studies that have informed the design of a robust clinical development plan. Following the successful completion of two Phase 1a trials in over 50 healthy volunteers, we initiated in 2019 two separate Phase 1b trials of ORIC-101 in combination with: (1) enzalutamide in metastatic prostate cancer and (2) nab-paclitaxel in advanced or metastatic solid tumors. These trials are intended to establish safety, pharmacokinetics, pharmacodynamics, preliminary anti-tumor activity and a recommended Phase 2 dose of ORIC-101 in combination with each of these therapeutics. To help inform which patients may be most suitable for treatment with ORIC-101, we have developed a proprietary immunohistochemistry (IHC) assay that measures GR protein expression levels as well as a proprietary GR gene activation signature that measures GR signaling activity, both of which are being utilized in our ongoing clinical trials and may be used for patient selection in future clinical trials. We expect to report interim data for one of these Phase 1b trials in the first half of 2021.

CD73 inhibitor program: ORIC-533

Many cancers usurp the anti-inflammatory adenosine pathway to avoid detection by the immune system, thereby reducing the effectiveness of certain chemotherapy- and immunotherapy-based treatments. Accumulation of adenosine in the tumor microenvironment is implicated in local immune suppression that leads to tumor proliferation. CD73 is an enzyme that controls the rate at which extracellular adenosine is produced and its overexpression is associated with poor prognosis in several cancers, including TNBC, NSCLC, melanoma and prostate, among others. Several global pharmaceutical companies are developing anti-CD73 antibodies, but due to significant medicinal chemistry challenges, to our knowledge, there are no orally bioavailable inhibitors of CD73 in clinical development. Our second product candidate, ORIC-533, is an orally bioavailable small molecule inhibitor of CD73, which has demonstrated more potent adenosine inhibition *in vitro* compared to an antibody-based approach. We expect to file an IND for ORIC-533 with the FDA in 2021.

Other preclinical programs

We are also developing several therapies targeting other key mechanisms of resistance. For example, we have a program directed to a target that is a potential innate oncogenic driver and also a potential bypass mechanism of resistance in certain cancers. This and other additional programs targeting resistance mechanisms are in various states of preclinical drug discovery and are directed towards a variety of solid tumors with a focus on breast, prostate and lung cancers.

Our team that is Overcoming Resistance In Cancer

We have assembled a management team that has led organizations that have advanced multiple oncology therapeutics from early stage research to clinical trials, and ultimately to regulatory approval and commercialization. Our Chief Executive Officer, Dr. Jacob Chacko, has worked and collaborated with the

members of our team for over 25 years collectively prior to ORIC, and multiple team members have worked together previously at Ignyta, Medivation, Aragon, Seragon and Genentech. Our team's select accomplishments include:

- Our Chief Medical Officer and Senior Vice President of Clinical Development previously held the same positions at Ignyta, where they led a global registrational trial that resulted in the approval of Rozlytrek in two indications for genetically defined cancers.
- Our Chief Scientific Officer was most recently the head of translational oncology at Genentech, where her team advanced more than 20 programs into clinical development.
- Our Chief Business Officer, while leading business development at Medivation, identified and led the acquisition of a compound that was subsequently developed and approved as Talzenna (talazoparib).
- Our Chief Financial Officer and our Chief Executive Officer, while previously CFOs at two separate publicly traded companies, led over \$1 billion in capital raises.
- Our management team has been involved in several multibillion-dollar strategic transactions, including as part of the leadership teams at Ignyta and Medivation.

We are supported by our founders who have discovered and developed multiple innovative cancer treatments and have successfully collaborated prior to founding ORIC. Drs. Sawyers and Heyman, leading experts in cancer resistance and nuclear hormone receptors, co-founded Aragon and Seragon, which developed therapeutics focused on AR and ER, respectively, the former effort leading to the approved drug Erleada. Dr. Sawyers was also involved in the discovery of Xtandi and is an expert in precision medicine, having played a key role in the development of Gleevec and Sprycel. Our third co-founder, Scott Lowe, Ph.D., is a colleague of Dr. Sawyers at MSKCC and an expert in tumor networks and molecular determinants of treatment response. Our founders are currently active scientific advisors to ORIC and Dr. Heyman is a member of our board of directors. All of our founders are equity holders of ORIC, Drs. Sawyers and Lowe receive compensation as scientific advisors, and Dr. Heyman receives compensation as a board member. Although they are regularly available for scientific consultation, our arrangements with these individuals do not entitle us to any of their existing or future intellectual property derived from their independent research or research with other third parties beyond what has previously been licensed to us.

In addition, we have assembled a scientific advisory board that, in addition to our founders, includes Dr. Richard Scheller, who was previously Chief Scientific Officer of Genentech, and Dr. Larry Lasky, who was previously one of only three Research Fellows in Genentech's history. We are also supported by our syndicate of leading investors, including The Column Group, Topspin, OrbiMed, EcoR1, Fidelity Management, ArrowMark Partners, Invus, Foresite and Casdin Capital, among others.

Our strategy

Our goal is to discover, develop and commercialize innovative therapies that overcome resistance in cancer. The key elements of our business strategy to achieve this goal include:

- Leveraging the insights, experience and networks of our founders and management team.
- Advancing our lead product candidate, ORIC-101, as rapidly as possible through clinical development by exploring rational combinations across multiple tumor types.
- Building the leading, fully-integrated company focused on delivering innovative medicines that aim to overcome resistance in cancer.

- Continuing to expand our portfolio of product candidates through both internal research activities and business development efforts.
- Utilizing a precision medicine approach in the development of each of our product candidates.
- Evaluating opportunities to accelerate development timelines and enhance the commercial potential of our programs in collaboration with third parties.

Risks related to our business

Our ability to execute on our business strategy is subject to a number of risks, which are discussed more fully in the section titled “Risk factors.” You should carefully consider these risks before making an investment in our common stock. These risks include, among others, the following:

- We have a limited operating history, have not initiated or completed any large-scale or pivotal clinical trials and have no products approved for commercial sale.
- We have incurred significant net losses since our inception, and we expect to continue to incur significant net losses for the foreseeable future.
- Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates.
- Even if this offering is successful, we will require substantial additional capital to finance our operations.
- We are substantially dependent on the success of our lead product candidate, ORIC-101, which is currently in early stage clinical trials. If we are unable to complete development of, obtain approval for and commercialize ORIC-101 for one or more indications in a timely manner, our business will be harmed.
- Our prospects depend in part upon discovering, developing and commercializing additional product candidates.
- The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable.
- The clinical trials of our product candidates may not demonstrate safety and efficacy to the satisfaction of the FDA, EMA or other comparable foreign regulatory authorities or otherwise produce positive results.
- We rely on third parties to conduct some or all aspects of our product manufacturing, research and preclinical and clinical development, and these third parties may not perform satisfactorily.
- Our success depends on our ability to protect our intellectual property as well as to operate without infringing the intellectual property rights of third parties.
- We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be impacted.

Corporate information

We were incorporated in Delaware in August 2014. Our principal executive offices are located at 240 E. Grand Avenue, 2nd Floor, South San Francisco, California 94080. Our telephone number is (650) 388-5600. Our website address is www.oricpharma.com. Information contained on the website is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus.

We use the ORIC Pharmaceuticals logo and other marks as trademarks in the United States and other countries. This prospectus contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the TM symbol, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Implications of being an emerging growth company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (JOBS Act). We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than \$1.07 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least \$700 million of equity securities held by non-affiliates; (3) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of our initial public offering. As a result of this status, we have taken advantage of reduced reporting requirements in this prospectus and may elect to take advantage of other reduced reporting requirements in our future filings with the U.S. Securities and Exchange Commission. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have elected to use the extended transition period to enable us to comply with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (1) are no longer an emerging growth company and (2) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

The offering

Common stock offered by us	shares.
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days to purchase up to additional shares of our common stock.
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full).
Use of proceeds	We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows: (1) to fund our two Phase 1b trials of ORIC-101, (2) to fund the development of ORIC-533 and (3) to fund other research and development activities, as well as for working capital and other general corporate purposes. See the section titled "Use of proceeds" for more information.
Risk factors	See the section titled "Risk factors" for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.
Proposed trading symbol	"ORIC"

The number of shares of our common stock to be outstanding after this offering is based on 85,169,744 shares of our common stock outstanding as of December 31, 2019 (including our convertible preferred stock on an as-converted basis), and excludes:

- 10,615,463 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2019 with a weighted-average exercise price of \$0.94 per share;
- 814,793 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, as amended, as of December 31, 2019, which shares will be added to the shares to be reserved for future issuance under our 2020 Equity Incentive Plan (2020 Plan);
- shares of common stock reserved for future issuance under our 2020 Plan, which will become effective in connection with this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan; and
- shares of common stock reserved for future issuance under our 2020 Employee Stock Purchase Plan (2020 ESPP), which will become effective in connection with this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

Unless otherwise indicated, this prospectus assumes or gives effect to the following:

- no exercise of outstanding options;
- no exercise by the underwriters of their option to purchase additional shares of common stock from us in this offering;
- the automatic conversion of all outstanding shares of our convertible preferred stock as of December 31, 2019 into an aggregate of 77,114,498 shares of our common stock immediately prior to the completion of this offering; and
- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, each of which will occur immediately prior to the completion of this offering.

Summary financial data

The following tables summarize our financial data for the periods and as of the dates indicated. We have derived our summary statements of operations data for the years ended December 31, 2017 and 2018, and balance sheet data as of December 31, 2018, from our audited financial statements appearing elsewhere in this prospectus. You should read the following summary financial data together with our financial statements and the related notes appearing elsewhere in this prospectus and the information in the sections titled "Selected financial data" and "Management's discussion and analysis of financial condition and results of operations."

(in thousands, except per share amounts)	Year ended December 31,	
	2017	2018
Statements of operations data:		
Operating expenses:		
Research and development	\$ 19,126	\$ 19,026
General and administrative	3,415	3,345
Total operating expenses	22,541	22,371
Loss from operations	(22,541)	(22,371)
Other income:		
Interest income, net	251	775
Other income	261	233
Total other income	512	1,008
Net loss and comprehensive loss	\$ (22,029)	\$ (21,363)
Net loss per share, basic and diluted ⁽¹⁾	\$ (3.90)	\$ (3.08)
Weighted-average shares outstanding, basic and diluted ⁽¹⁾	5,642	6,936
Pro forma net loss per share, basic and diluted (unaudited) ⁽¹⁾		\$ (0.35)
Pro forma weighted-average shares outstanding, basic and diluted (unaudited) ⁽¹⁾		60,629

(1) See Note 2 to our audited financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

(in thousands)	As of December 31, 2018		
	Actual	Pro forma ⁽¹⁾	Pro forma as adjusted ⁽²⁾⁽³⁾ (unaudited)
Balance sheet data:			
Cash and cash equivalents	\$ 42,636	\$	\$
Total assets	46,734		
Accrued other liabilities	2,150		
Total liabilities	3,894		
Convertible preferred stock	107,266		
Accumulated deficit	(65,807)		
Total stockholders' (deficit) equity	(64,426)		

(1) The pro forma balance sheet data gives effect to the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 77,114,498 shares of our common stock which will occur immediately prior to the completion of this offering, resulting in an aggregate of outstanding shares of our common stock.

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- (2) The pro forma as adjusted column in the balance sheet data table above gives effect to (a) the pro forma adjustments described in footnote (1) above and (b) the issuance and sale of _____ shares of common stock in this offering at the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.
- (3) Each \$1.00 increase or decrease in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, the pro forma as adjusted amount of each of our cash and cash equivalents, total assets and stockholders' deficit by \$ _____ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase or decrease of 1.0 million shares in the number of shares offered by us at the assumed initial public offering price would increase or decrease, as applicable, each of our cash and cash equivalents, total assets, and stockholders' deficit by \$ _____ million. The pro forma as adjusted information set forth above is illustrative only and will depend on the actual initial public offering price and other terms of this offering determined at pricing.

Risk factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our financial statements and the related notes appearing elsewhere in this prospectus and the section titled "Management's discussion and analysis of financial condition and results of operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock.

Risks related to our financial position and need for additional capital

We have a limited operating history, have not initiated or completed any large-scale or pivotal clinical trials, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and viability.

We are a clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2014, have no products approved for commercial sale and have not generated any revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. In 2019, we initiated our first two Phase 1b clinical trials for our lead product candidate, ORIC-101, and have not initiated clinical trials for any other product candidate. To date, we have devoted substantially all of our resources to research and development activities, including with respect to our GR antagonist and CD73 inhibitor programs and other preclinical programs, business planning, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital and providing general and administrative support for these operations.

We have not yet demonstrated our ability to successfully initiate and complete any large-scale or pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. As a result, it may be more difficult for you to accurately predict our likelihood of success and viability than it could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by clinical-stage biopharmaceutical companies in rapidly evolving fields. We also may need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We have not yet demonstrated an ability to successfully overcome such risks and difficulties, or to make such a transition. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

We have incurred significant net losses since our inception, and we expect to continue to incur significant net losses for the foreseeable future.

We have incurred significant net losses since our inception, have not generated any revenue from product sales to date and have financed our operations principally through private placements of our convertible preferred stock. Our net loss was \$21.4 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of \$65.8 million. Our lead product candidate, ORIC-101, is in early-stage clinical trials, and we plan on filing an investigational new drug application (IND) with the U.S. Food and Drug Administration (FDA) for our second product candidate, ORIC-533, in 2021. Our other programs are in preclinical discovery and

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research stages. As a result, we expect that it will be several years, if ever, before we have a commercialized product and generate revenue from product sales. Even if we succeed in receiving marketing approval for and commercializing one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses in order to discover, develop and market additional potential products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital, our ability to fund the development of our product candidates and our ability to achieve and maintain profitability and the performance of our stock.

Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates.

Our business depends entirely on the successful discovery, development and commercialization of product candidates. We have no products approved for commercial sale and do not anticipate generating any revenue from product sales for the next several years, if ever. Our ability to generate revenue and achieve profitability depends significantly on our ability, or any future collaborator's ability, to achieve several objectives, including:

- successful and timely completion of preclinical and clinical development of our lead product candidate, ORIC-101, ORIC-533 and our other future product candidates;
- establishing and maintaining relationships with contract research organizations (CROs) and clinical sites for the clinical development of ORIC-101, ORIC-533 and our other future product candidates;
- timely receipt of marketing approvals from applicable regulatory authorities for any product candidates for which we successfully complete clinical development;
- developing an efficient and scalable manufacturing process for our product candidates, including obtaining finished products that are appropriately packaged for sale;
- establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for our product candidates, if approved;
- successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether in-house or with one or more collaborators;
- a continued acceptable safety profile following any marketing approval of our product candidates;
- commercial acceptance of our product candidates by patients, the medical community and third-party payors;
- satisfying any required post-marketing approval commitments to applicable regulatory authorities;
- identifying, assessing and developing new product candidates;
- obtaining, maintaining and expanding patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protecting our rights in our intellectual property portfolio;

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- defending against third-party interference or infringement claims, if any;
- entering into, on favorable terms, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- obtaining coverage and adequate reimbursement by third-party payors for our product candidates;
- addressing any competing therapies and technological and market developments; and
- attracting, hiring and retaining qualified personnel.

We may never be successful in achieving our objectives and, even if we do, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations.

Even if this offering is successful, we will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials of, and seek marketing approval for, ORIC-101 and advance our other programs. Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing and distribution activities. Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency (EMA) or other regulatory agencies to perform clinical trials or preclinical studies in addition to those that we currently anticipate. Other unanticipated costs may also arise. Because the design and outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of any product candidate we develop. We have not yet met with the FDA to discuss any of our product candidates or development programs, and we are not permitted to market or promote ORIC-101, or any other product candidate, before we receive marketing approval from the FDA. Following this offering, we also expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to continue our operations.

As of December 31, 2018, we had \$42.6 million in cash and cash equivalents. Based on our current operating plan, we believe that the proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our planned operating expenses and capital expenditures through . Our estimate as to how long we expect the net proceeds from this offering, together with our existing cash and cash equivalents, to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

We plan to use the net proceeds from this offering to fund our two Phase 1b trials of ORIC-101 and to fund our development of ORIC-533 and other research and development activities, as well as for working capital and other general corporate purposes. Advancing the development of ORIC-101, ORIC-533 and our other programs, will require a significant amount of capital. The net proceeds from this offering and our existing cash and cash equivalents will not be sufficient to fund all of the activities that are necessary to complete the development of ORIC-101 or our other programs.

We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources, which may dilute our stockholders or restrict our operating activities. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing may result in imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through up-front payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to our product candidates, or grant licenses on terms that are not favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research-stage programs, clinical trials or future commercialization efforts.

Risks related to the discovery, development and commercialization of our product candidates

We are substantially dependent on the success of our lead product candidate, ORIC-101, which is currently in early stage clinical trials. If we are unable to complete development of, obtain approval for and commercialize ORIC-101 for one or more indications in a timely manner, our business will be harmed.

Our future success is dependent on our ability to timely and successfully complete clinical trials, obtain marketing approval for and successfully commercialize ORIC-101, our lead product candidate. We are investing the majority of our efforts and financial resources in the research and development of ORIC-101 for multiple indications. ORIC-101 is a potent and selective small molecule antagonist of GR, which has been linked to resistance to multiple classes of cancer therapeutics across a variety of solid tumors. In 2019, we initiated a Phase 1b clinical trial evaluating ORIC-101 in combination with nab-paclitaxel in patients with advanced or metastatic solid tumors. To date, eight patients have been enrolled in this study across three dosing cohorts. In the fourth quarter of 2019, we also initiated a Phase 1b clinical trial evaluating ORIC-101 in combination with enzalutamide in patients with metastatic prostate cancer progressing on enzalutamide. To date, one patient has been enrolled in this study. Prior to these two Phase 1b trials, ORIC-101 has only been studied in two Phase 1a trials in healthy volunteers. ORIC-101 will require additional clinical development, expansion of manufacturing capabilities, marketing approval from government regulators, substantial investment and significant marketing efforts before we can generate any revenues from product sales. We are not permitted to market or promote ORIC-101, or any other product candidate, before we receive marketing approval from the FDA and comparable foreign regulatory authorities, and we may never receive such marketing approvals.

The success of ORIC-101 will depend on several factors, including the following:

- the successful and timely completion of our ongoing clinical trials of ORIC-101;
- the initiation and successful patient enrollment and completion of additional clinical trials of ORIC-101 on a timely basis;
- maintaining and establishing relationships with CROs and clinical sites for the clinical development of ORIC-101 both in the United States and internationally;

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- the frequency and severity of adverse events in clinical trials;
- demonstrating efficacy, safety and tolerability profiles that are satisfactory to the FDA, EMA or any comparable foreign regulatory authority for marketing approval;
- the timely receipt of marketing approvals for ORIC-101 from applicable regulatory authorities;
- the timely identification, development and approval of companion diagnostic tests, if required;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- the maintenance of existing or the establishment of new supply arrangements with third-party drug product suppliers and manufacturers for clinical development and, if approved, commercialization of ORIC-101;
- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- the protection of our rights in our intellectual property portfolio;
- the successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize ORIC-101, which would materially harm our business. If we do not receive marketing approvals for ORIC-101, we may not be able to continue our operations.

In addition to ORIC-101, our prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.

Our future operating results are dependent on our ability to successfully discover, develop, obtain regulatory approval for and commercialize product candidates other than ORIC-101. All of our current programs other than ORIC-101, including ORIC-533, are in research or preclinical development. A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from preclinical testing or early clinical trials of a product candidate may not be predictive of the results that will be obtained in later stage clinical trials of the product candidate.

The success of other product candidates we may develop will depend on many factors, including the following:

- generating sufficient data to support the initiation or continuation of clinical trials;
- obtaining regulatory permission to initiate clinical trials;
- contracting with the necessary parties to conduct clinical trials;
- successful enrollment of patients in, and the completion of, clinical trials on a timely basis;

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- the timely manufacture of sufficient quantities of a product candidate for use in clinical trials; and
- adverse events in clinical trials.

Even if we successfully advance any other product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this “Risk factors” section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from any product candidates.

The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

Obtaining approval by the FDA, EMA and other comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Even if we eventually complete clinical testing and receive approval for our product candidates, the FDA, EMA and other comparable foreign regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested or may impose other prescribing limitations or warnings that limit the product’s commercial potential. We have not submitted for, or obtained, regulatory approval for any product candidate, and it is possible that none of our product candidates will ever obtain regulatory approval. Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or other comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, are only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- we may be unable to demonstrate to the FDA, EMA or other comparable foreign regulatory authorities that our product candidate’s risk-benefit ratio for its proposed indication is acceptable;
- the FDA, EMA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;

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- the FDA, EMA or other comparable regulatory authorities may fail to approve companion diagnostic tests required for our product candidates; and
- the approval policies or regulations of the FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects.

The clinical trials of our product candidates may not demonstrate safety and efficacy to the satisfaction of the FDA, EMA or other comparable foreign regulatory authorities or otherwise produce positive results.

Before obtaining marketing approval from the FDA, EMA or other comparable foreign regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate with substantial evidence the safety and efficacy of such product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete and its ultimate outcome is uncertain. A failure of one or more clinical trials can occur at any stage of the process. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent receipt of marketing approval or our ability to commercialize our product candidates, including:

- receipt of feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- negative or inconclusive clinical trial results that may require us to conduct additional clinical trials or abandon certain drug development programs;
- the number of patients required for clinical trials being larger than anticipated, enrollment in these clinical trials being slower than anticipated or participants dropping out of these clinical trials at a higher rate than anticipated;
- third-party contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the suspension or termination of our clinical trials for various reasons, including non-compliance with regulatory requirements or a finding that our product candidates have undesirable side effects or other unexpected characteristics or risks;
- the cost of clinical trials of our product candidates being greater than anticipated;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates being insufficient or inadequate; and
- regulators revising the requirements for approving our product candidates.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing in a timely manner, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may incur unplanned costs, be delayed in seeking and

obtaining marketing approval, if we receive such approval at all, receive more limited or restrictive marketing approval, be subject to additional post-marketing testing requirements or have the drug removed from the market after obtaining marketing approval.

Our product candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, financial condition and prospects significantly.

For example, in study ORIC-GR-17001, there were two Grade 1 adverse events: pain in the extremity and nausea. Both were mild, attributed to ORIC-101 and resolved without treatment. In study ORIC-GR-17002, Part A, the most commonly reported treatment-emergent adverse events were mild gastrointestinal adverse events. These were observed in two participants and consisted of Grade 1 nausea in one subject and Grade 1 nausea, abdominal pain, and diarrhea in a second subject. They were resolved without treatment. In study ORIC-GR-17002, Part B, the most common adverse events were gastrointestinal in nature and were deemed related to ORIC-101. See the section titled “Business—Safety.”

In our Phase 1b trial of ORIC-101 in combination with nab-paclitaxel in advanced or metastatic solid tumors, two patients experienced dose-limiting toxicity (DLT) during the first cycle of treatment. Specifically, one patient experienced Grade 3 fatigue and discontinued treatment after two weeks on study. A second patient with advanced pancreatic cancer that had metastasized to the liver experienced Grade 4 neutropenia and thrombocytopenia and Grade 5 hepatic failure in the setting of rapid disease progression. A CT scan of the patient’s abdomen on study Day 9 demonstrated disease progression, and the patient died on study Day 12. These toxicities are well-described for nab-paclitaxel (including reports of hepatic necrosis and hepatic encephalopathy leading to death). After review of safety and PK data from Dose Level 1 by the study’s Safety Review Committee (SRC), it was determined that Dose Level 1 exceeded the maximum tolerated doses of the combination of ORIC-101 and nab-paclitaxel. The protocol was amended and following FDA review and Institutional Review Board (IRB) approvals, three new patients were enrolled to the revised new Dose Level 1A. See the section titled “ Business—Phase 1b trial of ORIC-101 in combination with nab-paclitaxel in advanced or metastatic solid tumors.”

Patients in our ongoing and planned clinical trials may in the future suffer other significant adverse events or other side effects not observed in our preclinical studies or previous clinical trials. ORIC-101 or other product candidates may be used in populations for which safety concerns may be particularly scrutinized by regulatory agencies. In addition, ORIC-101 is being studied in combination with other therapies, which may exacerbate adverse events associated with the therapy. Patients treated with ORIC-101 or our other product candidates may also be undergoing surgical, radiation and chemotherapy treatments, which can cause side effects or adverse events that are unrelated to our product candidate but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such

patients' illnesses. For example, it is expected that some of the patients enrolled in our ORIC-101 clinical trials will die or experience major clinical events either during the course of our clinical trials or after such trials, which has occurred in the past.

If further significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, EMA, other comparable regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects. Further, if any of our product candidates obtains marketing approval, toxicities associated with such product candidates and not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the product or the withdrawal of the product from the market. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or early stage clinical trials.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities.

We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future clinical trials will be successful. For instance, we do not know whether ORIC-101 will perform in current or future clinical trials as ORIC-101 has performed in preclinical studies or prior clinical trials, nor do we know whether ORIC-533 will perform in current or future preclinical studies or future clinical trials as it has in prior preclinical studies. Product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA, EMA and other comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Additionally, while we are aware of several other clinical-stage GR antagonists being developed by Corcept Therapeutics, to our knowledge, there are no GR antagonists approved for the treatment of cancer and the most advanced GR antagonist in development for cancer is in a Phase 2 clinical trial for ovarian cancer. As such, the development of ORIC-101 and our stock price may be impacted by inferences, whether correct or not, that are drawn between the success of our product candidate and those of Corcept Therapeutics or other companies. Additionally, prior to our two Phase 1b trials, ORIC-101 was only studied in two Phase 1a trials in healthy volunteers. Regulatory authorities may also limit the scope of later-stage trials until we have demonstrated satisfactory safety, which could delay regulatory approval, limit the size of the patient population to which we may market our product candidates, or prevent regulatory approval.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our product

candidates may also be undergoing surgical, radiation and chemotherapy treatments and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our product candidates. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes.

We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain approval to market any of our product candidates.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available, and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, interim or topline data from our clinical trials, such as the interim data from our Phase 1b clinical trial of ORIC-101. These interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. For example, we may report tumor responses in certain patients that are unconfirmed at the time and which do not ultimately result in confirmed responses to treatment after follow-up evaluations. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, ORIC-101 or any other product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

If we experience delays or difficulties in the enrollment and/or maintenance of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to such trial's conclusion as required by the FDA, EMA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may

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result in slower enrollment than we anticipate. For instance, we have developed a proprietary immunohistochemistry (IHC) assay that measures GR protein expression levels as well as a proprietary GR gene activation signature that measures GR signaling activity, both of which are being utilized in our ongoing clinical trials and may be used for patient selection in future clinical trials, and utilizing such biomarker-driven identification and/or certain highly specific criteria related to the stage of disease progression may limit patient populations eligible for our clinical trials. Additionally, our approach of identifying and selecting a subset of patients more likely to benefit from ORIC-101 by measuring levels of GR expression or gene activity is, to our knowledge, untested in oncology. If these strategies for patient identification prove unsuccessful, we may have difficulty enrolling or maintaining patients appropriate for ORIC-101.

Patient enrollment may be affected if our competitors have ongoing clinical trials for programs that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' programs. Patient enrollment for our current or any future clinical trials may be affected by other factors, including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the trial in question as defined in the protocol;
- perceived risks and benefits of the product candidate under study;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved or other product candidates being investigated for the indications we are investigating;
- clinicians' willingness to screen their patients for biomarkers to indicate which patients may be eligible for enrollment in our clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion or, because they may be late-stage cancer patients, will not survive the full terms of the clinical trials.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods.

If we are unable to successfully develop companion diagnostic tests for our product candidates, experience significant delays in doing so, or rely on third parties in the development of such companion diagnostic tests, we may not realize the full commercial potential of our product candidates.

We are exploring predictive biomarkers to determine patient selection for our clinical trials. Specifically, to help inform which patients may be most suitable for treatment with ORIC-101, we have developed a proprietary IHC

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assay that measures GR protein expression levels as well as a proprietary GR gene activation signature that measures GR signaling activity, both of which are being utilized in our ongoing clinical trials and may be used for patient selection in future clinical trials. If either of these approaches proves to be a useful method for patient selection, we expect to incorporate the specific diagnostic test into our registrational studies and partner with the appropriate diagnostic provider to co-develop a companion diagnostic. In general, the FDA expects to review and approve simultaneously NDA and pre-market approval (PMA) submissions for a therapeutic and its companion diagnostic, respectively, so any delay in diagnostic approval could delay drug approval.

We may rely on third parties for the design, development and manufacture of companion diagnostic tests for our product candidates that require such tests. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. If we or such third parties are unable to successfully develop companion diagnostics, or experience delays in doing so, we may be unable to enroll enough patients for our current and planned clinical trials, the development of our product candidates may be adversely affected or we may not obtain marketing approval, and we may not realize the full commercial potential of our product candidates, including ORIC-101.

We expect to develop ORIC-101, ORIC-533 and potentially other programs in combination with other therapies, which exposes us to additional risks.

We intend to develop ORIC-101, ORIC-533 and potentially other programs, in combination with one or more currently approved cancer therapies or therapies in development. In 2019, we initiated a Phase 1b clinical trial evaluating ORIC-101 in combination with nab-paclitaxel in patients with advanced or metastatic solid tumors. In 2019, we also initiated a Phase 1b clinical trial evaluating ORIC-101 in combination with enzalutamide in patients with metastatic prostate cancer. Patients may not be able to tolerate ORIC-101 or any of our other product candidates in combination with other therapies or dosing of ORIC-101 in combination with other therapies may have unexpected consequences. Even if any of our product candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA, EMA or other comparable foreign regulatory authorities that could revoke approval of the therapy used in combination with any of our product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our product candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our product candidates or our own products being removed from the market or being less successful commercially.

We may also evaluate our product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA, EMA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval.

If the FDA, EMA or other comparable foreign regulatory authorities do not approve or revoke their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with ORIC-101 or any other product candidate, we may be unable to obtain approval of or successfully market any one or all of the product candidates we develop.

Additionally, if the third-party providers of therapies or therapies in development used in combination with our product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our product candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects. For example, for our Phase 1b trial of ORIC-101 in

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combination with enzalutamide in prostate cancer, we entered into a clinical trial collaboration and supply agreement with Astellas. Under the terms of the clinical trial collaboration and supply agreement, Astellas, which jointly commercializes enzalutamide in the United States with Pfizer, is providing enzalutamide for the trial. If this agreement terminates and we are unable to obtain enzalutamide on the current terms, the cost to us to conduct this trial may significantly increase.

We have limited resources and are currently focusing our efforts on developing ORIC-101 for particular indications and advancing our preclinical programs. As a result, we may fail to capitalize on other indications or product candidates that may ultimately have proven to be more profitable.

We are currently focusing our resources and efforts on developing ORIC-101 for particular indications and advancing our preclinical programs. As a result, because we have limited resources, we may forgo or delay pursuit of opportunities for other indications or with other product candidates that may have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development activities for ORIC-101, ORIC-533 and other preclinical programs, may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target markets for ORIC-101, ORIC-533 or any of our other programs, we may relinquish valuable rights to that product candidate or program through collaboration, licensing or other strategic arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate or program.

We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the products we develop, our commercial opportunities will be negatively impacted.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates. In addition, our products may need to compete with drugs physicians use off-label to treat the indications for which we seek approval. This may make it difficult for us to replace existing therapies with our products.

In particular, there is intense competition in the field of oncology. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, emerging and start-up companies, universities and other research institutions. We also compete with these organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in-licensing new product candidates.

We expect to face competition from existing products and products in development for each of our programs. For ORIC-101, we are aware of several other clinical-stage GR antagonists being developed by Corcept Therapeutics. To our knowledge, there are no GR antagonists approved for the treatment of cancer and the most advanced GR antagonist in development for cancer is in a Phase 2 clinical trial. For ORIC-533, we are aware of several companies developing antibodies against CD73, including AstraZeneca, Bristol-Myers Squibb, Novartis in collaboration with Surface Oncology, Corvus Pharmaceuticals, Innate Pharma and Tracon

Pharmaceuticals in collaboration with I-Mab Biopharma. Other companies, such as Arcus Biosciences, Calithera Biosciences and Merck through its acquisition of Peloton Therapeutics, have small-molecule programs against this target. To our knowledge, there are no orally available, small molecule CD73 inhibitors in clinical trials. Many of these current and potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources, and commercial expertise than we do. Large pharmaceutical and biotechnology companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing biotechnology products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical and biotechnology companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result of all of these factors, our competitors may succeed in obtaining approval from the FDA, EMA or other comparable foreign regulatory authorities or in discovering, developing and commercializing products in our field before we do.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient, have a broader label, are marketed more effectively, are more widely reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain marketing approval from the FDA, EMA or other comparable foreign regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if the product candidates we develop achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected.

The manufacture of drugs is complex, and our third-party manufacturers may encounter difficulties in production. If any of our third-party manufacturers encounter such difficulties, our ability to provide adequate supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or prevented.

Manufacturing drugs, especially in large quantities, is complex and may require the use of innovative technologies. Each lot of an approved drug product must undergo thorough testing for identity, strength, quality, purity and potency. Manufacturing drugs requires facilities specifically designed for and validated for this purpose, as well as sophisticated quality assurance and quality control procedures. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturer, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. The use of biologically derived ingredients can also lead to allegations of harm, including infections or allergic reactions, or closure of product facilities due to possible contamination. If our third-party manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization as a result of these challenges, or otherwise, our development and commercialization efforts

would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates progress through preclinical and clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. For example, we may introduce an alternative formulation of ORIC-101 into the dose expansion phases of our ongoing Phase 1b clinical trials. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates, if approved, and generate revenue.

Our product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if our product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which a product candidate is approved;
- restrictions on the use of product candidates in the labeling approved by regulatory authorities, such as boxed warnings or contraindications in labeling, or a risk evaluation and mitigation strategy, if any, which may not be required of alternative treatments and competitor products;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement by third-party payors, including government authorities;
- the availability of an approved product candidate for use as a combination therapy;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and undergo required diagnostic screening to determine treatment eligibility and of physicians to prescribe these therapies and diagnostic tests;
- the effectiveness of sales and marketing efforts;
- unfavorable publicity relating to our product candidates; and
- the approval of other new therapies for the same indications.

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If any of our product candidates is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from that product candidate and our financial results could be negatively impacted.

The market opportunities for ORIC-101 and other product candidates we develop, if approved, may be limited to certain smaller patient subsets.

Cancer therapies are sometimes characterized as first-line, second-line or third-line, and the FDA often approves new therapies initially only for a particular line of use. When cancer is detected early enough, first-line therapy, such as chemotherapy, hormone therapy, surgery, radiation therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. Our current clinical trials for ORIC-101 are with patients who have received one or more prior treatments. There is no guarantee that product candidates we develop, even if approved, would be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials that may be costly, time-consuming and subject to risk.

The number of patients who have the cancers we are targeting may turn out to be lower than expected. Additionally, the potentially addressable patient population for ORIC-101 and other product candidates we develop, including as a result of the selection of patients with specific biomarkers, levels of GR expression or gene activity, may be limited or may not be amenable to treatment with our product candidates. We have developed a proprietary IHC assay that measures GR protein expression levels as well as a proprietary GR gene activation signature that measures GR signaling activity, both of which are being utilized in our ongoing clinical trials and may be used for patient selection in future clinical trials. We are continuing to evaluate the appropriate levels of GR protein overexpression for determining which patients may be eligible for treatment. Regulatory approval may limit the market of a product candidate to target patient populations when such biomarker-driven identification and/or highly specific criteria related to the stage of disease progression are utilized.

Even if we obtain significant market share for any approved product, if the potential target populations are small, we may never achieve profitability without obtaining marketing approval for additional indications.

We may not be successful in augmenting our product pipeline through acquisitions and in-licenses.

We believe that accessing external innovation and expertise is important to our success; and while we plan to leverage our leadership team's prior business development experience as we evaluate potential in-licensing and acquisition opportunities to further expand our portfolio, we may not be able to identify suitable licensing or acquisition opportunities, and even if we do, we may not be able to successfully secure such licensing and acquisition opportunities. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully license or acquire additional product candidates to expand our portfolio, our pipeline, competitive position, business, financial condition, results of operations, and prospects may be materially harmed.

Any product candidates we develop may become subject to unfavorable third-party coverage and reimbursement practices, as well as pricing regulations.

The availability and extent of coverage and adequate reimbursement by third-party payors, including government health administration authorities, private health coverage insurers, managed care organizations and other third-party payors is essential for most patients to be able to afford expensive treatments. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of such product candidates will be covered and reimbursed by third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize an adequate return on our investment. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, for example, principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services (CMS), an agency within the U.S. Department of Health and Human Services (HHS). CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor's determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate. As a result, the coverage determination process is often time-consuming and costly. This process will require us to provide scientific and clinical support for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our product candidates may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be.

In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

Outside the United States, the commercialization of therapeutics is generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the European Union, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time

after a product receives marketing approval. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, product prices under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

If we are unable to establish or sustain coverage and adequate reimbursement for any product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Our business entails a significant risk of product liability and if we are unable to obtain sufficient insurance coverage such inability could have an adverse effect on our business and financial condition.

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an FDA, EMA or other regulatory authority investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs. FDA, EMA or other regulatory authority investigations could potentially lead to a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources and substantial monetary awards to trial participants or patients. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our product candidates, if approved. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have an adverse effect on our business and financial condition.

Risks related to regulatory approval and other legal compliance matters

We may be unable to obtain U.S. or foreign regulatory approval and, as a result, may be unable to commercialize our product candidates.

Our product candidates are and will continue to be subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in the United States and in many foreign jurisdictions before a new drug can be approved for marketing. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. We cannot provide any assurance that any product candidate we may develop will progress through required clinical testing and obtain the regulatory approvals necessary for us to begin selling them.

We have not conducted, managed or completed large-scale or pivotal clinical trials nor managed the regulatory approval process with the FDA or any other regulatory authority. The time required to obtain approvals from the FDA and other regulatory authorities is unpredictable and requires successful completion of extensive clinical trials which typically takes many years, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when evaluating clinical trial data can, and often does, change during drug development, which makes it difficult to predict with any certainty how they will be applied. We may also encounter unexpected delays or increased costs due to new government regulations, including future legislation or administrative action, or changes in FDA policy during the period of drug development, clinical trials and FDA regulatory review.

Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from any particular product candidates we are developing and for which we are seeking approval. Furthermore, any regulatory approval to market a drug may be subject to significant limitations on the approved uses or indications for which we may market, promote and advertise the drug or the labeling or other restrictions. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy (REMS) plan as part of approving an NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. These requirements or restrictions might include limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may significantly limit the size of the market for the drug and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries, and generally includes all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval.

The FDA, EMA and other comparable foreign regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction.

Our ongoing clinical trials are being undertaken in the United States. We may choose to conduct additional clinical trials internationally. For example, we conducted a Phase 1a healthy volunteer trial of ORIC-101 in the United Kingdom. The acceptance of study data by the FDA, EMA or other comparable foreign regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. In cases where data from United States clinical trials are intended to serve as the basis for marketing approval in the foreign countries outside the United States, the standards for clinical trials and approval may be different. There can be no assurance that any United States or foreign regulatory authority would accept data from trials conducted outside of its applicable jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the

FDA or EMA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential product candidates will be harmed.

Even if our product candidates receive regulatory approval, they will be subject to significant post-marketing regulatory requirements and oversight.

Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and on-going surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements and regulatory inspection. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or foreign regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with current good manufacturing practices (cGMPs) and good clinical practices (GCPs) for any clinical trials that we conduct post-approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, failure to comply with FDA, EMA and other comparable foreign regulatory requirements may subject our company to administrative or judicially imposed sanctions, including:

- delays in or the rejection of product approvals;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on the products, manufacturers or manufacturing process;

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- warning or untitled letters;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production; and
- imposition of restrictions on operations, including costly new manufacturing requirements.

Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates, if approved, and generate revenue.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. For example, if we receive marketing approval for ORIC-101 as a treatment for metastatic prostate cancer, physicians may nevertheless use our product for their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

If we are required by the FDA to obtain approval of a companion diagnostic test in connection with approval of any of our product candidates, and we do not obtain or we face delays in obtaining FDA approval of a diagnostic test, we will not be able to commercialize the product candidate and our ability to generate revenue will be materially impaired.

To help inform which patients may be most suitable for treatment with ORIC-101, we have developed a proprietary IHC assay that measures GR protein expression levels as well as a proprietary GR gene activation signature that measures GR signaling activity, both of which are being utilized in our ongoing Phase 1b clinical studies and may be used for patient selection in future clinical studies. Additionally, in connection with

development of our potential product candidates, we may develop or work with collaborators to develop or obtain access to companion diagnostic tests to identify patient subsets within a disease category who may derive selective and meaningful benefit from our programs. Such companion diagnostics would be used during our clinical trials as well as in connection with the commercialization of our product candidates. To be successful in developing and commercializing product candidates in combination with these companion diagnostics, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared at the same time the product candidate is approved. To date, the FDA has required marketing approval of all companion diagnostic tests for cancer therapies. Various foreign regulatory authorities also regulate *in vitro* companion diagnostics as medical devices and, under those regulatory frameworks, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of our current diagnostics and any future diagnostics we may develop, which we expect will require separate regulatory clearance or approval prior to commercialization.

The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express certain biomarkers or the specific genetic alteration that the companion diagnostic was developed to detect. If the FDA, EMA or a comparable regulatory authority requires approval of a companion diagnostic for any of our product candidates, whether before or concurrently with approval of the product candidate, we, and/or future collaborators, may encounter difficulties in developing and obtaining approval for these companion diagnostics. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval of a companion diagnostic could delay or prevent approval or continued marketing of our related product candidates.

Additionally, we may rely on third parties for the design, development and manufacture of companion diagnostic tests for our product candidates that may require such tests. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so, the development of our product candidates may be adversely affected, our product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of our product candidates that obtain marketing approval. As a result, our business, results of operations and financial condition could be materially harmed. In addition, a diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

We may seek Fast Track designation from the FDA for one or more of our product candidates. Even if one or more of our product candidates receive Fast Track designation, we may be unable to obtain or maintain the benefits associated with the Fast Track designation.

Fast Track designation is designed to facilitate the development and expedite the review of therapies for serious conditions and fill an unmet medical need. Programs with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review and the ability to submit a rolling application for regulatory review. Fast Track designation applies to both the product candidate and the specific indication for which it is being studied. If any of our product candidates receive Fast Track designation but do not continue to meet the criteria for Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program. Furthermore, Fast Track designation does not change the standards for approval. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures.

We may not be able to obtain orphan drug designation or obtain or maintain orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA, EMA or other comparable foreign regulatory authorities, from approving competing products.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Our target indications may include diseases with large patient populations or may include orphan indications. However, there can be no assurances that we will be able to obtain orphan designations for our product candidates.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances. The applicable exclusivity period is ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug designation for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to ensure that we will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same

condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process or entitles the product candidate to priority review.

Where appropriate, we plan to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated registration pathways. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

Where possible, we plan to pursue accelerated development strategies in areas of high unmet need. We may seek an accelerated approval pathway for our one or more of our product candidates. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

Prior to seeking such accelerated approval, we will seek feedback from the FDA and will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation (e.g., breakthrough therapy designation), there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

We may face difficulties from changes to current regulations and future legislation.

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

For example, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), was passed, which substantially changes the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. It is unclear how judicial decisions, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2029 unless additional congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Moreover, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, at the federal level, the Trump administration's budget proposals for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 (Right to Try Act), was signed into law. The law, among other things, provides a federal

framework for certain patients to access certain investigational new product candidates that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its products available to eligible patients as a result of the Right to Try Act.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Additionally, the collection and use of health data in the European Union is governed by the General Data Protection Regulation (GDPR), which extends the geographical scope of European Union data protection law to non-European Union entities under certain conditions and imposes substantial obligations upon companies and new rights for individuals. Failure to comply with the GDPR and the applicable national data protection laws of the EU Member States may result in fines up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties. The GDPR may increase our responsibility and liability in relation to personal data that we may process, and we may be required to put in place additional mechanisms in an effort to comply with the GDPR. This may be onerous and if our efforts to comply with GDPR or other applicable European Union laws and regulations are not successful, it could adversely affect our business in the European Union.

Finally, state and foreign laws may apply generally to the privacy and security of information we maintain, and may differ from each other in significant ways, thus complicating compliance efforts. For example, the California Consumer Privacy Act of 2018 (CCPA), which takes effect on January 1, 2020, gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. In addition, the CCPA (a) allows enforcement by the California Attorney General, with fines set at \$2,500 per violation (i.e., per person) or \$7,500 per intentional violation and (b) authorizes private lawsuits to recover statutory damages for certain data breaches. While it exempts some data regulated by the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and certain clinical trials data, the CCPA, to the extent applicable to our business and operations, may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. Some observers note that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or

commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the Securities and Exchange Commission (SEC) and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, upon completion of this offering and in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Our relationships with healthcare professionals, clinical investigators, CROs and third party payors in connection with our current and future business activities may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and health information privacy and security laws, which could expose us to significant losses, including, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, clinical investigators, CROs, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations may include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal false claims laws, including the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalties laws, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal HIPAA, prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

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- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and their implementing regulations, also imposes obligations, including mandatory contractual terms, on covered entities, which are health plans, healthcare clearinghouses, and health care providers, as those terms are defined by HIPAA, and their respective business associates, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to CMS information regarding payments and other transfers of value to physicians and teaching hospitals as well as information regarding ownership and investment interests held by physicians and their immediate family members. The information reported is publicly available on a searchable website, with disclosure required annually; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare and data privacy laws and regulations will involve on-going substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, research, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, which will be effective as of the date of the effectiveness of the registration statement of which this

prospectus forms a part, but it is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

If we fail to comply with other U.S. healthcare laws and compliance requirements, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

In the United States, our current and future activities with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers are subject to regulation by various federal, state and local authorities in addition to the FDA, which may include but are not limited to, CMS, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice (DOJ) and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, our business practices, including our clinical research, sales, marketing and scientific/educational grant programs may be required to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the patient data privacy and security provisions of HIPAA transparency requirements, and similar state laws, each as amended, as applicable.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any good, item, facility or service reimbursable, in whole or part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been interpreted broadly to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Rather, if "one purpose" of the remuneration is to induce referrals, the federal Anti-Kickback Statute is implicated. In addition, the ACA codified case law that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act (discussed below).

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The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal healthcare program that the person knows or should know is for a medical or other item or service that was not provided as claimed or is false or fraudulent.

The federal civil False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies are being investigated or, in the past, have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses.

HIPAA imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Analogous U.S. state laws and regulations, including state anti-kickback and false claims laws, may apply to claims involving healthcare items or services reimbursed by any third-party payor, including private insurers our business practices.

HIPAA, as amended by HITECH, and their implementing regulations, imposes requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates that are independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

Additionally, the federal Physician Payments Sunshine Act within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals, and to report annually certain ownership and investment interests held by physicians and their immediate family members.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states,

manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain.

State and local laws also require pharmaceutical and biotechnology companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, establish marketing compliance programs, restrict payments that may be made to healthcare providers professionals and entities and other potential referral sources, file periodic reports with the state relating to pricing and marketing, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register field representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, exclusion, debarment or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of hazardous and flammable materials, including chemicals and biological materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our business activities may be subject to the U.S. Foreign Corrupt Practices Act (FCPA) and similar anti-bribery and anti-corruption laws of other countries in which we operate, as well as U.S. and certain foreign export controls, trade sanctions, and import laws and regulations. Compliance with these legal requirements could limit our ability to compete in foreign markets and subject us to liability if we violate them.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits companies and their employees and third-party intermediaries from offering, promising, giving or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, hospitals are owned and operated by the government, and doctors and other hospital employees would be considered foreign officials under the FCPA. Recently, the SEC and DOJ have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents or contractors, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, disgorgement, and other sanctions and remedial measures, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international activities, our ability to attract and retain employees and our business, prospects, operating results and financial condition.

In addition, our products may be subject to U.S. and foreign export controls, trade sanctions and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U.S. export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments, and persons targeted by U.S. sanctions. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or products targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to, existing or potential customers with international operations. Any decreased use of our products or limitation on our ability to export or sell our products would likely adversely affect our business.

Risks related to employee matters, managing our growth and other risks related to our business

Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed.

Additionally, we rely on our scientific founders and other scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. These advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. In particular, if we are unable to maintain consulting relationships with our scientific founders or if they provide services to our competitors, our development and commercialization efforts will be impaired and our business will be significantly harmed.

If we are unable to establish sales or marketing capabilities or enter into agreements with third parties to sell or market our product candidates, we may not be able to successfully sell or market our product candidates that obtain regulatory approval.

We currently do not have and have never had a marketing or sales team. In order to commercialize any product candidates, if approved, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services for each of the territories in which we may have approval to sell or market our product candidates. We may not be successful in accomplishing these required tasks.

Establishing an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates will be expensive and time-consuming, and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could adversely impact the commercialization of any of our product candidates that we obtain approval to market, if we do not have arrangements in place with third parties to provide such services on our behalf. Alternatively, if we choose to collaborate, either globally or on a

territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration and such arrangements may prove to be less profitable than commercializing the product on our own. If we are unable to enter into such arrangements when needed, on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. If we are unable to successfully commercialize our approved product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

In order to successfully implement our plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2019, we had 57 full-time employees, including 46 employees engaged in research and development. In order to successfully implement our development and commercialization plans and strategies, and as we transition into operating as a public company, we expect to need additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA, EMA and other comparable foreign regulatory agencies' review process for ORIC-101 and any other product candidates, while complying with any contractual obligations to contractors and other third parties we may have; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and, if approved, commercialize ORIC-101 and other product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of clinical development and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third party service providers is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of ORIC-101 and any other product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing third-party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third-party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize ORIC-101 and other product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or

improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems, and those of our third-party CROs, other contractors (including sites performing our clinical trials) and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. To the extent that any disruption or security breach were to result in a loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our product candidates could be delayed. We cannot assure you that our data protection efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other third parties, will prevent significant breakdowns or breaches in systems or other cyber incidents that cause loss, destruction, unavailability, alteration or dissemination of, or damage to, our data that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information), which could result in financial, legal, business, and reputational harm to us. For example, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Notifications and follow-up actions related to a security incident could impact our reputation and cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security breach. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security incident were to result in a loss, destruction or alteration of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed, and we could be subject to

significant fines or penalties for any noncompliance with certain state, federal and/or international privacy and security laws.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in or, failure or security breach of our systems or third-party systems where information important to our business operations or commercial development is stored. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

Our operations are vulnerable to interruption by fire, earthquakes, power loss, telecommunications failure, terrorist activity and other events beyond our control, which could harm our business.

Our facilities are located in California. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major flood, fire, earthquake, power loss, terrorist activity or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes to offset future taxable income may be limited.

Our net operating loss (NOL) carryforwards may be unavailable to offset future taxable income because of restrictions under U.S. tax law. Our NOLs generated in tax years ending on or prior to December 31, 2017 are only permitted to be carried forward for 20 taxable years under applicable U.S. federal tax law, and therefore could expire unused. Under tax legislation commonly referred to as the Tax Cuts and Jobs Act (Tax Act), our federal NOLs generated in tax years ending after December 31, 2017 may be carried forward indefinitely, but the deductibility of federal NOLs generated in tax years beginning after December 31, 2017 is limited to 80% of our current year taxable income. It is uncertain if and to what extent various states will conform to the Tax Act. As of December 31, 2017, we had federal NOL carryforwards of approximately \$41.6 million, which will begin to expire in 2034. In addition, for the period of January 1 through December 31, 2018, we created federal NOL carryforwards of \$20.0 million which do not expire. We also have available California NOL carryforwards of approximately \$63.5 million as of December 31, 2018, which begin to expire in 2034.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (Code), if a corporation undergoes an "ownership change" (generally defined as a cumulative change in the corporation's ownership by "5-percent shareholders" that exceeds 50 percentage points over a rolling three-year period), the corporation's ability to use its pre-change NOLs and certain other pre-change tax attributes to offset its post-change taxable income may be limited. Similar rules may apply under state tax laws. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside our control. We have not conducted any studies to determine annual limitations, if any, that could result from such changes in the ownership. Our ability to utilize our NOLs and certain other tax attributes could be limited by an "ownership change" as described above and consequently, we may not be able to utilize a material portion of our NOLs and certain other tax attributes, which could have a material adverse effect on our cash flows and results of operations.

U.S. federal income tax reform could materially adversely affect our company.

On December 22, 2017, President Trump signed into law the Tax Act, which significantly revises the Code. The Tax Act, among other things, reduces the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, repeals the alternative minimum tax for corporations, limits the tax deduction for interest expense to 30% of adjusted taxable income (except for certain small businesses), limits the deduction for NOLs carried forward from taxable years beginning after December 31, 2017, eliminates net operating loss carrybacks, and modifies or repeals many business deductions and credits. Our financial statements included elsewhere in this prospectus reflect the effects of the Tax Act based on current guidance. However, there remain uncertainties and ambiguities in the application of certain provisions of the Tax Act and, as a result, we made certain judgments and assumptions in the interpretation thereof. The U.S. Treasury Department and the Internal Revenue Service, or the IRS, may issue further guidance on how the provisions of the Tax Act will be applied or otherwise administered that differs from our current interpretation. In addition, the Tax Act could be subject to potential amendments and technical corrections, any of which could materially lessen or increase certain adverse impacts of the legislation on us.

A variety of risks associated with marketing our product candidates internationally could materially adversely affect our business.

We may seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements and reimbursement regimes in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

Risks related to our intellectual property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. We also seek to protect our proprietary position by acquiring or in-licensing relevant issued patents or pending applications from third parties.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or the patent applications of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties.

Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our and our licensors' proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. These uncertainties and/or limitations in our ability to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

Although we own one issued patent in the United States, we cannot be certain that the claims in our other U.S. pending patent applications, corresponding international patent applications and patent applications in certain foreign territories, or those of our licensors, will be considered patentable by the United States Patent and Trademark Office (USPTO), courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued patent will not be found invalid or unenforceable if challenged.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;

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- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent prosecution process is also expensive and time-consuming, and we and our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we or our licensors will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications and those of our licensors may not result in patents being issued which protect our product candidates or which effectively prevent others from commercializing competitive product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own or in-license currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents or the patents of our licensors by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents or the patents of our licensors may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant review (PGR) and *inter partes* review

(IPR), or other similar proceedings challenging our owned patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, our patents or the patents of our licensors may become subject to post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our or priority of invention or other features of patentability with respect to our patents and patent applications and those of our licensors. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of our licensors is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to develop products that are similar to our product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors or collaborators might not have been the first to make the inventions covered by the issued patents or patent application that we own or license;
- we or our licensors or collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that the pending patent applications we own or license will not lead to issued patents;
- issued patents that we own or license may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, it could significantly harm our business, results of operations and prospects.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third-party patents that may be infringed by commercialization of any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation that may cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any of our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- subject us to significant liability to third parties; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

Although no third party has asserted a claim of patent infringement against us as of the date of this prospectus, others may hold proprietary rights that could prevent our product candidates from being marketed. For

example, we are aware of issued patents with broad mode of action claims that could be alleged to cover our product candidate ORIC-101 in certain treatment indications. We believe that these mode of action patents are difficult to enforce and that we would have valid defenses to these claims of patent infringement. Nonetheless, a third party, such as the patent owner or licensee of the mode of action patents, may assert a claim of patent infringement directed at our product candidate ORIC-101. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our products, treatment indications, or processes could subject us to significant liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates, treatment indications, or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may be involved in lawsuits to protect or enforce our patents or our licensors' patents, which could be expensive, time consuming and unsuccessful. Further, our issued patents or our licensors' patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our intellectual property rights. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent or the patent of our licensors is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, non-enablement, or obviousness-type double patenting. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution.

Third parties may also raise similar invalidity claims before the USPTO or patent offices abroad, even outside the context of litigation. Such mechanisms include re-examination, PGR, IPR, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of or amendment to our patents or our licensors' patents in such a way that they no longer cover our technology or platform, or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, or any product candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

The outcome following legal assertions of invalidity and/or unenforceability is unpredictable, and prior art could render our patent or our licensors' patent invalid. There is no assurance that all potentially relevant prior art relating to our patent and patent applications or the patent and patent applications of our licensors has been found. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patent and patent applications or the patent and patent applications of our licensors, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim.

If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we may lose at least part, and perhaps all, of the patent protection on such product candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications or the patent and patent applications of our licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available

for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.

Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of our licensors and the enforcement or defense of our issued patents or those of our licensors.

On September 16, 2011, the Leahy-Smith America Invents Act (the Leahy-Smith Act), was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a “first inventor to file” system in which,

assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we may not be certain that we or our licensors are the first to either (1) file any patent application related to our product candidates or (2) invent any of the inventions claimed in the patents or patent applications.

The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of our licensors and the enforcement or defense of our issued patents or those of our licensors, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in U.S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing pharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would

weaken our ability to obtain new patents or to enforce our existing patent and the patents we might obtain or license in the future.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U.S. patents or those of our licensors may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments). The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may not be able to protect our intellectual property rights throughout the world.

Although we have one issued patent in the United States and pending patent applications in the United States and other countries, filing, prosecuting and defending patents in all countries throughout the world would be

prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents, the patents of our licensors, or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or our licensors' patents or marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents or the patents of our licensors at risk of being invalidated or interpreted narrowly and our patent applications or the patent applications of our licensors at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or applications and those of our licensors. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our products. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition, we rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidentiality information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We may be subject to claims that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets.

We have entered into and may enter in the future into non-disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, lessees of shared multi-company property and other third parties. We may become subject to litigation where a third party asserts that we or our employees inadvertently or otherwise breached the agreements and used or disclosed trade secrets or other information proprietary to the third parties. A third party has inquired about a potential breach of a non-disclosure and confidentiality agreement in view of our developments in the CD73 inhibitor program. The inquiry may progress to a claim that we or our employees inadvertently or otherwise breached the agreement and used trade secrets

or other information proprietary to the third party. Defense of such matters, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions. Moreover, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology. Failure to defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Parties making claims against us may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, operating results, financial condition and prospects.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Our rights to develop and commercialize our technology and product candidates may be subject, in part, to the terms and conditions of licenses granted to us by others.

We have entered into license agreements with third parties and we may enter into additional license agreements in the future with others to advance our research or allow commercialization of product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future.

In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. In such an event, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our products that are subject of such licensed rights could be adversely affected.

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Our licensors may have relied on third party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

The patent protection and patent prosecution for some of our product candidates may be dependent on third parties.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our product candidates, there may be times when the filing and prosecution activities for patents relating to our product candidates are controlled by our licensors or collaboration partners. If any of our licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Intellectual property discovered through government funded programs may be subject to federal regulations such as “march-in” rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.

Our licensed patent applications, which do not cover ORIC-101, any of our current product candidates or any of our discovery and research programs, have been supported through the use of U.S. government funding awarded by the National Institute of Health and the Army Medical Research and Materiel Command. Although we do not currently own issued patents or pending patent applications that have been generated through the use of U.S. government funding, we may acquire or license in the future intellectual property rights that have been generated through the use of U.S. government funding or grants. Pursuant to the Bayh-Dole Act of 1980, the U.S. government has certain rights in inventions developed with government funding. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as “march-in rights”). If the U.S. government exercised its march-in rights in our future intellectual property rights that are generated through the use of U.S. government funding or grants, we could be forced to license or sublicense intellectual property developed by us or that we license on terms unfavorable to us, and there can be no assurance that we would receive compensation from the U.S. government for the exercise of such rights. The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting

requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

Risks related to our dependence on third parties

We rely on third parties to conduct our clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.

We do not have the ability to independently conduct our clinical trials. We currently rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our current and planned clinical trials of ORIC-101 and we expect to continue to rely upon third parties to conduct additional clinical trials of ORIC-101 and other product candidates. Third parties have a significant role in the conduct of our clinical trials and the subsequent collection and analysis of data. These third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we have limited ability to control the amount or timing of resources that any such third party will devote to our clinical trials. The third parties we rely on for these services may also have relationships with other entities, some of which may be our competitors. Some of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements with a third party, it would delay our drug development activities.

Our reliance on these third parties for such drug development activities will reduce our control over these activities but will not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCP standards, regulations for conducting, recording and reporting the results of clinical trials to assure that data and reported results are reliable and accurate and that the rights, integrity and confidentiality of trial participants are protected. The EMA also requires us to comply with similar standards. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials substantially comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under current cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the marketing approval process.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We contract with third parties for the production of our product candidates for preclinical studies and, in the case of ORIC-101, our ongoing clinical trials, and expect to continue to do so for additional clinical trials and

ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quality and quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. We rely, and expect to continue to rely, on third-party manufacturers for the production of our product candidates for preclinical studies and clinical trials under the guidance of members of our organization. In the case of ORIC-101, we rely on a single third-party manufacturer and we currently have no alternative manufacturer in place. We do not have long-term supply agreements, and we purchase our required drug product on a purchase order basis, which means that aside from any binding purchase orders we have from time to time, our supplier could cease supplying to us or change the terms on which it is willing to continue supplying to us at any time. If we were to experience an unexpected loss of supply of ORIC-101 or any other product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials.

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule and specifications, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
the failure of third-party contractors to comply with applicable regulatory requirements, including cGMPs;
- the failure of the third party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of our contract manufacturing partners and are dependent on these contract manufacturing partners for compliance with cGMP regulations for manufacturing both active pharmaceutical ingredients (API) and finished drug products. To date, we have obtained API and drug product for our product candidates from single-source third party contract manufacturers. We are in the process of developing our supply chain for each of our product candidates and intend to put in place framework agreements under which third-party contract manufacturers will generally provide us with necessary quantities of API and drug product on a project-by-project basis based on our development needs. As we advance our product candidates through development, we will consider our lack of

redundant supply for the API and drug product for each of our product candidates to protect against any potential supply disruptions. However, we may be unsuccessful in putting in place such framework agreements or protecting against potential supply disruptions.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or others, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we will need to find alternative manufacturing facilities, and those new facilities would need to be inspected and approved by FDA, EMA or comparable regulatory authority prior to commencing manufacturing, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

From time to time, we evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

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In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

If we decide to establish collaborations, but are not able to establish those collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We may seek to selectively form collaborations to expand our capabilities, potentially accelerate research and development activities and provide for commercialization activities by third parties. Any of these relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We would face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. Further, we may not be successful in our efforts to establish a collaboration or other alternative arrangements for product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy.

In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Even if we are successful in entering into a collaboration, the terms and conditions of that collaboration may restrict us from entering into future agreements on certain terms with potential collaborators.

If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We may enter into collaborations with third parties for the development and commercialization of product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

If we enter into any collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of

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our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates would pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, including as a result of a business combination or sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;
- we may grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly obtain, maintain, defend or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all;
- collaborators may not provide us with timely and accurate information regarding development progress and activities under the collaboration or may limit our ability to share such information, which could adversely impact our ability to report progress to our investors and otherwise plan our own development of our product candidates;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks related to this offering and ownership of our common stock

We do not know whether an active, liquid and orderly trading market will develop for our common stock or what the market price of our common stock will be and as a result it may be difficult for you to sell your shares of our common stock.

Prior to this offering, no market for shares of our common stock existed and an active trading market for our shares may never develop or be sustained following this offering. We will determine the initial public offering price for our common stock through negotiations with the underwriters, and the negotiated price may not be indicative of the market price of our common stock after this offering. The market value of our common stock may decrease from the initial public offering price. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies, technologies or other assets by using our shares of common stock as consideration.

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock following this offering is likely to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In addition to the factors discussed in this “Risk factors” section and elsewhere in this prospectus, these factors include:

- the timing and results of preclinical studies and clinical trials of our product candidates or those of our competitors;
- the success of competitive products or announcements by potential competitors of their product development efforts;
- regulatory actions with respect to our products or our competitors’ products;
- actual or anticipated changes in our growth rate relative to our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;

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- market conditions in the pharmaceutical and biotechnology sector;
- changes in the structure of healthcare payment systems;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- expiration of market stand-off or lock-up agreements; and
- general economic, political, industry and market conditions, including the impending presidential election in the United States in 2020.

The realization of any of the above risks or any of a broad range of other risks, including those described in this “Risk factors” section, could have a dramatic and adverse impact on the market price of our common stock.

If securities or industry analysts do not publish research or reports, or if they publish adverse or misleading research or reports, regarding us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. We do not currently have and may never obtain research coverage by securities or industry analysts. If no or few securities or industry analysts commence coverage of us, the stock price would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue adverse or misleading research or reports regarding us, our business model, our intellectual property, our stock performance or our market, or if our operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award as determined by our board of directors, and recognize the cost as an expense over the employee’s requisite service period. As the variables that we use as a basis for valuing these awards change over time, including, after the closing of this offering, our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and cost of, and level of investment in, research and development activities relating to our current and any candidates and research-stage programs, which will change from time to time;

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- our ability to enroll patients in clinical trials and the timing of enrollment;
- the cost of manufacturing our current and any product candidates, which may vary depending on FDA, EMA or other comparable foreign regulatory authority guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies or other assets;
- the timing and outcomes of clinical trials for ORIC-101, and any of our other product candidates, or competing product candidates;
- the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;
- competition from existing and potential future products that compete with ORIC-101 and any of our other product candidates, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any delays in regulatory review or approval of ORIC-101 or any of our other product candidates;
- the level of demand for ORIC-101 and any of our other product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future products that compete with ORIC-101 and any of our other product candidates;
- our ability to commercialize ORIC-101 and any of our other product candidates, if approved, inside and outside of the United States, either independently or working with third parties;
- our ability to establish and maintain collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic and political environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Prior to this offering, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 57.11% of our voting stock and, upon the closing of this

offering, that same group will beneficially own approximately % of our outstanding voting stock (based on the number of shares of common stock outstanding as of December 31, 2019 assuming no exercise of the underwriters' option to purchase additional shares, no exercise of outstanding options and no purchases of shares in this offering by any of this group), in each case assuming the conversion of all outstanding shares of our convertible preferred stock into shares of our common stock immediately prior to the closing of this offering. After this offering, this group of stockholders will have the ability to control us through this ownership position even if they do not purchase any additional shares in this offering. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of approximately \$ per share, representing the difference between the assumed initial public offering price of \$ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, and our pro forma net tangible book value per share after giving effect to this offering and the automatic conversion of all outstanding shares of our convertible preferred stock immediately prior to the closing of this offering. As of December 31, 2019, there were 10,615,463 shares subject to outstanding options with a weighted-average exercise price of \$0.94 per share. To the extent that these outstanding options are ultimately exercised or the underwriters exercise their option to purchase additional shares, you will incur further dilution. See the section of this prospectus titled "Dilution" for a further description of the dilution you will experience immediately after this offering.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have outstanding shares of common stock, based on the number of shares outstanding as of December 31, 2019, assuming: (1) no exercise of the underwriters' option to purchase additional shares and, (2) the conversion of all outstanding shares of our convertible preferred stock into shares of common stock immediately prior to the closing of this offering. This includes the shares that we sell in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. Of the remaining shares, shares of our common stock are currently restricted as a result of securities laws or market stand-off or lock-up agreements but will be able to be sold after this offering as described in the "Shares eligible for future sale" section of this prospectus. Moreover, after this offering, holders of an aggregate of shares of our common stock will have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity incentive plans. Once we register these shares, they can be freely sold in the public market upon issuance,

subject to volume limitations applicable to affiliates and the lock-up agreements described in the “Underwriting” section of this prospectus.

Our executive officers, directors and the holders of substantially all of our capital stock and securities convertible into or exchangeable for our capital stock have entered into market stand-off agreements with us and lock-up agreements with the underwriters under which they have agreed, subject to specific exceptions described in the section titled “Underwriting,” not to sell, directly or indirectly, any shares of common stock without the permission of the underwriters for a period of 180 days following the date of this prospectus. We refer to such period as the lock-up period. When the lock-up period expires, we and our securityholders subject to a lock-up agreement or market stand-off agreement will be able to sell our shares in the public market. In addition, the underwriters may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements at any time and for any reason. See the description of the market stand-off agreement with us and the lock-up agreement with the underwriters in the section of this prospectus titled “Shares eligible for future sale” for more information. Sales of a substantial number of such shares upon expiration of the lock-up and market stand-off agreements, the perception that such sales may occur, or early release of these agreements, could cause our market price to fall or make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

We are an “emerging growth company,” and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). For as long as we continue to be an emerging growth company, we intend to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (Sarbanes-Oxley Act);
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements; and
- exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, our financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than \$1.07 billion in annual revenue; (2) the date we qualify as a “large accelerated filer,”

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with at least \$700 million of equity securities held by non-affiliates; (3) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will incur increased costs as a result of operating as a public company, and our management will devote substantial time to related compliance initiatives. Additionally, if we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company, and these expenses may increase even more after we are no longer an “emerging growth company.” We will be subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (Exchange Act), the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and . Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly, which will increase our operating expenses. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. We cannot accurately predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

In addition, as a public company we will be required to incur additional costs and obligations in order to comply with SEC rules that implement Section 404 of the Sarbanes-Oxley Act. Under these rules, beginning with our second annual report on Form 10-K after we become a public company, we will be required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be an emerging growth company, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaging in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of our internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are designed and operating effectively, and implement a continuous reporting and improvement process for internal control over financial reporting.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system’s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

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If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon the closing of this offering, we will become subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the facts that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, and you will be relying on the judgment of our management regarding the application of these proceeds. You will not have the opportunity, as part of your investment decision, to assess whether we are using the proceeds appropriately. Our management might not apply the net proceeds in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to any appreciation in the value of their stock.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws, as they will be in effect upon closing of this offering, will contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions, among other things:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed “for cause” and only with the approval of two-thirds of our stockholders;
- authorize the issuance of “blank check” preferred stock that our board could use to implement a stockholder rights plan (also known as a “poison pill”);
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting;
- authorize our board of directors to amend the bylaws;
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and
- require a super-majority vote of stockholders to amend some provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL), prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated bylaws that will become effective upon the closing of this offering provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated bylaws that will become effective upon the closing of this offering provide that the Court of Chancery of the State of Delaware is the exclusive forum for:

- any derivative action or proceeding brought on our behalf;

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- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This exclusive-forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to this provision. If a court were to find this exclusive-forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business. Nothing in our amended and restated bylaws precludes stockholders that assert claims under the Securities Act or the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

Special note regarding forward-looking statements

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, development plans, planned preclinical studies and clinical trials, future results of clinical trials, expected research and development costs, regulatory strategy, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. Forward-looking statements contained in this prospectus include, but are not limited to, statements about:

- the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results;
- the timing, progress and results of preclinical studies and clinical trials for ORIC-101 and other product candidates we may develop, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs;
- the timing, scope and likelihood of regulatory filings and approvals, including timing of Investigational New Drug applications and final FDA approval of ORIC-101 and any other future product candidates;
- the timing, scope or likelihood of foreign regulatory filings and approvals;
- our ability to develop and advance our current product candidates and programs into, and successfully complete, clinical studies;
- our manufacturing, commercialization, and marketing capabilities and strategy;
- our plans relating to commercializing our product candidates, if approved, including the geographic areas of focus and sales strategy;
- the need to hire additional personnel and our ability to attract and retain such personnel;
- the size of the market opportunity for our product candidates, including our estimates of the number of patients who suffer from the diseases we are targeting;
- our expectations regarding the approval and use of our product candidates in combination with other drugs;
- our competitive position and the success of competing therapies that are or may become available;
- our estimates of the number of patients that we will enroll in our clinical trials;
- the beneficial characteristics, safety, efficacy and therapeutic effects of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our plans relating to the further development of our product candidates, including additional indications we may pursue;

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- existing regulations and regulatory developments in the United States, Europe and other jurisdictions;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering ORIC-101 and other product candidates we may develop, including the extensions of existing patent terms where available, the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- our continued reliance on third parties to conduct additional clinical trials of our product candidates, and for the manufacture of our product candidates for preclinical studies and clinical trials;
- our ability to obtain, and negotiate favorable terms of, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- the pricing and reimbursement of ORIC-101 and other product candidates we may develop, if approved;
- the rate and degree of market acceptance and clinical utility of ORIC-101 and other product candidates we may develop;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our financial performance;
- the period over which we estimate our existing cash and cash equivalents will be sufficient to fund our future operating expenses and capital expenditure requirements;
- the impact of laws and regulations;
- our expectations regarding the period during which we will qualify as an emerging growth company under the JOBS Act; and
- our anticipated use of our existing resources and the proceeds from this offering.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk factors" and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein until after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

Market, industry and other data

This prospectus contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates, including data regarding the estimated size of such markets and the incidence of certain medical conditions. We obtained the industry, market and similar data set forth in this prospectus from our internal estimates and research and from academic and industry research, publications, surveys and studies conducted by third parties, including governmental agencies. In some cases, we do not expressly refer to the sources from which this data is derived. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. While we believe our internal research is reliable, such research has not been verified by any third party. You are cautioned not to give undue weight to any such information, projections and estimates.

Use of proceeds

We estimate that the net proceeds to us from the sale of the shares of our common stock in this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise their option to purchase additional shares in full, based upon the assumed initial public offering price of \$ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each \$1.00 increase or decrease in the assumed initial public offering price of \$ per share would increase or decrease, as applicable, the net proceeds to us from this offering by approximately \$ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase or decrease of 1.0 million shares in the number of shares offered by us would increase or decrease, as applicable, the net proceeds to us from this offering by approximately \$ million, assuming the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations, establish a public market for our common stock and facilitate our future access to the public capital markets.

We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately \$ million to fund our two Phase 1b trials of ORIC-101 in combination with (1) enzalutamide in prostate cancer and (2) nab-paclitaxel in advanced or metastatic solid tumors;
- approximately \$ million to fund our development of ORIC-533; and
- the remaining amounts to fund our development of other research and development activities, as well as for working capital and other general corporate purposes.

Based on our current operating plan, we believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our planned operating expenses and capital expenditures through . This includes the completion of our two Phase 1b trials of ORIC-101. The net proceeds from this offering, together with our existing cash and cash equivalents, will not be sufficient to fund any of our product candidates through regulatory approval, and we anticipate needing to raise additional capital to complete the development of and commercialize our product candidates. It is difficult to predict the cost and timing required to complete development and obtain regulatory approval of, and commercialize, our product candidates due to, among other factors, our lack of experience with initiating, conducting and completing clinical trials, and uncertainty regarding the scope and design of clinical trials required to obtain regulatory approval for our product candidates, the rate of subject enrollment in our clinical trials, filing requirements with various regulatory agencies, clinical trial results, and the actual costs of manufacturing, supplying and commercializing our product candidates.

Our expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above. We believe opportunities may exist from time to time to expand our current business through licenses with or acquisitions of, or investments in, complementary businesses, products or technologies. While we have no current agreements, commitments or understandings for any

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specific licenses, acquisitions or investments at this time, we may use a portion of the net proceeds for these purposes.

Our management will have broad discretion over the use of the net proceeds from this offering. The amounts and timing of our expenditures will depend upon numerous factors including the results of our research and development efforts, the timing, cost and success of preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, the timing of regulatory submissions, our ability to obtain additional financing, the amount of cash obtained through our existing collaborations and future collaborations, if any, and any unforeseen cash needs.

Pending their use, we intend to invest the net proceeds of this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

Dividend policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings and do not expect to pay any dividends in the foreseeable future. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to applicable laws, and will depend on a number of factors, including our financial condition, results of operations, capital requirements, contractual restrictions, general business conditions and other factors that our board of directors may deem relevant.

Capitalization

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2019:

- on an actual basis;
- on a pro forma basis, giving effect to (1) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 77,114,498 shares of common stock immediately prior to the completion of this offering and (2) the filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the completion of this offering; and
- on a pro forma as adjusted basis to reflect (1) the pro forma adjustments set forth above and (2) our issuance and sale of _____ shares of common stock in this offering at the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information set forth below is illustrative only and will depend on the actual initial public offering price and other terms of this offering determined at pricing. You should read this information in conjunction with our financial statements and the related notes appearing elsewhere in this prospectus, as well as the sections titled "Selected financial data" and "Management's discussion and analysis of financial condition and results of operations."

(in thousands, except per share amounts)	As of December 31, 2019		
	Actual	Pro forma (unaudited)	Pro forma as adjusted ⁽¹⁾
Cash and cash equivalents	\$ _____	\$ _____	\$ _____
Convertible preferred stock, \$0.0001 par value per share; _____ shares authorized, _____ shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted			
Stockholders' (deficit) equity:			
Preferred stock, \$0.0001 par value per share; no shares authorized, issued and outstanding, actual; _____ shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted			
Common stock, \$0.0001 par value per share; _____ shares authorized, _____ shares issued and outstanding, actual; _____ shares authorized, _____ shares issued and outstanding, pro forma; _____ shares authorized, _____ shares issued and outstanding, pro forma as adjusted			
Additional paid-in capital			
Accumulated deficit			
Total stockholders' (deficit) equity			
Total capitalization	\$ _____	\$ _____	\$ _____

- (1) Each \$1.00 increase or decrease in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, each of our pro forma as adjusted cash and cash equivalents, additional paid-in capital, total stockholders' (deficit) equity and total capitalization by approximately \$ _____ million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase or

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decrease of 1.0 million shares in the number of shares of common stock offered by us would increase or decrease, as applicable, each of our pro forma as adjusted cash and cash equivalents, additional paid-in capital, total stockholders' (deficit) equity and total capitalization by approximately \$ million, assuming the assumed initial public offering price of \$ per share, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters' option to purchase additional shares is exercised in full, our pro forma as adjusted cash and cash equivalents, additional paid-in capital, total stockholders' (deficit) equity, and total capitalization as of December 31, 2019, would be \$ million, \$ million, \$ million, and \$ million, respectively.

The number of shares of our common stock issued and outstanding, pro forma and pro forma as adjusted in the table above is based on 85,169,744 shares of our common stock outstanding as of December 31, 2019 (including our convertible preferred stock on an as-converted basis), and excludes:

- 10,615,463 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2019 with a weighted-average exercise price of \$0.94 per share;
- 814,793 shares of common stock for future issuance under our 2014 Equity Incentive Plan, as amended (2014 Plan), as of December 31, 2019, which shares will be added to the shares to be reserved for future issuance under our 2020 Equity Incentive Plan (2020 Plan);
- shares of common stock reserved for future issuance under our 2020 Plan, which will become effective in connection with this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan; and
- shares of common stock reserved for future issuance under our 2020 Employee Stock Purchase Plan (2020 ESPP), which will become effective in connection with this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

Dilution

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book deficit as of December 31, 2019 was \$ _____ million, or \$ _____ per share of our common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and convertible preferred stock, which is not included within our stockholders' (deficit) equity. Historical net tangible book value (deficit) per share represents historical net tangible book value (deficit) divided by the number of shares of our common stock outstanding as of December 31, 2019.

Our pro forma net tangible book value as of December 31, 2019 was \$ _____ million, or \$ _____ per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of December 31, 2019, after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock as of December 31, 2019 into an aggregate of shares of our common stock immediately prior to the completion of this offering as if such conversion had occurred on December 31, 2019.

After giving further effect to our sale of _____ shares of common stock in this offering at the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2019 would have been approximately \$ _____ million, or approximately \$ _____ per share. This represents an immediate increase in pro forma net tangible book value per share of approximately \$ _____ to our existing stockholders and an immediate dilution in pro forma net tangible book value per share of approximately \$ _____ to investors purchasing shares of common stock in this offering.

Dilution per share to investors purchasing shares of common stock in this offering is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by investors purchasing shares of common stock in this offering.

The following table illustrates this dilution on a per share basis to new investors (without giving effect to any exercise by the underwriters of their option to purchase additional shares):

Assumed initial public offering price per share		\$
Historical net tangible book value (deficit) per share as of December 31, 2019	\$	
Pro forma increase in net tangible book value per share as of December 31, 2019	_____	
Pro forma net tangible book value per share as of December 31, 2019		_____
Increase in pro forma net tangible book value per share attributable to investors purchasing shares of common stock in this offering		_____
Pro forma as adjusted net tangible book value per share		_____
Dilution per share to investors participating in this offering		\$

Each \$1.00 increase or decrease in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, the pro forma as adjusted net tangible book value per share after this offering by approximately \$ _____ per share and the dilution to investors purchasing shares of common stock in this offering by _____.

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approximately \$ _____ per share, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase of 1.0 million shares in the number of shares offered by us would increase the pro forma as adjusted net tangible book value per share after this offering by approximately \$ _____ and decrease the dilution per share to investors purchasing shares of common stock in this offering by approximately \$ _____, assuming no change in the assumed initial public offering price and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each decrease of 1.0 million shares in the number of shares offered by us would decrease the pro forma as adjusted net tangible book value per share after this offering by approximately \$ _____ and increase the dilution per share to investors purchasing shares of common stock in this offering by approximately \$ _____, assuming no change in the assumed initial public offering price and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase _____ additional shares of common stock in this offering in full at the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus and assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, the pro forma as adjusted net tangible book value per share after this offering would be approximately \$ _____ per share, and the dilution per share to investors purchasing shares of common stock in this offering would be approximately \$ _____ per share.

The following table summarizes, on the pro forma as adjusted basis described above, as of December 31, 2019, the number of shares of common stock purchased from us, the total consideration paid, or to be paid, and the weighted-average price per share paid, or to be paid, by existing stockholders and by investors purchasing shares in this offering at the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(dollar amounts in thousands, except per share amounts)	Shares purchased		Total consideration		Weighted-average price per share
	Number	Percent	Amount	Percent	
Existing stockholders before this offering		%	\$	%	\$
Investors purchasing shares in this offering					\$
Total		100%	\$	100%	

The table above assumes no exercise of the underwriters' option to purchase _____ additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to _____ % of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by investors purchasing shares of common stock in the offering would be increased to _____ % of the total number of shares outstanding after this offering.

Each \$1.00 increase or decrease in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, the total consideration paid by investors purchasing shares in this offering by approximately \$ _____ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. Similarly, each increase or decrease of 1.0 million shares in the number of shares offered by us would increase or decrease, as applicable, the total consideration paid by investors

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purchasing shares in this offering by approximately \$ million, assuming no change in the assumed initial public offering price.

The foregoing tables and calculations (other than the historical net tangible book value calculation) are based on the 85,169,744 shares of our common stock outstanding as of December 31, 2019 (including our convertible preferred stock on an as-converted basis), and excludes:

- 10,615,463 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2019 with a weighted-average exercise price of \$0.94 per share;
- 814,793 shares of common stock for future issuance under our 2014 Plan as of December 31, 2019, which shares will be added to the shares to be reserved for future issuance under our 2020 Plan;
- shares of common stock reserved for future issuance under our 2020 Plan, which will become effective in connection with this offering as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan; and
- shares of common stock reserved for future issuance under our 2020 ESPP, which will become effective in connection with this offering as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

To the extent that any outstanding options are exercised or new options are issued under the equity benefit plans, or we issue additional shares of common stock or other securities convertible into or exercisable or exchangeable for shares of our capital stock in the future, there will be further dilution to investors purchasing shares of common stock in this offering.

Selected financial data

The following tables summarize our selected financial data for the periods and as of the dates indicated. We have derived our selected statements of operations data for the years ended December 31, 2017 and 2018, and the balance sheet data as of December 31, 2017 and 2018, from our audited financial statements appearing elsewhere in this prospectus. You should read the following selected financial data together with our financial statements and the related notes appearing elsewhere in this prospectus and the information in the section titled "Management's discussion and analysis of financial condition and results of operations."

(in thousands, except per share amounts)	Year ended December 31,	
	2017	2018
Statement of operations data:		
Operating expenses:		
Research and development	\$ 19,126	\$ 19,026
General and administrative	3,415	3,345
Total operating expenses	22,541	22,371
Loss from operations	(22,541)	(22,371)
Other income:		
Interest income, net	251	775
Other income	261	233
Total other income	512	1,008
Net loss and comprehensive loss	\$ (22,029)	\$ (21,363)
Net loss per share, basic and diluted ⁽¹⁾	\$ (3.90)	\$ (3.08)
Weighted-average shares outstanding, basic and diluted ⁽¹⁾	5,642	6,936
Pro forma net loss per share, basic and diluted (unaudited) ⁽¹⁾		\$ (0.35)
Pro forma weighted-average shares outstanding, basic and diluted (unaudited) ⁽¹⁾		60,629

(1) See Note 2 to our audited financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

(in thousands)	As of December 31,	
	2017	2018
Balance sheet data:		
Cash and cash equivalents	\$ 25,819	\$ 42,636
Total assets	30,025	46,734
Accrued other liabilities	1,670	2,150
Total liabilities	4,299	3,894
Convertible preferred stock	69,337	107,266
Accumulated deficit	(44,444)	(65,807)
Total stockholders' deficit	(43,611)	(64,426)

Management's discussion and analysis of financial condition and results of operations

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes appearing elsewhere in this prospectus and in the section titled "Selected financial data." Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks, uncertainties and assumptions. As a result of many factors, including those factors set forth in the section titled "Risk factors," our actual results could differ materially from the results described in or implied by these forward-looking statements. You should carefully read the "Risk factors" to gain an understanding of the factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section titled "Special note regarding forward-looking statements."

Overview

ORIC Pharmaceuticals is a clinical-stage biopharmaceutical company dedicated to improving patients' lives by Overcoming Resistance In Cancer.

Our fully integrated discovery and development team is advancing a diverse pipeline of innovative therapies designed to counter resistance mechanisms in cancer by leveraging our expertise within three specific areas: hormone-dependent cancers, precision oncology and key tumor dependencies. Our lead product candidate, ORIC-101, builds upon a legacy of successful drug development by our founders in the field of nuclear hormone receptors and their efforts to elucidate the cause of resistance to the groundbreaking prostate cancer therapies that they had developed. ORIC-101 is a potent and selective small molecule antagonist of the glucocorticoid receptor (GR), which has been linked to resistance to multiple classes of cancer therapeutics across a variety of solid tumors. In 2019, we initiated two separate Phase 1b trials of ORIC-101 in combination with (1) Xtandi (enzalutamide) in metastatic prostate cancer and (2) Abraxane (nab-paclitaxel) in advanced or metastatic solid tumors, and we expect to report interim data for one of these trials in the first half of 2021. Our second product candidate, ORIC-533, is an orally bioavailable small molecule inhibitor of CD73, a key node in the adenosine pathway believed to play a central role in resistance to chemotherapy- and immunotherapy- based treatment regimens. We expect to file an IND for ORIC-533 in 2021. Beyond these two product candidates, we are developing multiple precision medicines targeting other hallmark cancer resistance mechanisms.

Since our inception in 2014, we have devoted substantially all of our resources to research and development activities, including with respect to our GR antagonist and CD73 inhibitor programs and other preclinical programs, business planning, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital and providing general and administrative support for these operations.

We do not have any products approved for sale, and we have not generated any revenue from product sales. Our ability to generate product revenue sufficient to achieve profitability, if ever, will depend on the successful development and eventual commercialization of one or more of our product candidates which we expect will take a number of years.

We have incurred significant losses since the commencement of our operations. Our net losses were \$22.0 million and \$21.4 million in 2017 and 2018, respectively, and we expect to continue to incur significant losses for the foreseeable future as we advance our product candidates from discovery through preclinical development and clinical trials and seek regulatory approval of our product candidates. As of December 31,

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2018, we had an accumulated deficit of \$65.8 million. These losses have resulted primarily from costs incurred in connection with research and development activities and to a lesser extent from general and administrative costs associated with our operations. We expect to incur significant and increasing expenses and operating losses for the foreseeable future. Our net losses may fluctuate significantly from period to period, depending on the timing of and expenditures on our planned research and development activities.

We expect our expenses and capital requirements will increase substantially in connection with our ongoing activities as we:

- advance the development of ORIC-101;
- advance the development of ORIC-533;
- advance our earlier stage preclinical programs;
- expand our pipeline of product candidates, including through our own product discovery and development efforts or through acquisition or in-licensing;
- maintain, protect and expand our intellectual property portfolio, including patents, trade secrets and know how;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval and related commercial manufacturing build-out;
- implement operational, financial and management information systems;
- attract, hire and retain additional clinical, scientific, management and administrative personnel; and
- operate as a public company.

As a result, we will require substantial additional funding to develop our product candidates and support our continuing operations. Until such time that we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, which could include income from collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties or from grants. We may be unable to raise additional funds or to enter into such agreements or arrangements on favorable terms, or at all. Our failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations or financial condition, and could force us to delay, reduce or eliminate our product development or future commercialization efforts. We may also be required to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our development efforts. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

To date, we have financed our operations primarily through private placements of convertible preferred stock. As of December 31, 2018, we had raised net proceeds of \$107.3 million from these private placements of our convertible preferred stock and had cash and cash equivalents of \$42.6 million. In February 2019, an additional 5,086,054 shares of Series C convertible preferred stock were issued as part of the second tranche closing for \$3.00 per share, resulting in net proceeds of \$15.2 million. In June and July 2019, 16,869,345 shares of Series D convertible preferred stock were issued for \$3.30 per share, resulting in net proceeds of \$55.5 million. Based on our current operating plan, we believe that the proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our planned operating expenses and capital expenditures through

Components of our results of operations

Revenue

To date, we have not generated any revenue and do not expect to generate any revenue from the sale of products for the foreseeable future.

Operating expenses

Research and development

Research and development expenses account for a significant portion of our operating expenses and consist primarily of external and internal costs incurred in connection with the discovery and development of our product candidates.

External expenses include:

- payments to third parties in connection with the clinical development of our product candidates, including clinical research organizations (CROs) and consultants;
- the cost of manufacturing products for use in our preclinical studies and clinical trials, including payments to contract manufacturing organizations (CMOs) and consultants;
- payments to third parties in connection with the preclinical development of our product candidates, including outsourced professional scientific development services, consulting research fees and for sponsored research arrangements with third parties;
- laboratory supplies; and
- allocated facilities, depreciation and other expenses, which include direct or allocated expenses for IT, rent and maintenance of facilities.

Internal expenses include employee-related costs, including salaries, related benefits and stock-based compensation expense for employees engaged in research and development functions.

We expense research and development costs in the periods in which they are incurred. External expenses are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers or our estimate of the level of service that has been performed at each reporting date. We track external costs by the stage of program, clinical or preclinical. We do not track internal costs by program because these costs are deployed across multiple programs and, as such, are not separately classified.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect that our research and development expenses will increase substantially in the foreseeable future as we advance our product candidates through preclinical studies and clinical trials; continue to discover and develop additional product candidates and expand our pipeline; maintain, expand, protect and enforce our intellectual property portfolio; and hire additional personnel.

The successful development of our product candidates is highly uncertain, and we do not believe it is possible at this time to accurately project the nature, timing and estimated costs of the efforts necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. To the extent our product candidates continue to advance into clinical trials, as well as advance into larger and later-stage clinical trials, our expenses will increase substantially and may become more variable. We are also unable to predict when, if

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ever, we will generate revenue from our product candidates to offset these expenses. Our expenditures on current and future preclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. The duration, costs and timing of preclinical studies and clinical trials and development of our product candidates will depend on a variety of factors, including:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to maintain our current research and development programs and to establish new ones;
- establishing an appropriate safety profile with IND-enabling toxicology studies;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the receipt of regulatory approvals from applicable regulatory authorities;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- our ability to establish licensing or collaboration arrangements;
- the performance of our future collaborators, if any;
- obtaining and retaining research and development personnel;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- development and timely delivery of commercial-grade product formulations that can be used in our planned clinical trials and for commercial launch;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- launching commercial sales of our product candidates, if approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of our products following approval.

Any changes in the outcome of any of these factors could significantly impact the costs, timing and viability associated with the development of our product candidates.

General and administrative

General and administrative expenses consist primarily of salaries, related benefits and stock-based compensation expense for personnel in executive, finance and administrative functions. General and administrative expenses also include allocated facilities, depreciation and other expenses, which include direct or allocated expenses for rent and maintenance of facilities and insurance, not otherwise included in research and development expenses, as well as professional fees for legal, patent, consulting, investor and public relations, accounting and audit services.

We expect that our general and administrative expenses will increase substantially in the foreseeable future as we increase our headcount to support the continued research and development of our programs and the growth of our business. Following the completion of this offering, we also anticipate that we will incur substantially higher expenses relating to accounting, audit, legal, regulatory, compliance, director and officer insurance and investor and public relations as a result of being a public company.

Other income*Interest income, net and other income*

Interest income, net primarily consists of interest income generated from our investments in interest-bearing money market accounts. Other income primarily consists of rental income from the sub-lease of a portion of our headquarters located in South San Francisco, California.

Results of operations**Comparison of the years ended December 31, 2017 and 2018**

The following table summarizes our results of operations for the years ended December 31, 2017 and 2018:

(in thousands)	Year ended December 31,		Change
	2017	2018	
Operating expenses:			
Research and development	\$ 19,126	\$ 19,026	\$ (100)
General and administrative	3,415	3,345	(70)
Total operating expenses	22,541	22,371	(170)
Loss from operations	\$ (22,541)	\$ (22,371)	\$ 170
Other income:			
Interest income, net	\$ 251	\$ 775	\$ 524
Other income	261	233	(28)
Total other income	512	1,008	496
Net loss and comprehensive loss	\$ (22,029)	\$ (21,363)	\$ 666

Research and development expenses

Research and development expenses were \$19.1 million for the year ended December 31, 2017 compared to \$19.0 million for the year ended December 31, 2018, a decrease of \$0.1 million. This decrease was driven primarily by \$2.8 million lower manufacturing and IND filing-related costs for ORIC-101, largely offset by \$2.7 million higher personnel and early stage research costs. We expect that our research and development expenses will increase as we advance our product candidates through preclinical studies and clinical trials, continue to discover and develop additional product candidates and expand our pipeline.

We track external costs by stage of program, clinical and preclinical. We do not track internal costs by program because these costs are deployed across multiple programs, as such, are not separately classified. External research and development expenses consist of payments to outside consultants, CROs, CMOs, clinical trial sites and central laboratories in connection with our discovery and preclinical activities, process development, manufacturing and clinical development activities. External costs also include laboratory supplies as well as allocated facilities, depreciation and other expenses. Included in preclinical and other unallocated costs are external corporate overhead costs that are not specific to any one program.

Internal costs consist of employee-related costs including salaries, related benefits and stock-based compensation expense for employees engaged in research and development functions, which are not tracked by product candidate as several of our departments support multiple product candidate research and development programs.

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The following table summarizes our external costs and internal costs for the years ended December 31, 2017 and 2018:

(in thousands)	Year ended December 31,		Change
	2017	2018	
External costs:			
ORIC-101	\$ 6,733	\$ 4,365	\$ (2,368)
Preclinical and other unallocated costs	7,193	7,754	561
Total external costs	13,926	12,119	(1,807)
Internal costs	5,200	6,907	1,707
Total research and development expenses	\$ 19,126	\$ 19,026	\$ (100)

We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, including investments in manufacturing, as our programs advance into later stages of development and as we conduct additional clinical trials.

General and administrative expenses

General and administrative expenses were \$3.4 million for the year ended December 31, 2017 compared to \$3.3 million for the year ended December 31, 2018, a decrease of \$0.1 million. We anticipate that our general and administrative expenses will increase as we increase our headcount to support the continued research and development of our programs. We also anticipate that we will incur substantially higher expenses relating to accounting, audit, legal, regulatory, compliance, director and officer insurance and investor and public relations as a result of being a public company.

Other income

Other income was \$0.5 million for the year ended December 31, 2017 compared to \$1.0 million for the year ended December 31, 2018, an increase of \$0.5 million. This increase was primarily attributable to interest income as a result of higher cash balances as a result of the Series C convertible preferred stock financing in 2018.

Liquidity and capital resources

Sources of liquidity

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. Our net losses were \$22.0 million and \$21.4 million for the years ended December 31, 2017 and 2018, respectively. As of December 31, 2018, we had an accumulated deficit of \$65.8 million. We have funded our operations to date primarily with proceeds from the sale of convertible preferred stock. As of December 31, 2018, we had raised net proceeds of \$107.3 million from these private placements and had cash and cash equivalents of \$42.6 million. In February 2019, an additional 5,086,054 shares of Series C convertible preferred stock were issued as part of the second tranche closing for \$3.00 per share, resulting in net proceeds of \$15.2 million. In June and July 2019, 16,869,345 shares of Series D convertible preferred stock were issued for \$3.30 per share, resulting in net proceeds of \$55.5 million.

Our primary uses of cash are to fund our research and development activities, including with respect to ORIC-101, ORIC-533 and other preclinical programs, business planning, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital and providing general and administrative support for these operations.

Future funding requirements

To date, we have not generated any revenue. We do not expect to generate any meaningful revenue unless and until we obtain regulatory approval of and commercialize any of our product candidates, and we do not know when, or if at all, that will occur. We will continue to require substantial additional capital to develop our product candidates and fund operations for the foreseeable future. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the development of and seek regulatory approvals for our product candidates. We are subject to all the risks incident in the development of new pharmaceutical products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may harm our business. In addition, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Our expenses will also increase if, and as, we:

- advance our product candidates through preclinical and clinical development;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- seek to discover and develop additional product candidates;
- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval and intend to commercialize on our own or jointly;
- expand our operational, financial and management systems and increase personnel, including personnel to support our development, manufacturing and commercialization efforts and our operations as a public company;
- maintain, expand, protect and enforce our intellectual property portfolio; and
- acquire or in-license other product candidates and technologies.

In order to complete the development of our product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding. Until we can generate a sufficient amount of revenue from the commercialization of our product candidates, we may seek to raise any necessary additional capital through the sale of equity, debt financings or other capital sources, which could include income from collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties or from grants. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, including restricting our operations and limiting our ability to incur liens, issue additional debt, pay dividends, repurchase our common stock, make certain investments or engage in merger, consolidation, licensing or asset sale transactions. If we raise funds through collaborations, strategic partnerships and other similar arrangements with third parties, we may be required to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. We may be unable to raise additional funds or to enter into such agreements or

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arrangements on favorable terms, or at all. If we are unable to raise additional funds when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts.

We believe that the proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our planned operating expenses and capital expenditures through . We have based our projections of operating capital requirements on our current operating plan, which is based on several assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount and timing of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical studies and clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the costs of manufacturing commercial-grade products and sufficient inventory to support commercial launch;
- the revenue, if any, received from commercial sale of our products, should any of our product candidates receive marketing approval;
- the cost and timing of hiring new employees to support our continued growth;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the ability to establish and maintain collaborations on favorable terms, if at all;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the timing, receipt and amount of sales of, or milestone payments related to or royalties on, our current or future product candidates, if any.

A change in the outcome of any of these or other factors with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plan may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plan.

Cash flows

The following table summarizes our cash flow for the years ended December 31, 2017 and 2018:

(in thousands)	Year ended December 31,	
	2017	2018
Net cash used in operating activities	\$ (20,832)	\$ (20,683)
Net cash used in investing activities	(292)	(508)
Net cash provided by financing activities	260	38,008
Net (decrease) increase in cash and cash equivalents	\$ (20,864)	\$ 16,817

Operating activities

Net cash used in operating activities during the year ended December 31, 2017 of \$20.8 million was primarily attributable to our net loss of \$22.0 million, adjusted for addbacks for non-cash expenses of \$1.1 million, which includes stock-based compensation of \$0.2 million and depreciation of \$0.9 million.

Net cash used in operating activities during the year ended December 31, 2018 of \$20.7 million was primarily attributable to our net loss of \$21.4 million, adjusted for addbacks for non-cash expenses of \$1.4 million, which includes stock-based compensation of \$0.5 million and depreciation of \$0.9 million and a net decrease in working capital of \$0.7 million.

Investing activities

Net cash used in investing activities during the year ended December 31, 2017 of \$0.3 million and was attributable to purchases of property and equipment, partially offset by proceeds from notes receivable.

Net cash used in investing activities during the year ended December 31, 2018 of \$0.5 million was primarily attributable to purchases of property and equipment, partially offset by proceeds from notes receivable.

Financing activities

Net cash provided by financing activities during the year ended December 31, 2017 was \$0.3 million, consisting of proceeds from the issuance of common stock upon the exercise of options.

Net cash provided by financing activities during the year ended December 31, 2018 was \$38.0 million, primarily consisting of proceeds of \$37.9 million generated from the sale of shares of Series C convertible preferred stock, net of issuance costs, and proceeds of \$0.1 million from the issuance of common stock upon the exercise of stock options.

Contractual obligations and commitments

The following table summarizes our contractual obligations and commitments as of December 31, 2018:

(in thousands)	Payments due by period				
	Total	Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years
Operating lease obligations ⁽¹⁾	\$5,977	\$1,712	\$4,265	—	—

(1) Reflects minimum payments due for office and laboratory space in South San Francisco, California leased under an operating lease that expires in May 2022.

We lease certain office and lab space in South San Francisco, California under a non-cancelable operating lease, with a five-year term through May 2022 with an option to renew for an additional five-year term. Rent expense was \$1.4 million and \$1.5 million for the years ended December 31, 2017 and 2018, respectively, excluding the offset for amortization of the leasehold interest of \$0.1 million and \$0.2 million for the years ended December 31, 2017 and 2018, respectively.

In March 2019, we entered into a lease agreement for office space in San Diego, California under a non-cancelable operating lease with a 13-month term. In October 2019, the lease was amended to increase the office space and extend the lease term until May 2021. The minimum payments due under the amended lease total \$0.2 million over the lease term.

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In addition, we have entered into contracts in the normal course of business with CROs, CMOs and other third parties for preclinical research studies and testing, clinical trials and manufacturing services. These contracts do not contain any minimum purchase commitments and are cancelable by us upon prior notice and, as a result, are not included in the table of contractual obligations and commitments above. Payments due upon cancellation consist only of payments for services provided and expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation. We have entered into agreements with certain vendors for the provision of goods and services, which includes manufacturing services with CMOs and development services with CROs. These agreements may include certain provisions for purchase obligations and termination obligations that could require payments for the cancellation of committed purchase obligations or for early termination of the agreements. The amount of the cancellation or termination payments vary and are based on the timing of the cancellation or termination and the specific terms of the agreement.

Off-balance sheet arrangements

We currently do not have, and did not have during the periods presented, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Critical accounting policies and significant judgments and estimates

Our financial statements are prepared in accordance with generally accepted accounting principles (GAAP) in the United States. The preparation of our financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on a periodic basis. Our actual results may differ from these estimates.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing at the end of this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Research and development expenses

Research and development costs are expensed in the periods in which they are incurred. External costs consist primarily of payments to outside consultants, CROs, CMOs, clinical trial sites and central laboratories in connection with our discovery and preclinical activities, process development, manufacturing and clinical development activities. External costs also include laboratory supplies as well as allocated facilities, depreciation and other expenses. External expenses are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers or our estimate of the level of service that has been performed at each reporting date. We allocate external costs by the stage of program, clinical or preclinical. Internal costs consist primarily of employee-related costs including salaries, related benefits and stock-based compensation expense for employees engaged in research and development functions. We do not allocate internal costs by stage of program because these costs are deployed across multiple programs and, as such, are not separately classified. Research and development expenses amounted to \$19.1 million and \$19.0 million during the years ended December 31, 2017 and 2018, respectively.

Stock-based compensation

Stock-based compensation expense represents the cost of the grant date fair value of employee, officer, director and non-employee stock option grants, estimated in accordance with the applicable accounting

guidance, recognized on a straight-line basis over the vesting period. The vesting period generally approximates the expected service period of the awards. We recognize forfeitures as they occur.

The fair value of stock options is estimated using a Black-Scholes-Merton valuation model on the date of grant. The Black-Scholes-Merton option-pricing model requires inputs based on certain highly subjective assumptions. Changes to these assumptions can materially affect the fair value of stock options and ultimately the amount of stock-based compensation expense recognized in our financial statements. These assumptions include:

Fair value of common stock—Historically, as there has been no public market for our common stock, the fair value of our common stock was determined by our board of directors primarily based on valuations of our common stock prepared by a third-party valuation firm using the option pricing method (OPM) with discounts for lack of marketability and potential liquidation events in periods through August 2019, and the probability-weighted expected return method (PWERM) beginning in November 2019. See the subsection titled “—Determination of the fair value of our common stock” below.

Risk-free interest rate—The risk-free rate assumption is based on the U.S. Treasury instruments with maturities similar to the expected term of our stock options.

Expected volatility—Due to our limited operating history and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility data was computed using the daily closing prices for the selected companies’ shares during the equivalent period of the calculated expected term of the stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Expected term—The expected term represents the period that the stock-based awards are expected to be outstanding. We have opted to use the “simplified method” for estimating the expected term of options, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option, which is generally 10 years.

Expected dividend yield—To date, we have not issued any dividends and do not expect to issue dividends over the life of the options and therefore have estimated the dividend yield to be zero.

Stock-based compensation expense was \$0.2 million and \$0.5 million during the years ended December 31, 2017 and 2018, respectively. As of December 31, 2018, we had \$2.3 million of total unrecognized stock-based compensation costs which we expect to recognize over a weighted-average period of 3.34 years. The intrinsic value of all outstanding options as of _____ was approximately \$ _____, based on the assumed initial public offering price of \$ _____ per share, which is the midpoint of the estimated initial public offering price range set forth on the cover page of this prospectus, of which \$ _____ was related to vested options and \$ _____ was related to unvested options.

Determination of the fair value of our common stock

As there has been no public market for our common stock to date, for all periods prior to this initial public offering, the estimated fair value of our common stock has been historically determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuation of our common stock as well as our board of directors’ assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation to the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants’ Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* (the Practice

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Aid). The Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of common stock at each valuation date. In accordance with the Practice Aid, our board of directors considered the following methods:

- *Probability-weighted expected return method.* The PWERM is a scenario-based analysis that estimates the fair value of common stock based upon an analysis of future values for the business, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible forecasted outcomes as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at a non-marketable indication of value for the common stock.
- *Option pricing method.* Under the OPM, shares are valued by creating a series of call options, representing the present value of the expected future returns to the stockholders, with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options.
- *Hybrid return method.* The Hybrid Method is a blended approach using aspects of both the PWERM and OPM, in which the equity value in one of the scenarios is calculated using an OPM.

Based on our stage of development and other relevant factors, for valuations prior to November 2019, we determined that OPM was the most appropriate method for allocating our enterprise value to determine the estimated future fair value of our common stock. Specifically, we use the OPM backsolve method to estimate the fair value of our common stock, which derives the implied equity value for one type of equity security from a contemporaneous transaction involving another type of security, shares of our most recently issued series of convertible preferred stock in this instance. We used the OPM backsolve method because we were at an early stage of development and future liquidity events were difficult to forecast, and we had recently completed relevant third-party financings. We applied a discount for lack of marketability to account for a lack of access to an active public market and a discount for a liquidation scenario in which common stockholders do not receive their return.

Starting in November 2019, we determined that the PWERM was the most appropriate method for determining the fair value of our common stock. Using the PWERM, we determined the common stock fair value based on a probability-weighted present value of certain potential investment returns considering each of the possible forecasted outcomes as well as the rights, privileges and preferences of each of our classes of common stock and convertible preferred stock. We applied a discount back to for lack of marketability to account for a lack of access to an active public market and a discount for a liquidation scenario in which common stockholders do not receive their return.

In addition to considering the third-party valuations of our common stock, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- our stage of development and material risks related to our business;
- the progress of our research and development programs, including their stages of development, and our business strategy;
- the prices at which we sold convertible preferred stock and the superior rights, preferences and privileges of the convertible preferred stock relative to our common stock at the time of each grant;

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- external market conditions affecting the biotechnology industry, and trends within the biotechnology industry;
- the lack of an active public market for our common stock and the likelihood of achieving a liquidity event, such as an initial public offering or a sale of our company taking into consideration prevailing market conditions; and
- the analysis of initial public offerings and the market performance of similar companies in the biopharmaceutical industry, as well as recently completed mergers and acquisitions of peer companies.

The assumptions underlying these valuations represent our board's and management's best estimates, which involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different.

Following the closing of this offering, the fair value of our common stock will be determined based on the quoted market price of our common stock on the date of grant.

Recently issued accounting pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our financial statements appearing at the end of this prospectus.

Emerging growth company status

Section 107 of the JOBS Act permits an "emerging growth company" such as us to take advantage of an extended transition time to comply with new or revised accounting standards as applicable to public companies. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period to enable us to comply with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (1) are no longer an emerging growth company and (2) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than \$1.07 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least \$700 million of equity securities held by non-affiliates; (3) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

Quantitative and qualitative disclosures about market risks

Interest rate risk

As of December 31, 2018, our cash equivalents consisted of interest-bearing money market accounts. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term maturities and the low-risk profile of our investments, an immediate one percentage point relative change in market interest rates would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

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As of December 31, 2018, we had no debt outstanding and are therefore not exposed to interest rate risk with respect to debt.

Foreign currency exchange risk

Our expenses are generally denominated in U.S. dollars. However, we have entered into a limited number of contracts with vendors for research and development services that permit us to satisfy our payment obligations in U.S. dollars (at prevailing exchange rates) but have underlying payment obligations denominated in foreign currencies, including the Euro. We are subject to foreign currency transaction gains or losses on our contracts denominated in foreign currencies. To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not had a formal hedging program with respect to foreign currency. A 10% increase or decrease in current exchange rates would not have a material effect on our financial results for the years ended December 31, 2017 and 2018.

Effects of inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented.

Business

Overview

ORIC Pharmaceuticals is a clinical-stage biopharmaceutical company dedicated to improving patients' lives by *Overcoming Resistance In Cancer*.

Profound advancements in oncology drug development have expanded the treatment options available to patients, yet therapeutic resistance and relapse continue to limit the efficacy and duration of clinical benefit of such treatments. Collectively, our founders and management team have a decades-long heritage of identifying and characterizing resistance mechanisms in oncology, having discovered and developed groundbreaking medicines at companies such as Ignyta, Medivation, Aragon and Genentech.

At ORIC, our fully integrated discovery and development team is advancing a diverse pipeline of innovative therapies designed to counter resistance mechanisms in cancer by leveraging our expertise within three specific areas: hormone-dependent cancers, precision oncology and key tumor dependencies. Our lead product candidate, ORIC-101, builds upon a legacy of successful drug development by our founders in the field of nuclear hormone receptors and their efforts to elucidate the cause of resistance to the groundbreaking prostate cancer therapies that they had developed. ORIC-101 is a potent and selective small molecule antagonist of the glucocorticoid receptor (GR), which has been linked to resistance to multiple classes of cancer therapeutics across a variety of solid tumors. In 2019, we initiated two separate Phase 1b trials of ORIC-101 in combination with (1) Xtandi (enzalutamide) in metastatic prostate cancer and (2) Abraxane (nab-paclitaxel) in advanced or metastatic solid tumors, and we expect to report interim data for one of these trials in the first half of 2021. Our second product candidate, ORIC-533, is an orally bioavailable, potent and selective, small molecule inhibitor of CD73, a key node in the adenosine pathway believed to play a central role in resistance to chemotherapy- and immunotherapy-based treatment regimens. We expect to file an IND for ORIC-533 in 2021. Beyond these two product candidates, we are developing multiple precision medicines targeting other hallmark cancer resistance mechanisms. We believe our team and capabilities uniquely position us to be a leader in developing novel therapies to overcome resistance in cancer.

Cancer resistance continues to be one of the most daunting challenges facing patients, clinicians and researchers in oncology today. A multitude of biological factors and pathways have been linked to resistance, which enables tumors to restore cell growth and survival by circumventing a treatment's intended mechanism of action. Within resistance, we focus on three areas: (1) innate resistance, which derives from an unaddressed oncogenic driver that promotes tumorigenesis; (2) acquired resistance, the result of an induced or enriched oncogenic driver that arises in response to treatment; and (3) bypass resistance, the activation of a compensatory signaling pathway in response to treatment.

We are building a portfolio of novel agents targeting multiple resistance mechanisms by leveraging our specialized expertise in hormone-dependent cancers, precision oncology and key tumor dependencies:

- **Hormone-dependent cancers:** Two of our founders, Drs. Charles Sawyers and Richard Heyman, are leading experts in nuclear hormone receptors and hormone-dependent cancers. They previously co-founded two oncology companies, Aragon (acquired by Johnson & Johnson in 2013) and Seragon (acquired by Roche in 2014), that developed therapeutics targeting two nuclear hormone receptors, the androgen receptor (AR) and estrogen receptor (ER), respectively, the former effort leading to the approved drug Erleada (apalutamide). Our lead product candidate, ORIC-101, while independently developed by ORIC, builds on academic work from Dr. Sawyers' laboratory at Memorial Sloan Kettering Cancer Center (MSKCC) implicating GR as a potential mechanism of resistance to Xtandi (also discovered by Dr. Sawyers and developed by Medivation, which was acquired by Pfizer in 2016) in prostate cancer. Given the breadth of solid tumor

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indications in which hormone signaling pathways have been implicated in driving disease, or in the development of resistance, we believe our differentiated insight into this biology is a crucial component of our future success.

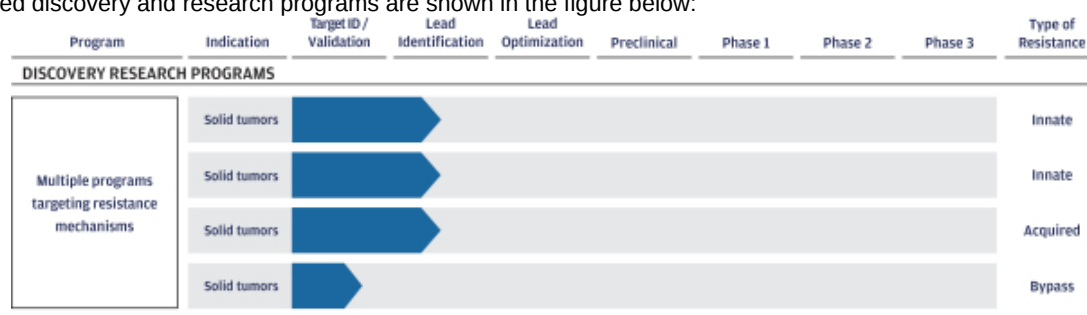
- Precision oncology:** Our precision medicine approach of utilizing biomarkers for demonstration of target and pathway engagement and ultimately for patient selection is rooted in our management team’s prior experience at Ignyta (acquired by Roche in 2018) in successfully developing Rozlytrek (entrectinib), which was approved by the U.S. Food and Drug Administration (FDA) for the treatment of ROS1-positive metastatic non-small cell lung cancer (NSCLC) and neurotrophic tyrosine receptor kinase (NTRK)-positive solid tumors in 2019. Our team’s experience in precision oncology dates back decades, including Dr. Sawyers’ pivotal role in the development of Gleevec (imatinib) and Sprycel (dasatinib). We believe our team’s expertise and experience in precision oncology will allow us to develop drugs with a higher probability of clinical success within biomarker-defined patient populations, while also potentially reducing the time and cost of development.
- Key tumor dependencies:** Key tumor dependencies are abnormal alterations that promote cancer cell growth and survival and also confer specific vulnerabilities that normal cells lack; these cancer-specific dependencies are compelling therapeutic targets. Our scientific team—led by our Chief Scientific Officer, Head of Biology and Head of Translational Medicine—has amassed deep knowledge of key oncogenic drivers and pathways in order to identify and validate oncology targets. They most recently worked together at Genentech, where they progressed more than 20 oncology discovery programs into clinical development, with three approvals to date, including Cotellic (cobimetinib), Zelboraf (vemurafenib) and Polivy (polatuzumab vedotin). Our knowledge of innate, acquired and bypass resistance mechanisms, as well as our in-depth experience in forward and reverse translation, underpins our discovery efforts to identify key drivers of cancer resistance that can be exploited for therapeutic gain. For example, our understanding of innate resistance has led to the discovery of ORIC-533, an orally bioavailable small molecule inhibitor of CD73.

We are leveraging these three areas of expertise to develop innovative therapies targeting the critical cancer resistance mechanisms that we believe will bring the largest benefit to patients, including by making existing therapies more effective for a longer period of time.

Our portfolio currently consists of multiple internally discovered programs targeting key resistance mechanisms. We own full worldwide development and commercialization rights to each of our programs. Our product candidates are shown in the figure below:



Our most advanced discovery and research programs are shown in the figure below:



GR antagonist program: ORIC-101

GR is a nuclear hormone receptor that mediates responses to glucocorticoid hormones involved in regulating a range of cellular functions, such as metabolism, cell growth and differentiation. The original hypothesis for our lead program targeting GR was borne out of work conducted in the laboratory of Dr. Sawyers at MSKCC in search of explanatory factors underlying resistance to anti-androgen prostate cancer therapies, including Xtandi and Erleada. His work demonstrated that GR signaling is a bypass mechanism to anti-androgen therapy, and that increased expression of GR in prostate cancer is correlated with resistance to Xtandi. We and others have shown that, in addition to prostate cancer, GR is also overexpressed across over 20 advanced solid tumors including pancreatic, triple negative breast (TNBC) and ovarian cancers, and that GR overexpression is associated with worse survival outcomes.

Our lead product candidate, ORIC-101, is a potent and selective small molecule GR antagonist designed to inhibit GR transcriptional activity and block pro-survival signals downstream of its activation that confer resistance to anti-androgen therapies and chemotherapies. Since its initial discovery at ORIC, we have rapidly advanced ORIC-101 through preclinical studies that have informed the design of a robust clinical development plan. Following the successful completion of two Phase 1a trials in over 50 healthy volunteers, we initiated in 2019 two separate Phase 1b trials of ORIC-101 in combination with: (1) enzalutamide in metastatic prostate cancer and (2) nab-paclitaxel in advanced or metastatic solid tumors. These trials are intended to establish safety, pharmacokinetics (PK), pharmacodynamics (PD), preliminary anti-tumor activity and a recommended Phase 2 dose of ORIC-101 in combination with each of these therapeutics. We expect to report interim data for one of these Phase 1b trials in the first half of 2021. To help inform which patients may be most suitable for treatment with ORIC-101, we have developed a proprietary immunohistochemistry (IHC) assay that measures GR protein expression levels as well as a proprietary GR gene activation signature that measures GR signaling activity, both of which are being utilized in our ongoing clinical trials and may be used for patient selection in future clinical trials. If either of these approaches proves to be a useful method for patient selection, we expect to incorporate the specific diagnostic test into our registrational studies and partner with the appropriate diagnostic provider to co-develop a companion diagnostic. In general, the FDA expects to review and approve simultaneously NDA and PMA submissions for a therapeutic and its companion diagnostic, respectively, so any delay in diagnostic approval could delay drug approval.

CD73 inhibitor program: ORIC-533

Many cancers usurp the anti-inflammatory adenosine pathway to avoid detection by the immune system, thereby reducing the effectiveness of certain chemotherapy- and immunotherapy-based treatments.

Accumulation of adenosine in the tumor microenvironment is implicated in local immune suppression that leads to tumor proliferation. CD73 is an enzyme that controls the rate at which extracellular adenosine is produced and its overexpression is associated with poor prognosis in several cancers, including TNBC, NSCLC, melanoma and prostate, among others. Several global pharmaceutical companies are developing anti-CD73 antibodies, but due to significant medicinal chemistry challenges, to our knowledge, there are no orally bioavailable inhibitors of CD73 in clinical development. Our second product candidate, ORIC-533, is an orally bioavailable small molecule inhibitor of CD73, which has demonstrated more potent adenosine inhibition *in vitro* compared to an antibody-based approach. We expect to file an IND for ORIC-533 with the FDA in 2021.

Other preclinical programs

We are also developing several therapies targeting other key mechanisms of resistance. For example, we have a program directed to a target that is a potential innate oncogenic driver and also a potential bypass mechanism of resistance in certain cancers. This and other additional programs targeting resistance mechanisms are in various states of preclinical drug discovery and are directed towards a variety of solid tumors with a focus on breast, prostate and lung cancers.

Our team that is Overcoming Resistance In Cancer

We have assembled a management team that has led organizations that have advanced multiple oncology therapeutics from early stage research to clinical trials, and ultimately to regulatory approval and commercialization. Our Chief Executive Officer, Dr. Jacob Chacko, has worked and collaborated with the members of our team for over 25 years collectively prior to ORIC, and multiple team members have worked together previously at Ignyta, Medivation, Aragon, Seragon and Genentech. Our team's select accomplishments include:

- Our Chief Medical Officer and Senior Vice President of Clinical Development previously held the same positions at Ignyta, where they led a global registrational trial that resulted in the approval of Rozlytrek in two indications for genetically defined cancers.
- Our Chief Scientific Officer was most recently the head of translational oncology at Genentech, where her team advanced more than 20 programs into clinical development.
- Our Chief Business Officer, while leading business development at Medivation, identified and led the acquisition of a compound that was subsequently developed and approved as Talzenna (talazoparib).
- Our Chief Financial Officer and our Chief Executive Officer, while previously CFOs at two separate publicly traded companies, led over \$1 billion in capital raises.
- Our management team has been involved in several multibillion-dollar strategic transactions, including as part of the leadership teams at Ignyta and Medivation.

We are supported by our founders who have discovered and developed multiple innovative cancer treatments and have successfully collaborated prior to founding ORIC. Drs. Sawyers and Heyman, leading experts in cancer resistance and nuclear hormone receptors, co-founded Aragon and Seragon, which developed therapeutics focused on AR and ER, respectively, the former effort leading to the approved drug Erleada. Dr. Sawyers was also involved in the discovery of Xtandi and is an expert in precision medicine, having played a key role in the development of Gleevec and Sprycel. Our third co-founder, Scott Lowe, Ph.D., is a colleague of Dr. Sawyers at MSKCC and an expert in tumor networks and molecular determinants of treatment response. Our founders are currently active scientific advisors to ORIC and Dr. Heyman is a member of our board of directors. All of our founders are equity holders of ORIC, Drs. Sawyers and Lowe receive compensation as scientific advisors, and Dr. Heyman receives compensation as a board member. Although they are regularly available for scientific

consultation, our arrangements with these individuals do not entitle us to any of their existing or future intellectual property derived from their independent research or research with other third parties beyond what has previously been licensed to us.

In addition, we have assembled a scientific advisory board that, in addition to our founders, includes Dr. Richard Scheller, who was previously Chief Scientific Officer of Genentech, and Dr. Larry Lasky, who was previously one of only three Research Fellows in Genentech's history. We are also supported by our syndicate of leading investors, including The Column Group, Topspin, OrbiMed, EcoR1, Fidelity Management, ArrowMark Partners, Invus, Foresite and Casdin Capital, among others.

Our strategy

Our goal is to discover, develop and commercialize innovative therapies that overcome resistance in cancer. The key elements of our business strategy to achieve this goal include:

- **Leveraging the insights, experience and networks of our founders and management team.** Our founders and management team have extensive experience identifying, discovering, developing and commercializing innovative cancer therapeutics aimed at novel targets, including Rozlytrek, Erleada, Talzenna, Xtandi, Sprycel and Gleevec. We are using this broad oncology experience together with our internal discovery and development capabilities to build a diverse pipeline of therapies targeting multiple cancer resistance mechanisms. For example, our lead product candidate, ORIC-101, while independently developed by ORIC, builds on academic work originally conducted by the laboratory of Dr. Sawyers at MSKCC.
- **Advancing our lead product candidate, ORIC-101, as rapidly as possible through clinical development by exploring rational combinations across multiple tumor types.** The GR signaling pathway has been implicated in resistance to anti-androgen therapies in prostate cancer as well as chemotherapy regimens in other advanced solid tumor indications. Our clinical development effort for ORIC-101, an internally developed potent and selective small molecule antagonist of GR, will initially focus on indications where there is evidence suggesting GR-mediated signaling contributes to resistance and disease progression. In 2019, we initiated two separate Phase 1b trials of ORIC-101 in combination with (1) enzalutamide in metastatic prostate cancer and (2) nab-paclitaxel in advanced or metastatic solid tumors, and we expect to report interim data for one of these trials in the first half of 2021. Where possible, we plan to pursue accelerated development strategies in areas of high unmet need.
- **Building the leading, fully-integrated company focused on delivering innovative medicines that aim to overcome resistance in cancer.** As of December 13, 2019, we had 57 full-time employees, including world-class discovery, preclinical and clinical development teams, encompassing all major functions necessary to take a molecule from target identification through registrational clinical trials. Together, they bring in-house expertise in medicinal chemistry, biology, translational medicine, computational chemistry, *in vitro* and *in vivo* pharmacology, computational biology, biomarker development and CMC. We have also established internal expertise in clinical development, clinical operations, pharmacovigilance, clinical pharmacology, regulatory and quality. The members of our research and development organization have collectively led and contributed to dozens of IND filings and multiple drug approvals in oncology. These internal capabilities led to the discovery and clinical development of our first product candidate and will enable us to continue to expand and advance our portfolio of additional product candidates.
- **Continuing to expand our portfolio of product candidates through both internal research activities and business development efforts.** Our second internally-generated product candidate, ORIC-533, is an orally bioavailable small molecule inhibitor of CD73. We expect to file an IND for ORIC-533 with the FDA in 2021. We

also continue to advance our other internally generated programs as well as expand our pipeline through internal discovery activities. Simultaneously, we believe that accessing external innovation and expertise is important to our success and plan to leverage our leadership team's prior business development experience as we evaluate potential in-licensing and acquisition opportunities to further expand our portfolio. We aim to be the partner of choice for academic groups and companies in the field of cancer resistance.

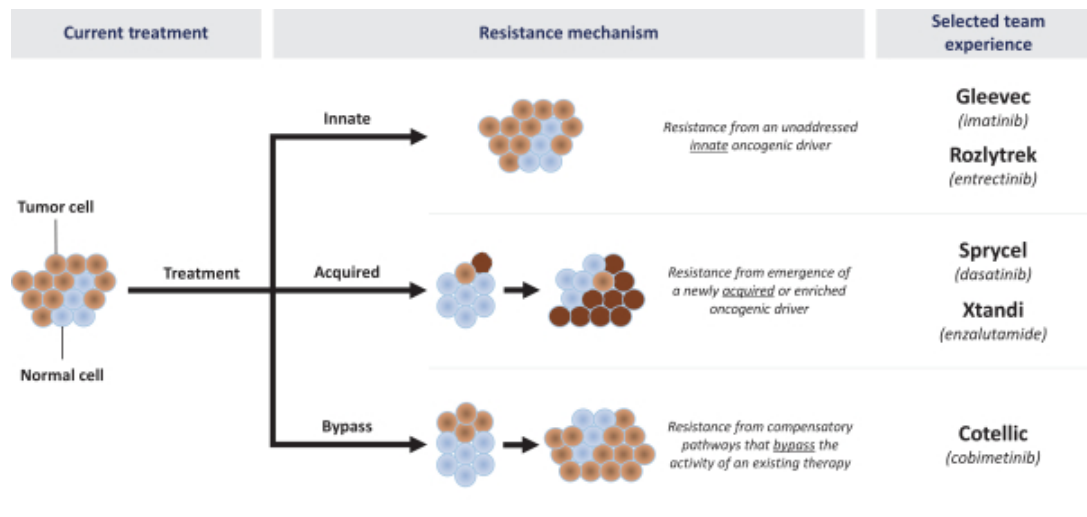
- **Utilizing a precision medicine approach in the development of each of our product candidates.** We use biomarkers to demonstrate target and pathway engagement and plan to use them for patient selection in our clinical trials. This approach is rooted in our team's prior experiences developing targeted therapies, such as Rozlytrek, an orally bioavailable, tyrosine kinase inhibitor approved for select tumors that harbor ROS1 or NTRK fusions. We seek to design rigorous and cost-efficient clinical programs that increase the probability of success by exploring connections between cellular-level biology and patient-level clinical outcomes. The use of biomarker-based patient selection is designed to enable demonstration of clinical proof-of-concept earlier and with fewer patients, leading ultimately to smaller pivotal trials. As part of our strategy, our in-house team of experienced translational scientists and computational biologists leverages existing technologies as well as develops proprietary assays to enable the selection and assessment of biomarkers for each of our programs. For ORIC-101, we have developed a proprietary IHC assay that measures GR protein expression levels as well as a proprietary GR gene activation signature that measures GR signaling activity. Both of these assays are being utilized in our two ongoing Phase 1b clinical trials of ORIC-101.
- **Evaluating opportunities to accelerate development timelines and enhance the commercial potential of our programs in collaboration with third parties.** We own full worldwide development and commercialization rights to each of our programs. We have established collaborations and intend to continue evaluating opportunities to work with partners that meaningfully enhance our capabilities with respect to the development and commercialization of our product candidates. For example, for our Phase 1b trial of ORIC-101 in combination with enzalutamide in prostate cancer, we have entered into a clinical trial collaboration and supply agreement with Astellas. In addition, we intend to commercialize our product candidates in key markets either alone or with partners in order to maximize the worldwide commercial potential of our programs.

Background on cancer resistance

Cancer resistance continues to be one of the most daunting challenges facing patients, clinicians and researchers in oncology today. A multitude of biological factors and pathways have been linked to resistance, which enables tumors to restore cell growth and survival by circumventing a treatment's intended mechanism of action. Furthermore, treatment resistance in cancer emerges irrespective of therapeutic class, including targeted therapy, hormone therapy, immunotherapy and chemotherapy.

Within resistance, we focus on three areas: (1) innate resistance, which derives from an unaddressed oncogenic driver that promotes tumorigenesis; (2) acquired resistance, the result of an induced or enriched oncogenic driver that arises in response to treatment; and (3) bypass resistance, the activation of a compensatory signaling pathway in response to treatment.

Overview of key resistance mechanisms and ORIC team's prior relevant experience



- Innate resistance** occurs when a key tumor dependency is not addressed, such as a driver mutation with no available targeted therapeutic. A recent example of a drug targeting innate resistance is Rozlytrek, developed by Ignyta for patients with ROS1-positive, metastatic NSCLC and NTRK gene fusion-positive solid tumors. We believe these innate resistance targets have a higher probability of technical success than other cancer targets, hold potential for meaningful clinical outcomes, and have the potential for rapid clinical development and approval timelines. Innate resistance targets have been the subject of a number of targeted therapies that have been approved over the past couple of decades. Studies have shown that treatments that target and inhibit unaddressed driver mutations have high response rates with generally good durability, including in a resistant setting. This efficacy in a refractory patient population in turn has been shown to enable a shorter development pathway, with many such agents being approved based upon single arm trials of modest size. New advances in small molecule drug discovery have created an opportunity to better target next-generation oncogenic drivers. Our pipeline includes several programs targeting innate resistance, including our orally bioavailable small molecule CD73 inhibitor, ORIC-533, which we designed to address adenosine-driven innate resistance to chemotherapy- and immunotherapy-based treatment regimens.
- Acquired resistance** arises in response to treatment resulting in a newly acquired or enriched oncogenic driver. Genomic changes in the therapeutic target, such as DNA mutation or amplification, can be evolutionarily selected to propel proliferation in heterogeneous tumors or may be acquired through the course of the disease. Specific changes in the target itself often result in loss of potency of the initial therapeutic. An example of acquired resistance is seen in chronic myeloid leukemia (CML) treated with the first-generation BCR-ABL inhibitor Gleevec, with resistance frequently driven by mutations in BCR-ABL that lead to loss of Gleevec binding activity. The second-generation BCR-ABL inhibitor Sprycel was developed to specifically address acquired resistance to Gleevec, with our co-founder, Dr. Sawyers, playing a critical role in the development of both therapeutics. Our pipeline includes one preclinical program and several ongoing discovery efforts directed towards targets for acquired resistance in solid tumors.
- Bypass resistance** occurs when a therapeutically targeted cancer pathway is reactivated in cells to compensate for the presence of a therapeutic. Targeted therapies that induce reactivation of the same pathway indicate a key dependence on that specific pathway for tumor growth and survival. Similar to GR,

this key dependency concept is illustrated in the context of BRAF mutant melanoma. Mutations in the BRAF kinase allow for unrestricted signaling of the protein that is required for tumor growth and survival. Discovery of small molecule BRAF inhibitors led to significant reduction of tumor growth and improvement of melanoma patient survival, as the innate resistance was addressed. However, following the initial profound responses observed in patients, patients began relapsing. Mechanistic exploration into the basis of patient progression revealed that some tumors were evolving to reactivate the same pathway further downstream, as the tumors compensated for the BRAF therapeutic. The development of Cotellic to target MEK further downstream in this pathway overcame the bypass mechanism and significantly improved patient outcomes.

Collectively, our team has spent decades identifying and characterizing resistance mechanisms and has a strong heritage of bringing forth new and improved therapies designed to exploit resistance biology from the research lab to the clinic and, ultimately, to patients in need.

Our areas of focus within cancer resistance

Our vision for patients with cancer is that therapeutics specifically addressing resistance will provide durable treatment responses, such that solid tumors can become a chronic disease with patient survival measured in years rather than months. Within the broader resistance landscape, we have specialized expertise in hormone-dependent cancers, precision oncology and key tumor dependencies, areas in which we have focused our internal discovery and external business development efforts.

Hormone-dependent cancers

Two of our founders, Drs. Sawyers and Heyman, are leading experts in nuclear hormone receptors and hormone-dependent cancers. They previously co-founded two oncology companies, Aragon and Seragon, that developed therapeutics targeting two nuclear hormone receptors, AR and ER, respectively. Following the acquisitions of Aragon—whose lead product, Erleada, was ultimately approved for prostate cancer—and Seragon, and built upon academic work from Dr. Sawyers' laboratory at MSKCC implicating GR as a potential mechanism of resistance to Xtandi (also discovered by Dr. Sawyers) in prostate cancer, Drs. Sawyers and Heyman conceived of ORIC and proposed GR as our first target of interest.

The nuclear hormone receptor gene family is a therapeutically rich target class implicated in a broad range of human diseases. Within this family, AR and ER are among the best-known targets that have resulted in a number of approved oncology therapies. ER has been implicated in breast and endometrial cancers, for which Nolvadex (tamoxifen) and Faslodex (fulvestrant) have been approved for breast cancer. Similarly, AR has been implicated in prostate cancer, for which Casodex (bicalutamide), Xtandi, Erleada and Nubeqa (darolutamide) have been approved.

A third member of this family is GR, which is encoded by the NR3C1 (nuclear receptor subfamily 3, group C, member 1) gene and is a nuclear hormone receptor to which cortisol and other glucocorticoids bind. When glucocorticoids bind to GR, its primary mechanism of action is translocation into the nucleus and regulation of gene transcription. GR is expressed in almost every cell in the body and regulates genes controlling metabolism, cell growth, inflammation, apoptosis and differentiation. Because the receptor gene is expressed in several forms, it has many different (pleiotropic) effects in different parts of the body.

There is substantial *in vitro*, *in vivo* and clinical evidence that GR signaling allows certain solid tumors to resist treatment. In some cancers GR signaling promotes tumor growth, while in others it stimulates genes that protect from cell death. Many types of solid tumors overexpress GR and are potential targets for ORIC-101, including prostate, pancreatic, ovarian, TNBC and endometrial cancers, among others.

Given the breadth of solid tumor indications in which hormone signaling pathways have been implicated in driving disease, or in the development of resistance, we believe our differentiated insight into this biology is a crucial component of our future success.

Precision oncology (biomarker-driven, patient-selected trials)

Our clinical development team—including our Chief Medical Officer, Head of Clinical Development and heads of five core functions—previously worked together with our Chief Executive Officer at Ignyta, an oncology company that developed a pipeline of precision therapies, including Rozlytrek, which is now approved by the FDA in two different indications for genetically defined tumors, ROS1-positive metastatic NSCLC and NTRK-positive solid tumors. The clinical development of Rozlytrek, which was largely driven by this team, relied upon biomarker-driven patient selection via a companion diagnostic, leading to the approval of the compound approximately five years after it first entered the clinic.

The Rozlytrek and Ignyta experience can be seen as a paradigm for precision oncology, in which the identification of biomarkers forms the basis of the entire drug discovery and development process, from early understandings of PK and PD modulation of target biology through to appropriate patient selection during clinical development. As part of our strategy, our in-house team of experienced translational scientists and computational biologists utilize existing technologies as well as develop proprietary assays to enable the selection and assessment of biomarkers for each of our programs. We seek to design rigorous and cost-efficient clinical programs that increase the probability of success by exploring connections between cellular-level biology and patient-level clinical outcomes. The use of biomarker-based patient selection is designed to enable demonstration of clinical proof-of-concept earlier and with fewer patients, leading ultimately to smaller pivotal trials.

Our emphasis on a precision oncology approach to the mechanisms that underlie cancer resistance enables us to develop biological methods and assays that can be employed in the selection of appropriate patients for our development candidates rather than relying solely on limited clinical diagnosis information. For example, like many cancers, prostate cancer is a heterogeneous disease with different pathways contributing to potential resistance mechanisms to anti-androgen therapy that may vary from patient to patient or evolve over the course of a patient's treatment history. In this complex resistance landscape, measuring levels of GR expression or gene activity represent potential strategies for selecting patients whose tumors are susceptible to GR inhibition through ORIC-101 therapy, enabling the possibility of identifying a subset of patients more likely to benefit from ORIC-101. To this end, we have developed a proprietary IHC assay that measures GR protein expression levels as well as a proprietary GR gene activation signature that measures GR signaling activity. Both of these assays are being utilized in our two ongoing Phase 1b clinical trials for ORIC-101. We intend to apply a similar precision oncology approach to the advancement of our entire pipeline.

Key tumor dependencies

Our scientific team—led by our Chief Scientific Officer, Head of Biology and Head of Translational Medicine—has amassed deep knowledge of key oncogenic drivers and pathways in order to identify and validate oncology targets. They most recently worked together at Genentech, where they progressed more than 20 oncology discovery programs into clinical development, with three approvals to date, including Cotellic, Zelboraf and Polivy. The team's approach to uncovering tumor dependencies that are key drivers of cancer resistance is biology-focused and mechanistically-driven.

Tumors are dependent on distinct biological drivers, or key tumor dependencies, which can be exploited to develop therapeutics. Examples of key tumor dependencies include oncogenic drivers, metabolic dependencies

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and lineage-specific markers. The earliest known tumor dependency occurs after normal cells acquire mutations that initiate tumor development. These early lesions continuously evolve within a given tissue in the presence of other cell types, such as endothelial and immune cells, ultimately generating a heterogeneous tumor ecosystem. The interplay between tumor cells and other heterologous cell types within a tissue impart physiological restrictions, such as limited oxygen or increased acidity, that tumor cells are forced to withstand to enable growth. This concept of evolution under selective pressure also applies in the context of an advanced tumor being subjected to therapeutic interventions—the relapsing tumors are forced to adapt in order to grow in the presence of treatment. Through these evolutionary processes, tumor cells can become exclusively dependent on distinct pathways, and these are the key dependencies that can be exploited for therapeutic gain.

Our understanding of key tumor dependencies has also led to the development of an orally bioavailable small molecule inhibitor of CD73, ORIC-533, that targets adenosine within a key metabolic pathway upon which tumors become dependent. Many cancers usurp the anti-inflammatory adenosine pathway to avoid detection by the immune system, thereby reducing the effectiveness of certain chemotherapy and immunotherapy-based treatments. Accumulation of adenosine in the tumor microenvironment is implicated in local immune suppression that leads to tumor proliferation. CD73 is an enzyme that controls the rate at which extracellular adenosine is produced and its overexpression is associated with poor prognosis in several cancers, including TNBC, NSCLC, melanoma and prostate, among others. In addition to our GR and CD73 programs, we are developing multiple programs focused on addressing key dependencies in solid tumors, defined as either unaddressed drivers of innate resistance, acquired mutations or bypass mechanisms that cause relapse.

Our knowledge of resistance mechanisms as well as in-depth experience in forward and reverse translation underpins our discovery efforts to identify key drivers of cancer resistance.

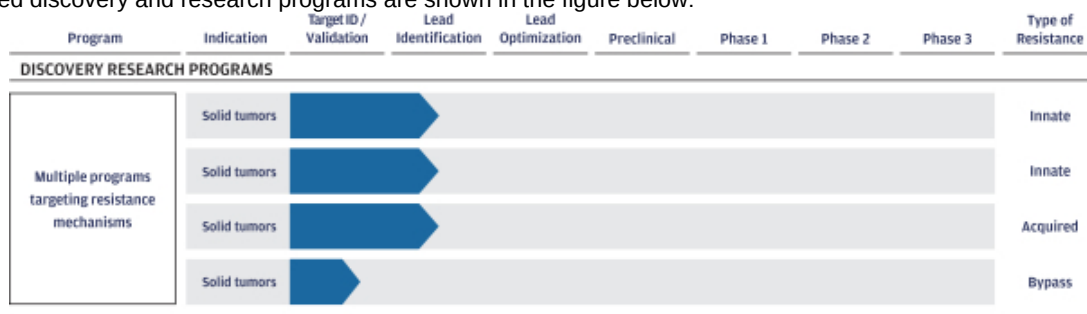
Our pipeline to treat cancer resistance

Our portfolio currently consists of multiple internally discovered programs targeting key resistance mechanisms. We own full worldwide development and commercialization rights to each of our programs. Our product candidates are shown in the figure below:



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Our most advanced discovery and research programs are shown in the figure below:



GR antagonist program: ORIC-101

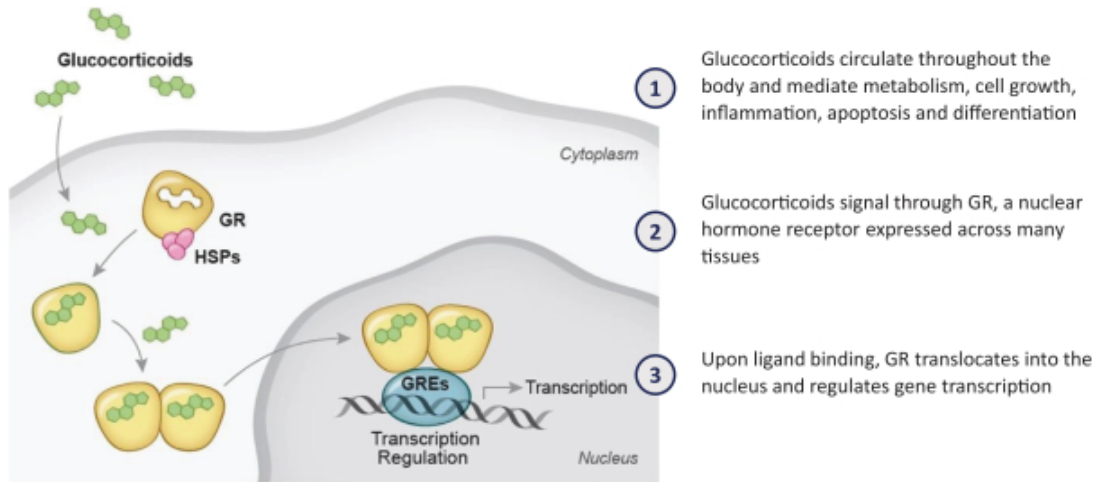
Our lead product candidate, ORIC-101, builds upon a legacy of successful drug development by our founders in the field of nuclear hormone receptors and their efforts to elucidate the cause of resistance to the groundbreaking prostate cancer therapies that they had developed. ORIC-101 is a potent and selective small molecule GR antagonist designed to inhibit GR transcriptional activity and block pro-survival signals downstream of its activation that confer resistance to anti-androgen therapies and chemotherapies. Following the successful completion of two Phase 1a trials in over 50 healthy volunteers, in 2019 we initiated two separate Phase 1b trials of ORIC-101 in combination with:

- (1) enzalutamide in metastatic prostate cancer and
- (2) nab-paclitaxel in advanced or metastatic solid tumors. We expect to report interim data for one of these trials in the first half of 2021.

Glucocorticoid receptor background

Glucocorticoids are steroid hormones secreted by the adrenal gland in a circadian and stress-associated manner to regulate metabolism, cell growth, apoptosis, differentiation and inflammation. Glucocorticoids signal through GR, a member of the superfamily of nuclear receptors expressed across a wide variety of tissues. Upon ligand binding, GR undergoes nuclear translocation, which is shown in the figure below. In the nucleus, GR binds to glucocorticoid response elements on DNA and transcriptionally activates a spectrum of genes that mediate multiple biological effects.

Glucocorticoid receptor signaling mediates multiple physiological processes

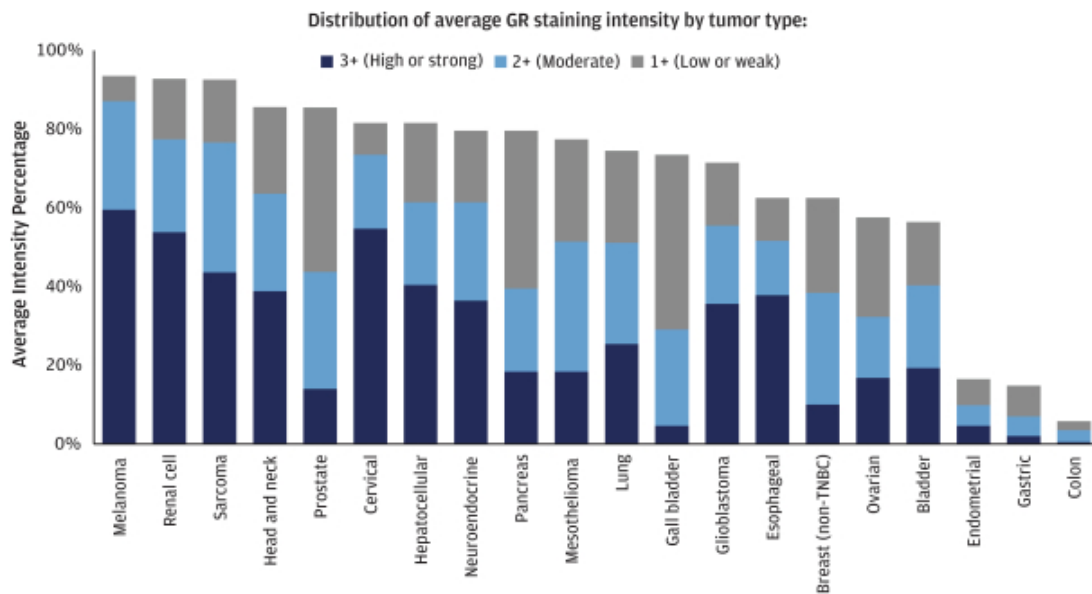


Note: GR: glucocorticoid receptor. HSPs: heat shock proteins. GREs: glucocorticoid response elements.

The glucocorticoid receptor as a mechanism of resistance

Multiple preclinical studies have implicated GR activation as a potential cause of cancer treatment resistance in cancers of epithelial origin. Dr. Sawyers' work has demonstrated that GR signaling is a bypass mechanism to anti-androgen therapy and that increased expression of GR in prostate cancer is correlated with resistance to Xtandi. We and others have shown that, in addition to prostate cancer, GR is also overexpressed across over 20 advanced solid tumors, including pancreatic, TNBC and ovarian cancers, which is shown in the figure below, and that GR overexpression is associated with worse survival outcomes.

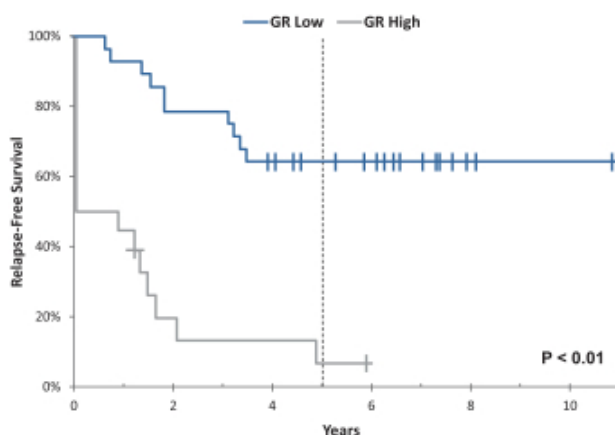
GR is overexpressed in solid tumors



Source: Block et al. Cancer Management and Research (2017). Melanoma n=11, Renal n=10, Sarcoma n=14, Neck and head n=10, Prostate n=11, Cervical n=15, Hepatocellular n=10, Neuroendocrine n=11, Pancreas n=16, Lung n=17, Gall bladder n=10, Esophageal n=8, Breast (non-TNBC) n=10, Ovarian n=11, Bladder n=10, Endometrial n=13, Gastric n=11, and Colon n=16.

In addition, overexpression of GR has been correlated with poor prognosis in patients with ER-negative breast cancer treated with chemotherapy, which is shown in the figure below, metastatic castration-resistant prostate cancer (mCRPC) treated with Xtandi and advanced endometrial cancer.

High GR expression associated with worse clinical outcomes in patients with ER-negative breast cancer treated with chemotherapy



Source: Pan et al. Clin Cancer Res (2011).

Note: ER: estrogen receptor; GR: glucocorticoid receptor. Tumors in the top quartile of NR3C1 expression were identified as “GR high” (n=18) whereas tumors in the bottom quartile of NR3C1 expression were identified as “GR low” (n=28); post-adjuvant chemotherapy.

P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.01 or less represents statistical significance, meaning there is a less than 1-in-100 likelihood that the observed result occurred by chance.

The FDA utilizes statistical significance, as measured by p-value, as an evidentiary standard of efficacy and typically requires a p-value of 0.05 or less to demonstrate statistical significance.

Limitations of other GR antagonists

Preclinical studies performed in TNBC and ovarian cancer models have helped to establish that genetic ablation or pharmacologic inhibition of GR enhances chemotherapy response. We are aware of only one other company, Corcept Therapeutics, developing GR antagonists for oncology. Corcept has compounds, including mifepristone and relacorilant, that are either approved or being evaluated in clinical trials for endocrine disorders and are also being evaluated in clinical trials for their potential to reverse oncology resistance.

Korlym (mifepristone) is a steroidal GR antagonist approved by the FDA in 2012 for the treatment of patients with Cushing’s syndrome, a disease characterized by elevated levels of the glucocorticoid cortisol. Mifepristone has been broadly used preclinically as a pharmacologic inhibitor of GR to examine the impact of modulation of GR on response to anti-cancer agents. Mifepristone has also been studied in multiple clinical trials across a variety of solid tumors and therapeutic regimens. Clinical trials of mifepristone were initiated in mCRPC, where the standard of care is AR antagonism, but mifepristone has since been shown to be a potent AR agonist and is therefore not expected to be a suitable treatment for mCRPC. Its potential as a combination therapy in oncology is further limited by its significant interactions with cytochrome P450 (CYP), most notably with CYP2C8, which is a key metabolic pathway for both taxanes (a major chemotherapeutic class used across multiple solid tumors) and Xtandi, and thus creates the potential for drug-drug interactions.

Relacorilant, currently in a Phase 3 trial for Cushing’s syndrome, is a non-steroidal GR antagonist that lacks the AR agonism of mifepristone. However, it retains the CYP liabilities of mifepristone, making combination development in oncology challenging. Despite these drawbacks, it is being developed in multiple oncology indications and has shown promising initial signs of durable clinical benefit in combination with nab-paclitaxel in pancreatic ductal adenocarcinoma, ovarian cancer and other advanced or metastatic solid tumors.

ORIC-101 differentiation

ORIC-101 is a highly potent and selective steroidal GR antagonist, as shown by the single-digit nanomolar inhibition for receptor binding in the figure below. Like relacorilant, ORIC-101 is not an AR agonist. However, unlike relacorilant, we expect ORIC-101 to have reduced CYP2C8 inhibition based on our preclinical studies. While certain ORIC-101 metabolites inhibit CYP2C8, they represent a fraction of the plasma exposure of the parent ORIC-101 compound. Thus, we believe ORIC-101 has the potential to enable potent GR inhibition but with less potential risk for drug-drug interaction with other combination agents, most notably taxanes and Xtandi.

ORIC-101 is a potent and selective GR antagonist designed for oncology

	Mifepristone (steroidal)	Relacorilant (non-steroidal)	ORIC-101 (steroidal)
GR antagonism IC ₅₀ (nM)	2.9	16	7.3
AR agonism IC ₅₀ (nM)	25	>2500	>2500
PR antagonism IC ₅₀ (nM)	0.4	>2500	22
CYP inhibition IC ₅₀ (nM)	Inhibitor of CYP2C8, CYP2C9 and CYP3A4	Inhibitor of CYP2C8, CYP2C9 and CYP3A4	Inhibitor of CYP3A4

■	Less favorable than ORIC-101
■	More favorable than ORIC-101

Note: GR: glucocorticoid receptor; AR: androgen receptor; PR: progesterone receptor. GR antagonism, AR antagonism and PR antagonism measured by luciferase assay.

The above table demonstrates the results of a series of preclinical *in vitro* experiments that we conducted evaluating ORIC-101, mifepristone and relacorilant across a variety of properties that we believe to be important in developing a potent and selective GR antagonist. The determination of more favorable or less favorable relates to the ideal properties of a GR antagonist for a combination therapy in oncology.

In these experiments, we employed luciferase reporter assays to measure antagonist and agonist activities of the molecules on GR, AR and PR. These assays are commonly used in *in vitro* experiments to measure the potency of molecules for nuclear hormone receptor targets such as GR, AR and PR (among other receptors). These assays have been well characterized in peer-reviewed scientific publications and are widely utilized in the scientific community.

The endpoints of these preclinical *in vitro* experiments were the half maximal inhibitory concentration (IC₅₀). The IC₅₀ value represents the concentration of molecule needed to inhibit activity by 50% (i.e., a lower IC₅₀ represents more potent inhibition). Cells were treated in the studies for 20 hours. Each molecule was compared against the other molecules.

In these preclinical *in vitro* experiments, mifepristone was shown to be a potent AR agonist, while ORIC-101 and relacorilant were not. AR agonism is commonly accepted to be an undesirable feature of a potential cancer treatment as this activity has been shown to stimulate the growth of prostate cancer. Since ORIC-101 is not an AR agonist, it was shown that mifepristone is less favorable than ORIC-101 with respect to this criterion.

In these experiments, relacorilant was shown to not be a PR antagonist, while mifepristone and ORIC-101 were shown to be PR antagonists. Since PR antagonism is not a required feature of a GR antagonist, it was shown that relacorilant is more favorable than ORIC-101 with respect to this criterion.

In addition, we used a common *in vitro* experiment that is accepted by Health Authorities to evaluate potential drug interaction liability mediated by CYP inhibition. Preclinical *in vitro* experiments were used to determine direct inhibition of major cytochrome P450 (CYP) activity including CYP2C8, CYP2C9, CYP2C19 and CYP3A4/5 by ORIC-101 in human liver microsomes. The endpoint of this preclinical *in vitro* experiment was IC₅₀. The IC₅₀ value represents the drug concentration needed to inhibit the activity of a specific CYP isoform to metabolize its corresponding probe substrate by 50% (i.e., a lower IC₅₀ represents more potent inhibition). The incubation was carried out for five minutes, which was within the linear range of metabolite formation of the probe substrates.

In these preclinical *in vitro* experiments to show CYP inhibition, ORIC-101 directly inhibited CYP3A4/5 with IC₅₀ value of 1.6 μM. IC₅₀ inhibition against CYP2C8 and CYP2C9 could not be determined via mathematical analysis as they were higher than 3 μM and >10 μM, respectively. In contrast, mifepristone directly inhibited CYP2C8, CYP2C9 and CYP3A4/5, with IC₅₀ values of 1.5, 4.9 and 9.5 μM, respectively; whereas, relacorilant directly inhibited CYP2C8, CYP2C9 and CYP3A4/5, with IC₅₀ values of 0.21, 2 and 1.3 μM, respectively. These data suggest that *in vitro*, while ORIC-101 inhibits CYP3A4/5, ORIC-101 exhibited improved properties against CYP2C8 and CYP2C9 compared with mifepristone and relacorilant.

Our current opportunities for ORIC-101

Resistance to hormone therapy in prostate cancer

We have chosen GR antagonism in prostate cancer as our initial therapeutic focus due to the well-documented biology of GR signaling as the principal driver of resistance to Xtandi in patients with prostate cancer, as published in *Cell* by our co-founder Dr. Sawyers. His work demonstrated that GR signaling is a bypass mechanism to anti-androgen therapy and that increased expression of GR in prostate cancer is correlated with resistance to Xtandi. We have demonstrated in preclinical prostate cancer models that GR antagonism can limit bypass resistance to Xtandi. Based on these data, we believe that ORIC-101, in combination with current standard-of-care agents such as Xtandi, has the potential to significantly improve clinical outcomes.

Prostate cancer overview

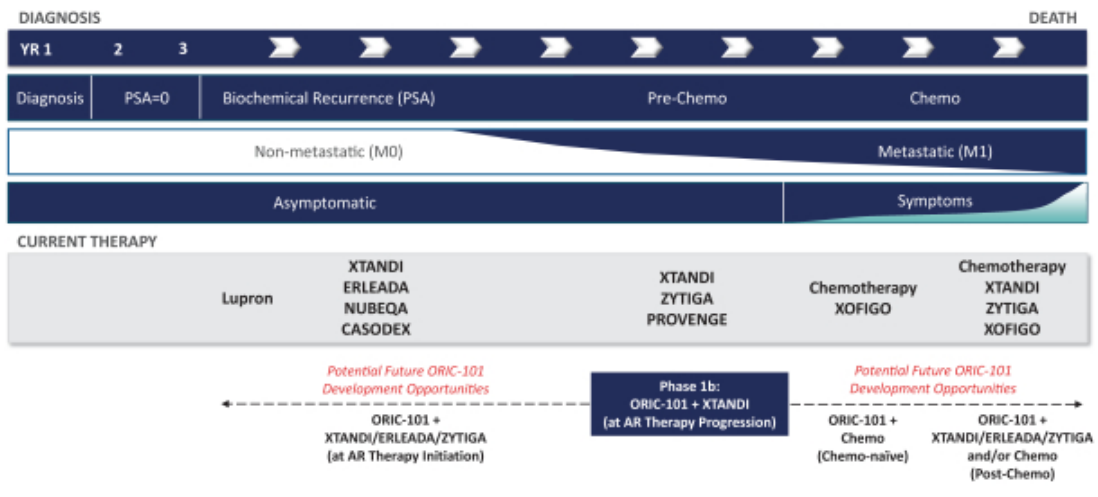
In the United States, prostate cancer is the second most prevalent cancer in men and the second leading cause of cancer death in men. The American Cancer Society estimated that in 2019 there would be approximately 175,000 new cases of prostate cancer and over 30,000 deaths from the disease in the United States by year end. Further, according to another study, over 50,000 new cases of metastatic prostate cancer are expected in 2020, which includes patients with both hormone-sensitive prostate cancer and mCRPC.

Treatment options for prostate cancer depend on many different factors, including the stage of the cancer. The disease is considered metastatic once the cancer has spread outside of the prostate gland to other parts of the body, such as the bones, lymph nodes, bladder and rectum. Tumors are considered hormone- (or castration-) sensitive if they still respond to medical or surgical treatment to lower testosterone levels. Tumors are considered castration-resistant if they progress despite androgen deprivation therapy (ADT), which is often correlated with rising levels of prostate-specific antigen (PSA).

In making treatment evaluations, physicians monitor disease burden in several ways, including changes in PSA levels. Increased PSA blood levels are considered by many physicians as indicative of cancer progression and alternative treatment options may be considered at that time. Current standard of care treatment for men with castration-resistant prostate cancer provides that patients should initially receive a combination of ADT and either Zytiga (abiraterone), which works by decreasing androgen levels, or Xtandi, which works by blocking androgen binding to AR. If the disease progresses despite these second-generation hormonal therapies, chemotherapy is typically the next treatment option. However, treatment with chemotherapy is generally postponed for as long as possible due to the potential for severe side effects including neuropathies, nausea, diarrhea, decreased mental capacity and increased risk of infections.

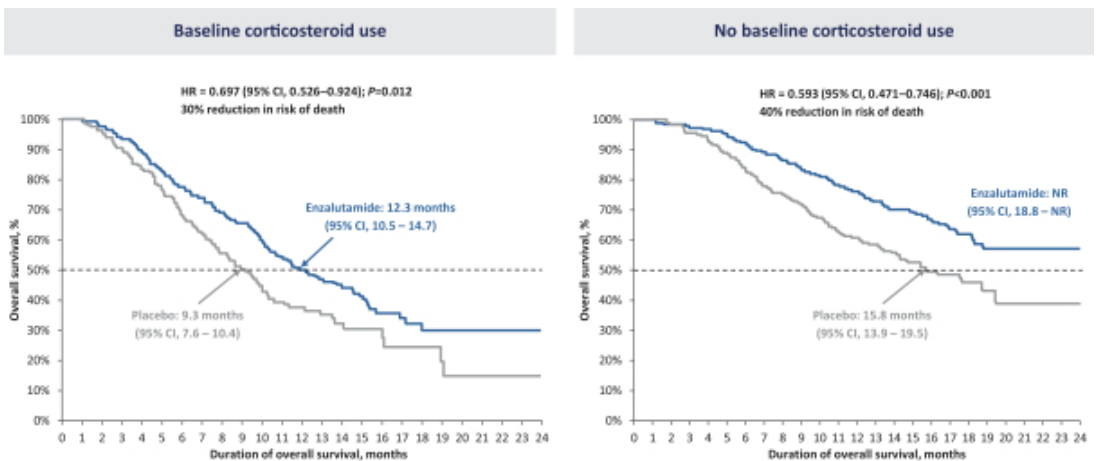
AR remains the principal driver of castration-resistant prostate cancer progression during the transition from localized to metastatic disease. While a majority of patients with prostate cancer will initially respond to either Zytiga, Xtandi or Erleada, the vast majority of these patients will ultimately become resistant, resulting in limited survival. Based on our preclinical data, we believe ORIC-101 may overcome a key resistance mechanism to these therapies and lead to meaningful clinical benefit for patients with prostate cancer.

Illustrative prostate cancer treatment landscape



An investigator analysis of Medivation’s Phase 3 clinical trial AFFIRM, in which patients with mCRPC who had previously received docetaxel were randomized to receive enzalutamide or a placebo, highlighted the potential role of GR in mediating enzalutamide resistance. A post-hoc analysis evaluated the impact of baseline corticosteroid use on clinical outcomes. Thirty percent of patients in this 1,199-patient trial were on corticosteroids at baseline. The results demonstrated that patients on baseline corticosteroids (i.e., GR agonism) had faster time to PSA progression and decreased overall survival when adjusted for other prognostic factors (e.g., age, performance status, prior therapy, disease burden, comorbidities).

Association of corticosteroid use and inferior clinical outcomes observed in Medivation’s Phase 3 AFFIRM study in mCRPC patients treated with enzalutamide



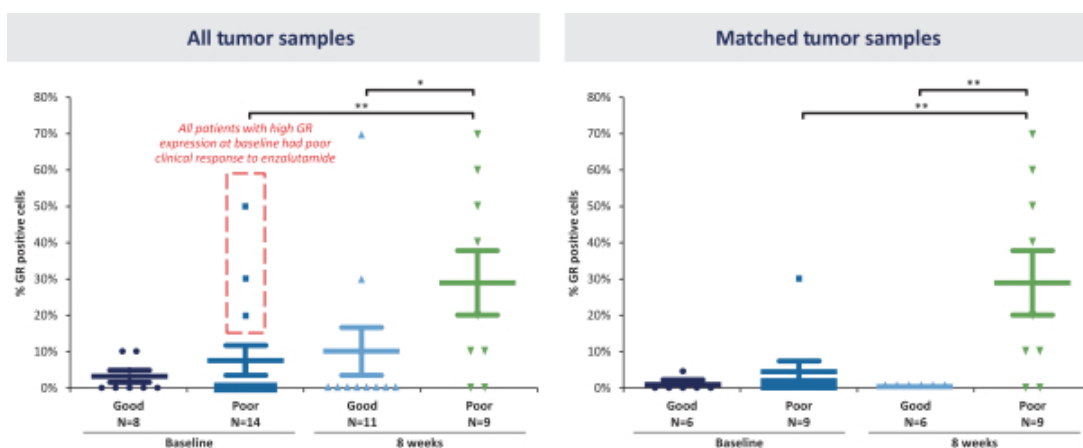
Source: Scher et al. ESMO (2012).

Note: NR: not reached; mCRPC: metastatic castration-resistant prostate cancer. 241 patients on enzalutamide and 119 patients on placebo.

Preclinical data

Several mechanisms of resistance to AR antagonists have been identified that are based on abnormalities in AR and its signaling. Dr. Sawyers' laboratory at MSKCC identified GR expression as a potential resistance mechanism bypassing AR altogether. As shown in the figure below, a retrospective analysis was conducted on tumor biopsies collected from mCRPC patients who were bifurcated into two groups: "good" responders to enzalutamide (experiencing clinical benefit for greater than six months) and "poor" responders to enzalutamide (experiencing clinical benefit for less than six months). GR expression levels were evaluated at baseline prior to the start of and after eight weeks of enzalutamide therapy. This analysis demonstrated a correlation between overexpression of GR and poor clinical outcomes. Patients with a "poor" response to enzalutamide demonstrated relatively higher GR expression levels at baseline as compared to "good" responders. Furthermore, "poor" responders demonstrated significantly higher GR expression levels after eight weeks on enzalutamide as compared to both: (1) the GR expression levels of "poor" responders at baseline, and (2) the GR expression levels of "good" responders after eight weeks on enzalutamide. These findings suggest that AR-inhibition by enzalutamide induced GR overexpression and that the levels of this GR overexpression were more pronounced in patients with poor clinical outcomes.

GR expression is associated with clinical resistance to enzalutamide in the treatment of prostate cancer



*: $p < 0.05$, **: $p < 0.01$.

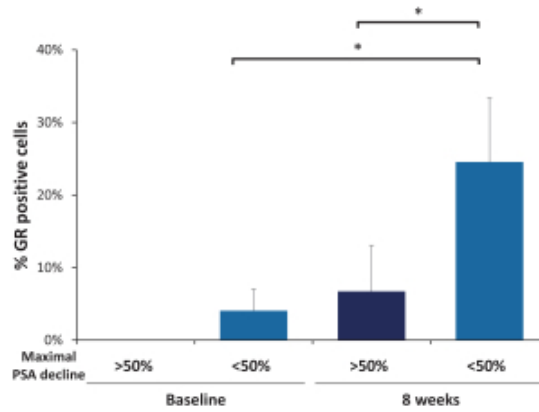
Source: Arora et al. Cell (2013).

Note: Patients who continued to benefit from enzalutamide for greater than six months were classified as "good" responders. Patients who discontinued enzalutamide earlier than six months due to a lack of clinical benefit were classified as "poor" responders. Matched tumor samples include those obtained from the same patient at baseline and after eight weeks of treatment.

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This same observation was confirmed if “good” versus “poor” response was defined by a maximal PSA decline of greater than 50% versus less than 50%. Again, as shown in the figure below, GR expression was significantly higher in “poor” responders after eight weeks on enzalutamide as compared to “good” responders.

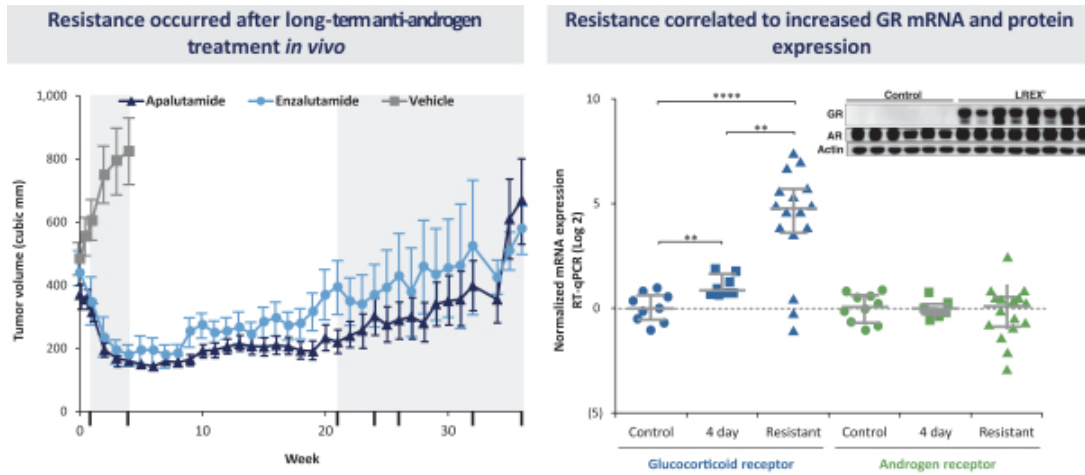
Elevated GR expression associated with a limited PSA response in enzalutamide-treated patients



*: p < 0.05

Source: Arora et al. Cell (2013).

Furthermore, in the LNCaP xenograft model with exogenous AR overexpression (LNCaP AR), acquired resistance to enzalutamide and apalutamide correlated with the upregulation of GR expression, which is shown below.

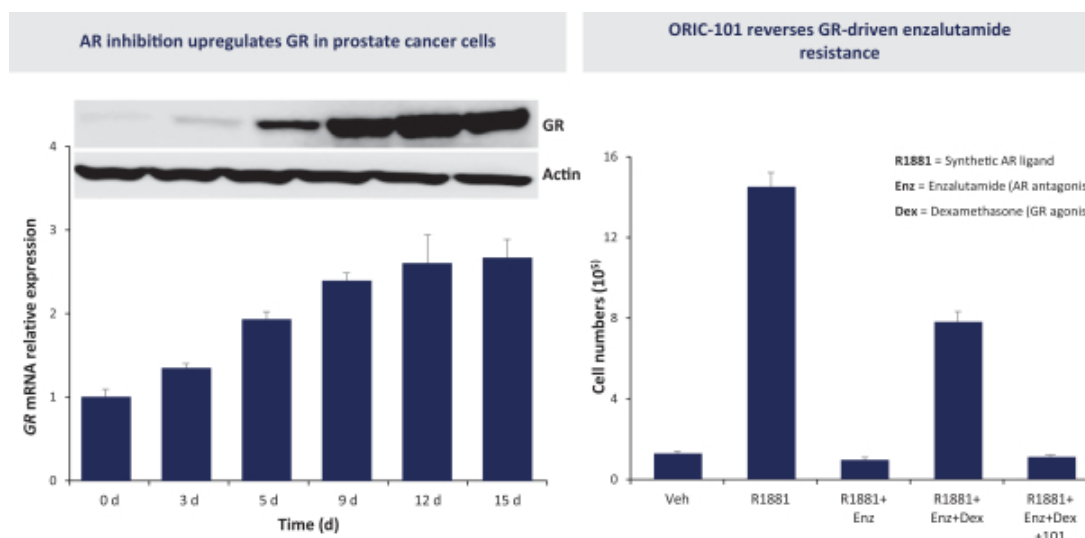


** : p < 0.01, ****: p < 0.0001.

Source: Arora et al. Cell (2013).

Note: Left graph's grey shading indicates treatment period when tumors were harvested (as annotated by long hash marks on the x axis). LREX' is a prostate cancer model that was derived from an enzalutamide-resistant tumor with high GR expression. Actin was used to verify consistent sample loading for the western blot experiment.

Similarly, as demonstrated in the figure on the left below, our *in vitro* studies demonstrate that inhibition of AR leads to upregulation of GR expression. In addition, as demonstrated in the figure on the right below, our *in vitro* studies of GR-expressing VCaP cells showed that the GR agonist dexamethasone conferred enzalutamide resistance, while the addition of a GR antagonist to counteract the dexamethasone reversed this effect.

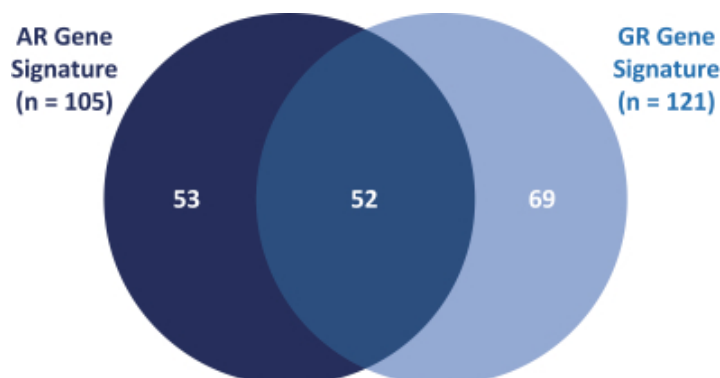


Source: Zhou et al. AACR-NCI-EORTC (2019).

Note: CWR22PC cells. GR mRNA levels relative to untreated samples shown on left slide with GR protein levels shown as inset. Actin was used to verify consistent sample loading for the western blot experiment.

Mechanistically, published data suggest that AR and GR drive a partially overlapping transcriptional program. Thus, GR activation can circumvent enzalutamide-mediated AR inhibition and sustain prostate cancer cell growth. But inhibiting GR activation is only effective in the presence of sustained AR inhibition. When AR expression levels rise, and the cancer cell is able to revert to AR mediated signaling, GR expression levels fall to baseline. These findings suggest that combined inhibition of both GR and AR could prolong the duration of response with next-generation AR antagonists such as enzalutamide or apalutamide.

AR and GR have overlapping gene signatures



Source: Arora et al. Cell (2013).

Note: Venn diagram of AR and GR signature gene lists. AR and GR signatures were defined as all genes showing >1.6 (or <1.6)-fold change (FDR < 0.05) after eight hours of addition of dihydrotestosterone (1 nM) or dexamethasone (100 nM) to charcoal-stripped media, respectively.

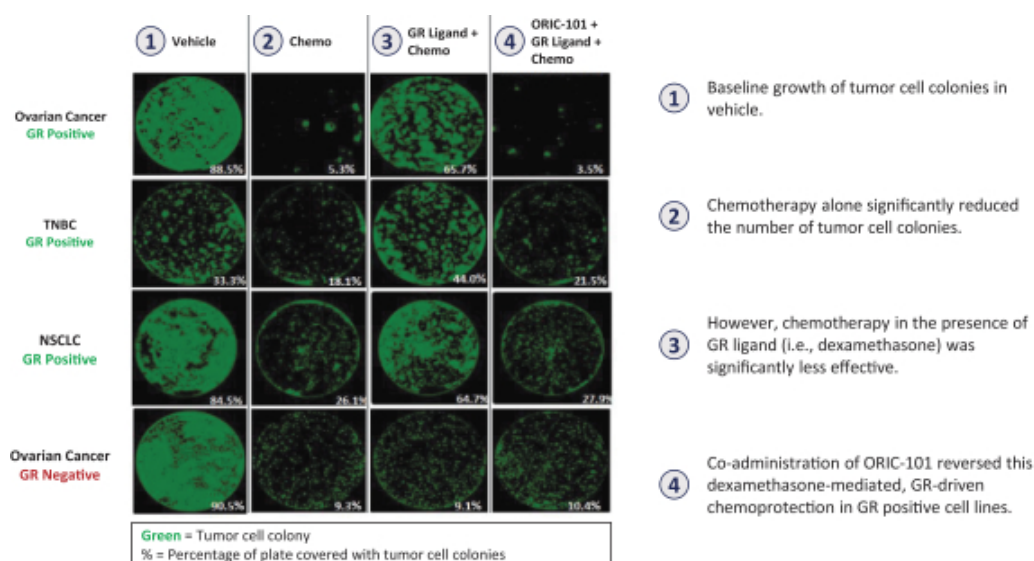
Resistance to chemotherapy in solid tumors

Preclinical data over the past decade indicate that activation of GR confers resistance to a variety of chemotherapeutic agents across an array of solid tumors that include ovarian, TNBC, prostate, pancreatic, small and non-small cell lung and urological cancers. In those settings, activation of GR signaling leads to decreased response to antimetabolites, taxanes and platinum agents. At the molecular level, GR signaling drives transcriptional activation of anti-apoptotic genes such as serum and glucocorticoid inducible protein kinase-1 (SGK1) and mitogen-activated protein kinase phosphatase-1 (MKP1/DUSP1), which in part mediate cell survival. In addition, GR activation has been demonstrated to regulate transcription of proteins that mediate cell adhesion and invasion. In that regard, GR-driven upregulation of integrins, the extracellular matrix Fibronectin-1 and the transmembrane glycoprotein Mucin-1, have been associated with pro-adhesion and protection from chemotherapy. Most recently, it has been shown that the master regulator of epithelial-mesenchymal transition (EMT), SNAI2, is a direct GR target, as well as a partial GR-induced chemoprotector.

Preclinical data

ORIC-101, as shown in the figure below, demonstrated activity in combination with chemotherapy *in vitro* using a colony formation assay. Ovarian, NSCLC and TNBC cell lines were used to assess how inhibition of GR activity by ORIC-101 affects dexamethasone-mediated chemoprotection. Based on the relative potencies of cortisol and dexamethasone, and the range of average unbound cortisol concentration in patients, a dexamethasone concentration of 30 nM was selected to simulate the expected level of GR activation at the average circulating cortisol level (approximately 375 nM) occurring in adult patients with cancer. The experiment demonstrated that co-administration of ORIC-101 reversed dexamethasone-mediated, GR-driven chemoprotection in GR positive cell lines.

ORIC-101 overcomes GR-driven chemotherapy resistance across a wide range of human cancer cell lines



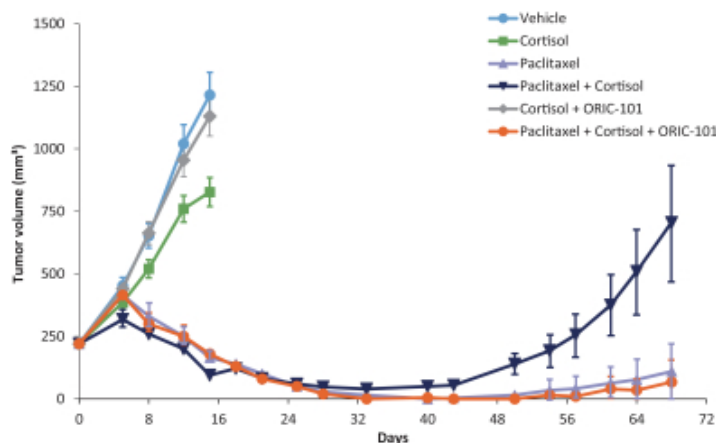
Source: Jahchan et al. AACR-NCI-EORTC (2017) and additional ORIC data.

Note: Chemotherapeutic agent is gemcitabine for ovarian cancer and paclitaxel for TNBC and NSCLC. GR ligand is dexamethasone.

The effect of ORIC-101 on the response to the chemotherapeutic compound paclitaxel was evaluated *in vivo* in the HCC1806 TNBC xenograft mouse model. The efficacy of paclitaxel was significantly diminished in tumors

grown under conditions simulating human cortisol levels sufficient to drive GR activation. Treatment with ORIC-101 was effective in reversing the effects of cortisol on paclitaxel efficacy, as shown in the figure below. Paclitaxel + cortisol + ORIC-101 treatment resulted in 88.7% tumor growth inhibition relative to paclitaxel + cortisol. At Day 68, palpable tumors were present in 93.3% of mice treated with cortisol + paclitaxel and only in 6.7% of mice treated with cortisol + paclitaxel + ORIC-101.

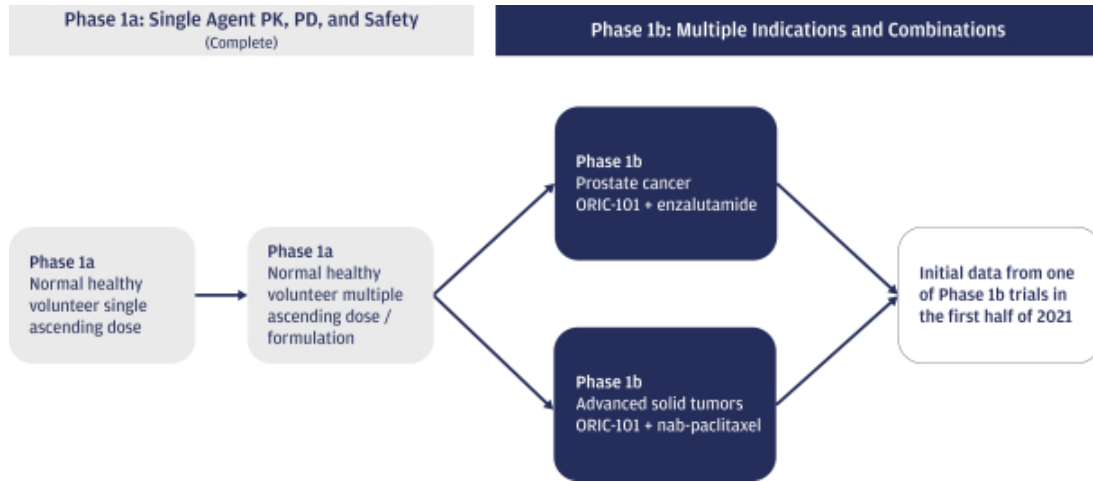
ORIC-101 overcomes GR-driven resistance to chemotherapy in TNBC xenografts



Note: HCC1806 tumor growth curves. Tumors were grown in the presence or absence of cortisol, paclitaxel and ORIC-101. Mice were treated with paclitaxel (20 mg/kg IP, Q3D×8), cortisol (100 mg/L in drinking water, *ad libitum*) or ORIC-101 (75 mg/kg of ORIC-101, PO, BID) starting on Day 0 for the duration of the study. Data is displayed as mean ± SEM. Cortisol supplementation required to activate human GR since primary glucocorticoid utilized by rodents is corticosterone. Cortisol levels intended to simulate physiological corticosteroid levels in humans. Comparable activity has been demonstrated in xenograft models of ovarian cancer, TNBC and in combination with other classes of chemotherapy.

Clinical development plan for ORIC-101

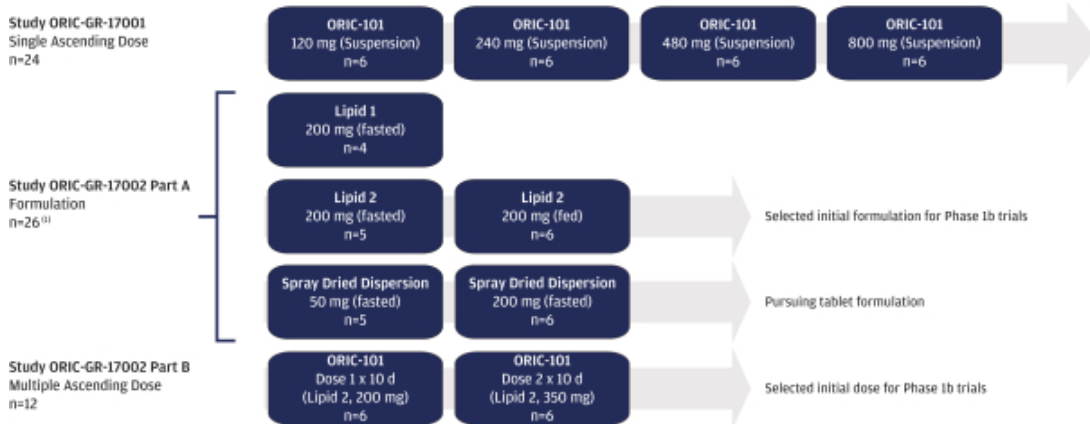
As shown in the figure below, following our preclinical studies that demonstrated that GR signaling is a bypass resistance mechanism to anti-androgen modulators in prostate cancer, as well as to chemotherapeutics in a variety of solid tumors, we completed two Phase 1a trials of ORIC-101 as a single agent in over 50 healthy volunteers, and in 2019, we initiated two separate Phase 1b trials of ORIC-101 in combination with: (1) enzalutamide in metastatic prostate cancer and (2) nab-paclitaxel in advanced or metastatic solid tumors.



Phase 1a healthy volunteer trials

We have conducted two healthy volunteer trials with ORIC-101. Study ORIC-GR-17001 was a single ascending dose trial that evaluated preliminary safety and PK of ORIC-101, and study ORIC-GR-17002 was a multi-ascending dose trial that evaluated the safety, PK and PD of ORIC-101 as well as of alternative formulations of ORIC-101.

Our Phase 1a trials are summarized in the table below.



⁽¹⁾ 26 dosing events with 20 unique individual participants. Participants in fed portion were previously dosed in fasted portion (five with Lipid 2, one with Lipid 1).

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Study 17001

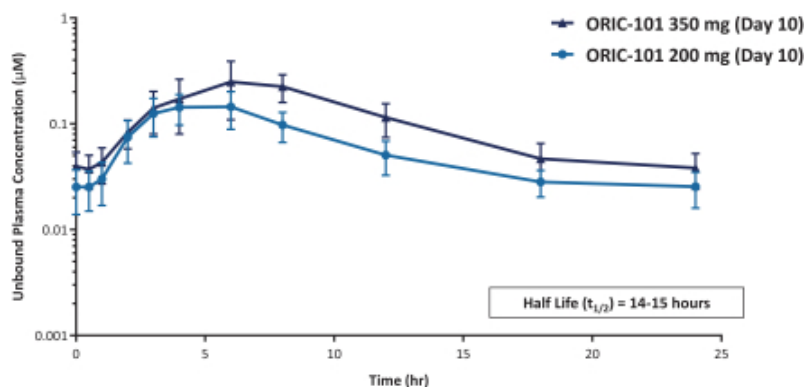
In study ORIC-GR-17001, ORIC-101 was administered in a fed state via oral suspension as four single-ascending doses of 120, 240, 480 and 800 mg, in cohorts of six subjects each. Overall, there was dose-proportional increase in the C_{max} and AUC(0-inf) of ORIC-101 in plasma. The trial was conducted at a single site in the United States.

Study 17002

Study ORIC-GR-17002 explored alternate formulations of ORIC-101 with a preliminary assessment of food-effect (Part A) along with a multiple-ascending dose portion (Part B). The trial was conducted at a single site in the United Kingdom. In Part A, a prototype spray-dried dispersion (SDD) powder in an oral suspension was evaluated along with two lipid capsule formulations. The oral SDD suspension and both lipid capsule formulations provided similar exposure to ORIC-101. There was also a modest food-effect observed.

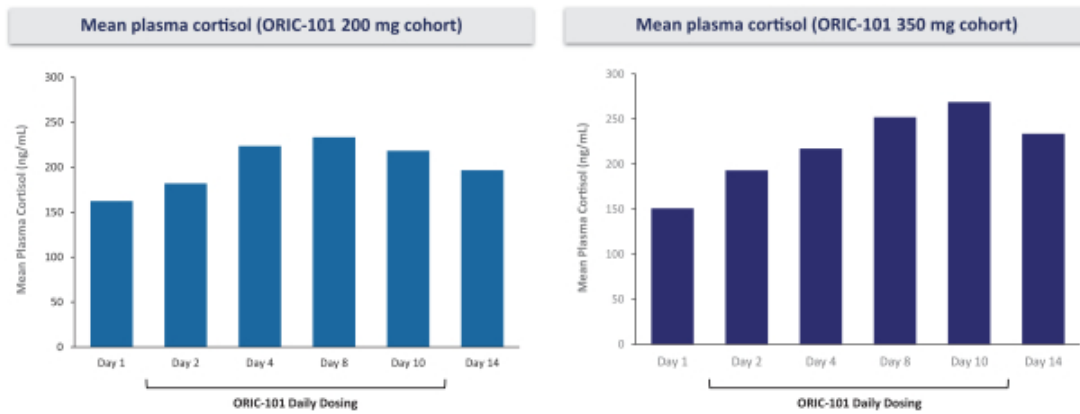
In Part B, ORIC-101 Lipid B capsules were administered once daily for ten consecutive days at a dose of 200 mg/day or 350 mg/day, under fed conditions. Six subjects were treated at each dose level. The exposure to ORIC-101, in terms of C_{max} and AUC(0-tau) in plasma, increased in a dose-dependent manner with approximately 2-fold accumulation, which is shown in the figure below. The half-life of 14-15 hours supported once daily dosing.

Exposure of ORIC-101 from Phase 1a multiple-ascending dose study supports once-daily dosing



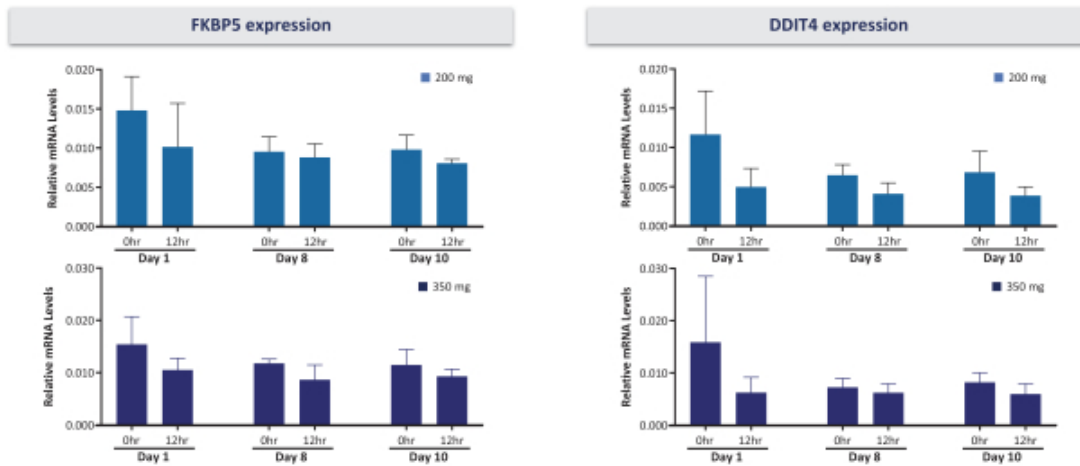
Cortisol levels can be used as a pharmacodynamic indicator of GR inhibition. Following ten days of administration of ORIC-101 at the doses of 200 mg/day and 350 mg/day, mean plasma cortisol concentrations upon waking increased over time, to a maximum on Day 8 at the dose of 200 mg/day (approximately 44% higher than Day 1) and Day 10 at the dose of 350 mg/day (approximately 78% higher than Day 1), and then subsequently decreased in both regimens, which is shown in the figure below.

Mean plasma cortisol levels increased with ORIC-101 GR inhibition in the Phase 1a multiple-ascending dose study



Finally, as another PD measure of GR inhibition, peripheral blood mononuclear cells (PBMCs) were collected and analyzed for expression of genes known to be targets of GR signaling. In this analysis, ORIC-101 was associated with decreased expression of these key PD biomarkers of GR activity, with the decrease occurring within the first day of ORIC-101 exposure and persisting for the entire duration of ten days of dosing, as shown in the figure below.

ORIC-101 was associated with downregulation of key pharmacodynamic biomarkers of GR activity in the Phase 1a multiple-ascending dose study



Note: ORIC-101 was dosed once daily for 10 days. PBMC: peripheral blood mononuclear cell; FKBP5: FK506 binding protein; DDIT4: DNA-damage-inducible transcript 4 protein.

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Safety

Overall, 56 subjects received at least a single dose of ORIC-101 across both healthy volunteer trials. A total of 12 subjects received 10 daily doses of ORIC-101 at either 200 mg/day (n=6) or 350 mg/day (n=6). All observed adverse events (AEs) were Grade 1 in severity, reversible, and no AE required study subject discontinuation.

In study ORIC-GR-17001, a single administration of ORIC-101 oral suspension at a dose of 120, 240, 480 or 800 mg was well-tolerated with only two Grade 1 AEs reported: pain in the extremity and nausea, one participant in the 480 mg and 800 mg dose, respectively. Both were mild, attributed to ORIC-101 and resolved without treatment.

In study ORIC-GR-17002, Part A, a single administration of ORIC-101 in oral SDD suspension or lipid capsules at the dose of 50 mg or 200 mg was well-tolerated. The most commonly reported treatment-emergent AEs attributed to ORIC-101 were mild gastrointestinal AEs. These were observed in 2 participants and consisted of Grade 1 nausea in one subject and Grade 1 nausea, abdominal pain, and diarrhea in a second subject. They resolved without treatment.

In study ORIC-GR-17002, Part B, multiple doses of ORIC-101 Lipid B were administered in a fed state in two cohorts of six healthy human volunteers at doses of 200 mg and 350 mg once daily for ten days and no serious AEs were observed at either dose level. Treatment-emergent AEs occurred in two and five participants at each dose level, respectively, and were all Grade 1 and reversible. The most common AEs (reported in one of six participants at 200 mg and five of six participants at 350 mg) were gastrointestinal in nature and were deemed related to ORIC-101. These events are generally consistent with known tolerability issues with the caprylic acid formulation and could also be attributable (at least in part) to pill burden at the higher ORIC-101 dose of 350 mg (7 x 50 mg capsules). In addition, there were no clinically significant post-dose changes in ECGs, vital signs, or safety laboratory results.

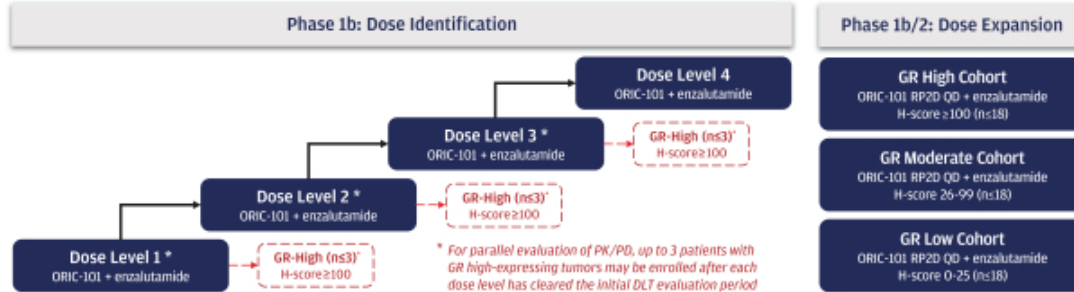
Treatment-emergent AEs	All doses (n=56)	200 mg (n=6)		350 mg (n=6)	
		Grade 1	Grade 3 ²	Grade 1	Grade 3 ²
Nausea	7	—	—	3	—
Diarrhea	3	—	—	1	—
Abdominal pain	2	—	—	1	—
Dysgeusia	2	—	—	2	—
Dyspepsia	2	—	—	2	—
Fatigue	2	—	—	2	—
Back pain	1	—	—	—	—
Catheter site swelling	1	—	—	—	—
Decreased appetite	1	—	—	1	—
Dry eye	1	—	—	—	—
Gastroesophageal reflux disease	1	—	—	1	—
Headache	1	—	—	—	—
Hot flush	1	—	—	1	—
Insomnia	1	—	—	—	—
Musculoskeletal chest pain	1	1	—	—	—
Pain in extremity	1	—	—	—	—
Proctalgia	1	—	—	1	—
Somnolence	1	—	—	1	—
Vomiting	1	1	—	—	—

Note: Severity grade as per the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v.5.0.

Phase 1b trial of ORIC-101 in combination with enzalutamide for metastatic prostate cancer

In the fourth quarter of 2019, we initiated study ORIC-101-02, an open-label, single arm, multicenter, dose escalation followed by dose expansion trial of ORIC-101 in combination with enzalutamide in patients with metastatic prostate cancer progressing on enzalutamide. This study is initially being conducted in three centers in the United States. The purpose of this trial is to assess safety, PK, PD and preliminary antitumor activity of ORIC-101 in combination with enzalutamide as well as establish its recommended Phase 2 dose. Once patients are deemed eligible, they receive treatment with ORIC-101 in addition to continuing their current enzalutamide therapy without any washout period.

To date, one patient has been enrolled on this study at Dose Level 1, in which patients receive 80 mg ORIC-101 in combination with 160 mg enzalutamide on a continuous daily dosing regimen. No additional data are currently available.

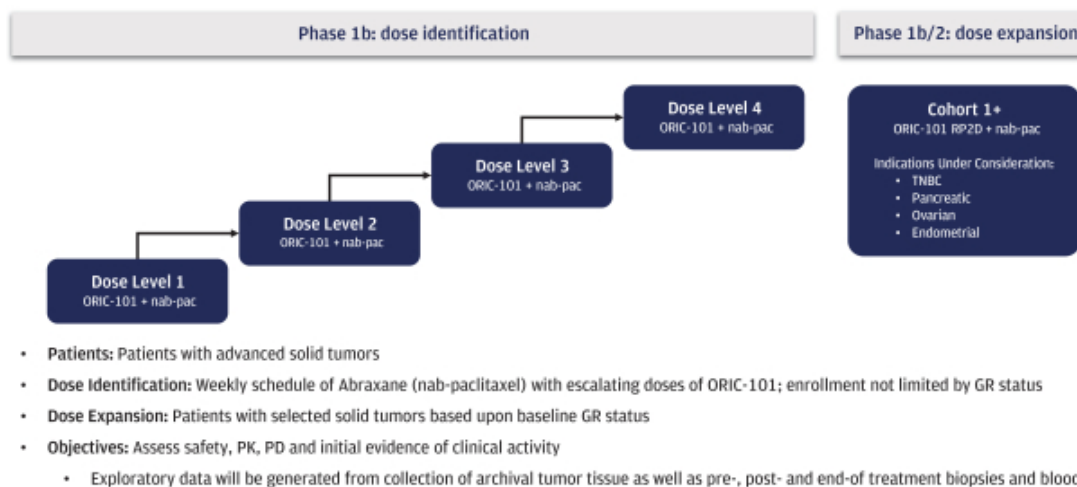


- **Patients:** Chemotherapy-naïve metastatic prostate cancer with evidence of disease progression while on treatment with enzalutamide
 - Patients will enroll in study while remaining on enzalutamide therapy (i.e., no treatment-free period)
 - Patients with progressive disease within 3 months of starting enzalutamide therapy will be excluded (i.e., no primary refractory patients)
- **Dose Identification:** Patients will remain on standard dose of enzalutamide and receive escalating doses of ORIC-101
- **Dose Expansion:** Additional patients treated with ORIC-101 at RP2D in combination with enzalutamide; cohorts based on GR expression
- **Objectives:** Assess safety, PK, PD and initial evidence of clinical activity (e.g., PSA decline, imaging, CTC conversion)
 - Exploratory data will be generated from collection of archival tumor tissue as well as pre-, post- and end of treatment biopsies and PBMCs

Note: Dose expansion cohorts will be governed by Simon's 2-stage designs to enable futility decision-making. RP2D: recommended Phase 2 dose.

Phase 1b trial of ORIC-101 in combination with nab-paclitaxel in advanced or metastatic solid tumors

In 2019, we initiated study ORIC-101-01, an open-label, single arm, multi-center, dose-finding trial of ORIC-101 in combination with nab-paclitaxel in patients with advanced or metastatic solid tumors in the United States. The purpose of this trial is to assess safety, PK, PD and preliminary anti-tumor activity of ORIC-101 in combination with nab-paclitaxel as well as establish a recommended Phase 2 dose.



RP2D: Recommended Phase 2 dose.

To date, eight patients have been enrolled on this study across three dosing cohorts. In the initial cohort, Dose Level 1, patients received 240 mg ORIC-101 administered on Days 1-5, 8-12, 15-19 in combination with 100 mg/m² nab-paclitaxel on Days 1, 8, and 15 of a 28-day cycle. Three patients with advanced pancreatic cancer were enrolled at this dose level. During the first cycle of treatment, two patients experienced DLT. Specifically, one patient experienced Grade 3 fatigue and discontinued treatment after two weeks on study. A second patient with advanced pancreatic cancer that had metastasized to the liver experienced Grade 4 neutropenia and thrombocytopenia and Grade 5 hepatic failure in the setting of rapid disease progression. A CT scan of the abdomen on study Day 9 demonstrated disease progression, and the patient died on study Day 12. These toxicities are well-described for nab-paclitaxel (including reports of hepatic necrosis and hepatic encephalopathy leading to death).

After review of safety and PK data from Dose Level 1 by the study's Safety Review Committee (SRC), it was determined that Dose Level 1 exceeded the maximum tolerated doses of the combination of ORIC-101 and nab-paclitaxel. The SRC further recommended restarting the dose escalation at lower doses of ORIC-101 and nab-paclitaxel (80 mg and 75 mg/m², respectively) but did not require the addition of prophylactic growth factor (G-CSF) for potential nab-paclitaxel-induced neutropenia. The protocol was amended and following FDA review and Institutional Review Board (IRB) approvals, three new patients were enrolled to the revised new Dose Level 1A: one patient with endometrial cancer, one patient with colorectal cancer, and one patient with a poorly differentiated neuroendocrine carcinoma of the lung. All patients completed the DLT evaluation period without DLT events. Furthermore, adverse events were mostly Grade 1 or 2 in severity, as shown in the table below. To date, there have been no Grade ≥4 treatment-related AEs reported in cohort 1A.

Treatment-emergent adverse events related to study drug in Cohort 1A (as of January 23, 2020)

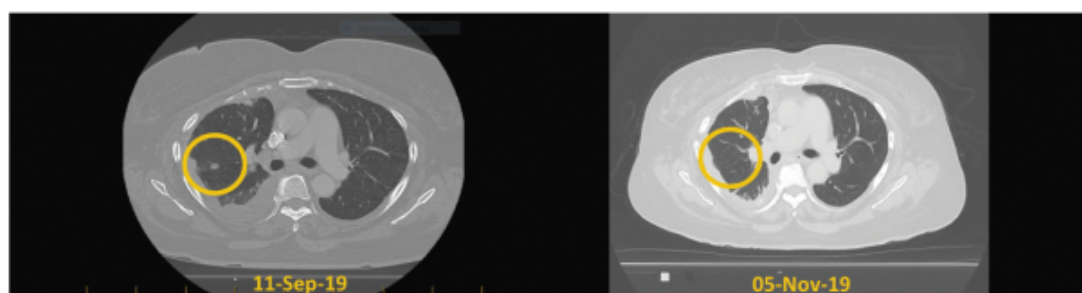
Preferred Term	Cohort 1A (N=3)		
	G1-G2	G3	Any
Any treatment-emergent AE related to study treatment	3 (100.0)	2 (66.7)	3 (100.0)
Anaemia	1 (33.3)	1 (33.3)	2 (66.7)
Aspartate aminotransferase increased	1 (33.3)	0 (0.0)	1 (33.3)
Nausea	1 (33.3)	0 (0.0)	1 (33.3)
Alanine aminotransferase increased	1 (33.3)	0 (0.0)	1 (33.3)
Diarrhoea	1 (33.3)	0 (0.0)	1 (33.3)
Alopecia	1 (33.3)	0 (0.0)	1 (33.3)
Blood alkaline phosphatase increased	0 (0.0)	1 (33.3)	1 (33.3)
Glossodynia	1 (33.3)	0 (0.0)	1 (33.3)
Hypokalaemia	1 (33.3)	0 (0.0)	1 (33.3)
Muscle spasms	1 (33.3)	0 (0.0)	1 (33.3)
Stomatitis	1 (33.3)	0 (0.0)	1 (33.3)
Weight decreased	1 (33.3)	0 (0.0)	1 (33.3)

Note: Severity grade as per the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v.5.0.

The status of GR expression in tumor was assessable for two patients based upon baseline tumor biopsy. The patient with endometrial cancer showed significant GR staining of her tumor, while there was little tumor staining of the patient with colorectal cancer. A baseline tumor biopsy could not be obtained in the third patient.

The patient with endometrial cancer had previously received a five-month course of paclitaxel and carboplatin to which her best response was stable disease. She subsequently received two sequential experimental agents but had disease progression on each of them. The patient then received nab-paclitaxel and ORIC-101 starting two months after her last experimental agent and eight months after her last exposure to taxane-platinum chemotherapy. This patient experienced a 33% reduction in tumor burden (per the Response Evaluation Criteria in Solid Tumors [RECIST] v1.1) after Cycle 2 (eight weeks on study) as shown in the figure below. The tumor marker, CA-125, had also declined from 686 U/mL at baseline down to 525 U/mL. The patient experienced only Grade 1 and 2 AEs, all of which were reversible.

First on-study tumor scans for patient with endometrial cancer



In patients with endometrial cancer, there are reports of successful retreatment with a taxane-platinum doublet but only in patients who previously received a taxane-platinum doublet in the adjuvant setting or in patients who had at least a six month treatment-free interval between first- and second-line treatment in the metastatic setting. Furthermore, published data are based upon taxane-platinum doublet rather than single-agent taxane

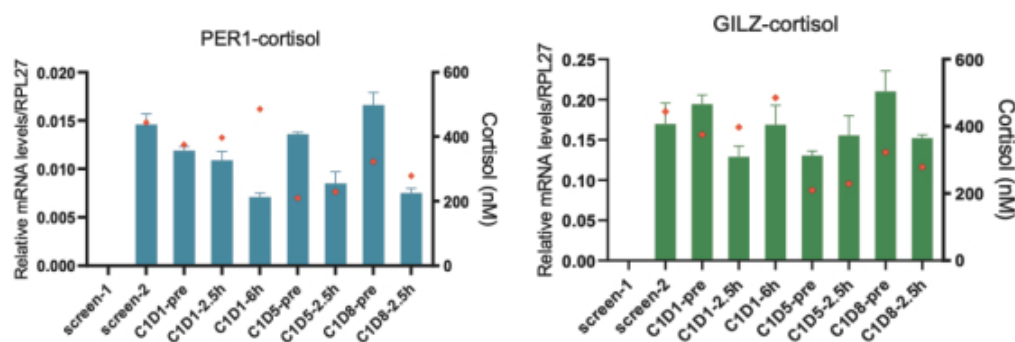
retreatment. Thus, in this patient who did not respond to her initial taxane-platinum treatment in the first-line metastatic setting and who had only a four-month treatment-free interval, there would be little to no expectation of tumor regression with single-agent taxane therapy.

A baseline tumor sample from this patient showed a high level of staining for GR by immunohistochemistry (H-score 150), which declined in a follow-up biopsy after treatment with ORIC-101 and nab-paclitaxel (H-score 65), with particular reduction in the percentage of cells that stained 3+ and 2+ for GR, as shown below.

Timepoint	Tumor H-score	Intensities (%)*			
		0	1	2	3
PRE-DOSE	150	20	20	50	10
END OF TREATMENT	65	40	55	5	0

* H-scores are defined as % of cells within the tumor with 0 staining intensity + % of cells with low (1+) staining intensity + % of cells with intermediate (2+) staining intensity + % of cells with high (3+) staining intensity.

In conjunction with this decline in GR tumor expression levels upon treatment, there was also evidence of GR-pathway inhibition. As part of the study, PBMCs were collected at various timepoints to assess the expression level of three genes indicative of GR-pathway signaling activity: PER1, GILZ, and FKBP5. With GR inhibition, it would be expected that expression of one or more of these genes would decrease, although the specific pattern may vary by tumor and between patients. In this patient, during ORIC-101 treatment, there was a marked decrease in expression of PER1 compared to baseline, with less pronounced changes seen in expression of GILZ, as shown in the figures below.



Collectively, these translational studies suggest that this patient with GR-positive endometrial cancer, who experienced tumor regression on ORIC-101 and nab-paclitaxel after prior taxane exposure, had a measurable reduction in GR-positive cells in the tumor on treatment with concurrent evidence of *in vivo* GR inhibition. A follow-up radiographic assessment four weeks after the initial eight-week assessment revealed further regression of the target lesions (38% reduction from baseline) along with stable non-target lesions; however, the appearance of new lesions led to an overall determination of disease progression as per RECIST v1.1. The patient subsequently came off study treatment due to disease progression.

Of the remaining two patients in cohort 1A, one patient (with colorectal cancer that showed no evidence of GR-positive staining at baseline) came off treatment for disease progression after seven weeks. The other patient (with poorly differentiated neuroendocrine carcinoma of the lung and unknown GR status) came off treatment for disease progression after ten weeks.

Currently, this trial is enrolling patients at Dose Level 2A: 160 mg ORIC-101 and 75 mg/m² nab-paclitaxel. Two patients have been enrolled to date at Dose Level 2A.

We expect to report interim data for one of these Phase 1b trials in the first half of 2021.

CD73 inhibitor program: ORIC-533

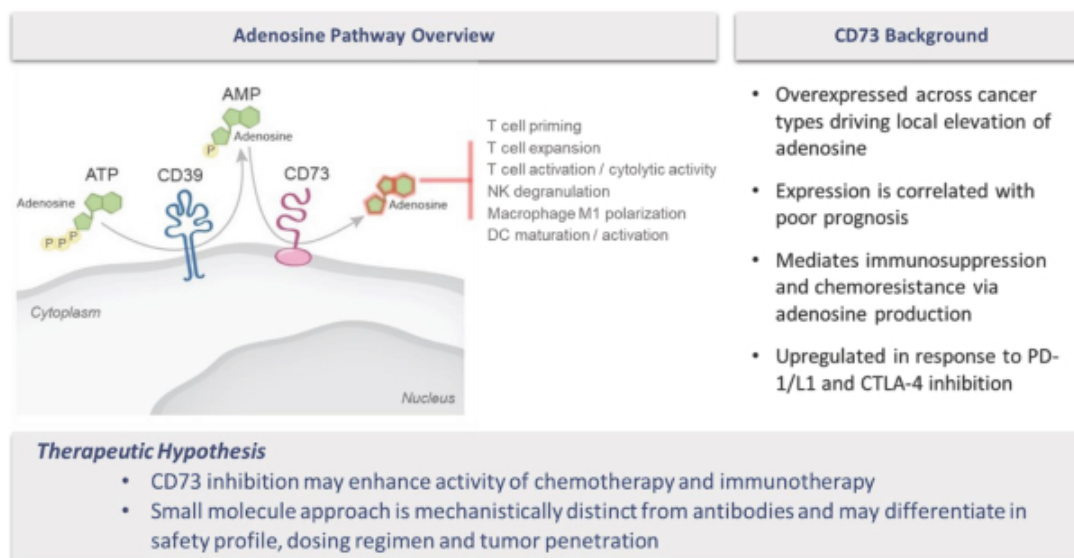
Background on adenosine and CD73

Adenosine, a purine nucleoside base, is an extracellular signaling molecule derived from adenosine triphosphate (ATP). Adenosine is a potent suppressor of immune function and accumulates in tissues at sites of inflammation and damage. Analogously, in the context of tumors, adenosine in the tumor micro environment is implicated in local immunosuppression that leads to tumor proliferation. Extracellular ATP is metabolized to AMP by the enzyme CD39, and AMP is metabolized to adenosine by the enzyme CD73. Adenosine, via its interaction with adenosine receptors, functions to suppress immune function. Multiple cell types within the tumor milieu, including cancer cells, endothelial cells and immune cells, express CD73.

Rationale for targeting CD73 in oncology

Many cancers usurp the anti-inflammatory adenosine pathway to avoid detection by the immune system, thereby reducing the effectiveness of certain chemotherapy- and immunotherapy-based treatments. Accumulation of adenosine in the tumor microenvironment is implicated in local immune suppression that leads to tumor proliferation. As shown in the figure below, CD73 is an enzyme that controls the rate at which extracellular adenosine is produced, and its overexpression is associated with poor prognosis in several cancers, including TNBC, NSCLC, melanoma and prostate, among others. Several global pharmaceutical companies are developing anti-CD73 antibodies, but due to significant medicinal chemistry challenges, to our knowledge, there are no orally bioavailable inhibitors of CD73 in clinical development.

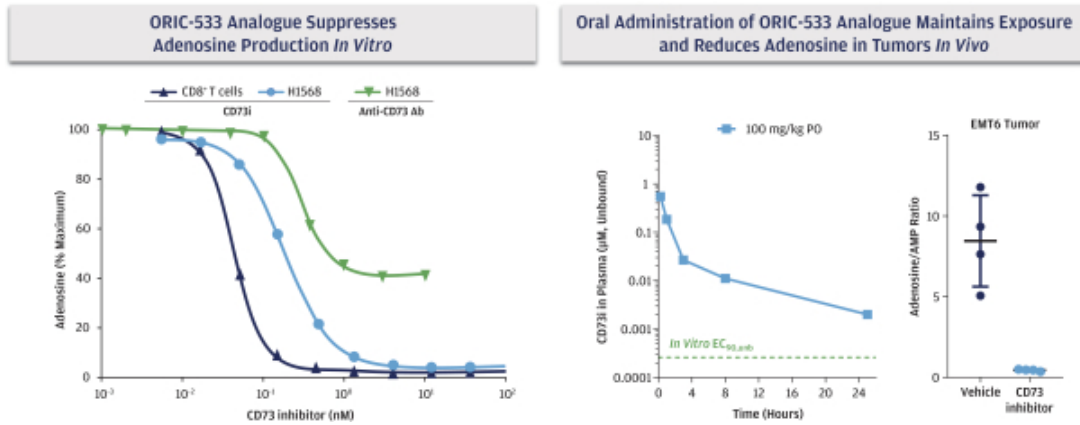
CD73 has been linked to therapy resistance



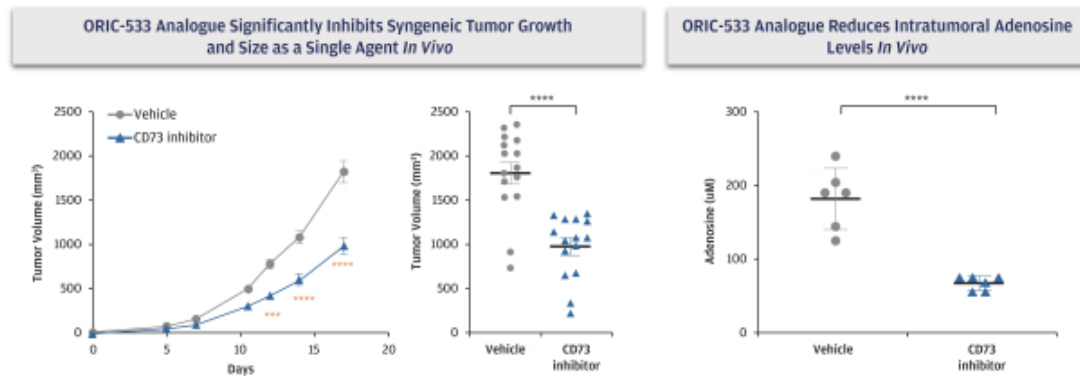
Preclinical data

ORIC-533 is an orally bioavailable small molecule that potently and selectively antagonizes CD73 enzymatic function (< 1nM) and fully inhibits CD73-mediated AMP to adenosine conversion both in human tumor cells and immune cells. Preclinical studies show that ORIC-533 restores CD8+ T-cell expansion and activation of

adenosine-induced immunosuppression. Reversal of adenosine-induced intratumoral immunosuppression with an ORIC-533 analogue leads to significant anti-tumor responses *in vivo*.



In the figure above on the left, an ORIC-533 analogue decreased adenosine production in a concentration-dependent manner in cultured human CD8+ T cells and human H1568 cancer cells. While an ORIC-533 analogue can completely block adenosine production by immune and tumor cells, an anti-CD73 antibody is unable to achieve the same degree of functional inhibition. In the figure above on the right, a single oral dose of our compound in mice achieved unbound plasma exposures that exceed the *in vitro* EC₉₀ levels required for suppression of adenosine production for 24 hours. Moreover, CD73 inhibition *in vivo* substantially reduced the adenosine/AMP ratio in EMT6 mouse tumors following sustained CD73 inhibitor treatment.



: $p = 0.0002$, *: $p < 0.0001$
 ORIC data using syngeneic EG7 tumor model.

In the figure above on the left, sustained CD73 inhibitor treatment impairs syngeneic tumor growth and tumor size significantly as a single agent. In the figure above on the right, intratumoral adenosine levels are substantially reduced following *in vivo* CD73 inhibitor treatment.

We expect to file an IND for ORIC-533 with the FDA in 2021.

Other preclinical programs

We are also developing several therapies targeting other key mechanisms of resistance. For example, we have a program directed to a target that is a potential innate oncogenic driver and also a potential bypass mechanism

of resistance in certain cancers. This and other additional programs targeting resistance mechanisms are in various states of preclinical drug discovery, and are directed towards a variety of solid tumors with a focus on breast, prostate and lung cancers.

Our collaboration and license agreements

In September 2019, we entered into a clinical trial collaboration and supply agreement with Astellas to evaluate ORIC-101 in combination with enzalutamide for the treatment of patients with metastatic prostate cancer. Under the terms of the clinical trial collaboration and supply agreement, we are sponsoring and conducting the Phase 1b trial of ORIC-101 in combination with enzalutamide. Astellas, which jointly commercializes enzalutamide in the United States with Pfizer, is providing enzalutamide for the trial. We maintain global development and commercial rights to ORIC-101 and rights to develop ORIC-101 in combination with other agents.

Sales and marketing

We intend to retain significant development and commercial rights to our product candidates and, if marketing approval is obtained, to commercialize our product candidates on our own, or potentially with a partner, in the United States and other regions. We currently have no sales, marketing or commercial product distribution capabilities. We intend to build the necessary infrastructure and capabilities over time for the United States, and potentially other regions, following further advancement of our product candidates. Clinical data, the size of the addressable patient population, the size of the commercial infrastructure and manufacturing needs may all influence or alter our commercialization plans.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates obtain marketing approval. We also rely, and expect to continue to rely, on third parties to package, label, store and distribute our investigational product candidates, as well as for our commercial products if marketing approval is obtained. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment and personnel while also enabling us to focus our expertise and resources on the development of our product candidates.

To date, we have obtained active pharmaceutical ingredients (API) and drug product for our product candidates from single-source third party contract manufacturers. We are in the process of developing our supply chain for each of our product candidates and intend to put in place framework agreements under which third-party contract manufacturers will generally provide us with necessary quantities of API and drug product on a project-by-project basis based on our development needs.

As we advance our product candidates through development, we will consider our lack of redundant supply for the API and drug product for each of our product candidates to protect against any potential supply disruptions.

We generally expect to rely on third parties for the manufacture of any companion diagnostics we may develop.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, the

expertise of our executive and scientific team, research, clinical capabilities, development experience and scientific knowledge provide us with competitive advantages, we face increasing competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Product candidates that we successfully develop and commercialize may compete with existing therapies and new therapies that may become available in the future.

Many of our competitors, either alone or with their collaborators, have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Additional mergers and acquisitions may result in even more resources being concentrated in our competitors.

Our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. The key competitive factors affecting the success of all of our programs are likely to be efficacy, safety and convenience.

For ORIC-101, our small molecule GR antagonist, we are aware of several other clinical-stage GR antagonists being developed by Corcept Therapeutics. To our knowledge, there are no GR antagonists approved for the treatment of cancer and the most advanced such GR antagonist is in a Phase 2 clinical trial.

For ORIC-533, our orally bioavailable small molecule CD73 inhibitor, we are aware of several companies developing antibodies against this target, including AstraZeneca, Bristol-Myers Squibb, Novartis in collaboration with Surface Oncology, Corvus Pharmaceuticals, Innate Pharma and Tracoon Pharmaceuticals in collaboration with I-Mab Biopharma. Other companies, such as Arcus Biosciences, Calithera Biosciences and Merck through its acquisition of Peloton Therapeutics, have small-molecule programs against this target. To our knowledge, there are no orally available, small molecule CD73 inhibitors in clinical trials.

Intellectual property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending our patent rights. We own the issued patent and patent applications relating to our lead product candidate ORIC-101, as well as our other product candidates. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the United States and in jurisdictions outside of the United States directed to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates and continuing innovation to develop, strengthen and maintain our proprietary position in the field of oncology. We also plan to rely on data exclusivity, market exclusivity and patent term extensions when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to defend and enforce our proprietary rights, including any patents that

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we may own or license in the future; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

As of January 24, 2020, our patent portfolio consisted of pending or issued patents that we own or license related to our ORIC-101 product candidate and various other compounds and programs. Specifically, we owned one issued U.S. patent, and six pending U.S. patent applications, five pending U.S. provisional patent applications and 36 pending foreign patent applications, four of which are international patent applications filed under the Paris Cooperation Treaty (PCT application), four of which are Australian applications, one of which is a Brazilian application, four of which are Canadian applications, four of which are Chinese applications, one of which is an Eurasian patent application, four of which are European regional patent applications, one of which is a Hong Kong application, one of which is an Israeli application, one of which is an Indian application, four of which are Japanese applications, one of which is a Korean application, one of which is a Mexican application, one of which is a New Zealander application, one of which is a Singaporean application, two of which are Taiwanese applications, and one of which is a South African application. Our patent portfolio also includes one pending U.S. application, one pending Canadian application, and one pending European regional patent application exclusively licensed to us from MSKCC. These licensed applications are based on the academic work conducted in the laboratory of Dr. Sawyers at MSKCC and do not cover ORIC-101, any of our current product candidates or any of our discovery and research programs.

More specifically with respect to ORIC-101, our issued U.S. patent in our owned portfolio described above has claims directed to our lead product candidate ORIC-101 as a composition of matter, as well as claims directed to pharmaceutical compositions comprising ORIC-101. This U.S. patent is expected to expire in October 2037, absent any patent term extensions for regulatory delay. Our owned portfolio described above also includes other pending patent applications related to ORIC-101, including two pending U.S. patent applications, one pending U.S. provisional patent application and 22 pending foreign patent applications, one of which is a PCT application, two of which are Australian applications, one of which is a Brazilian application, two of which are Canadian applications, two of which are Chinese applications, one of which is an Eurasian patent application, two of which are European regional patent applications, one of which is a Hong Kong application, one of which is an Israeli application, one of which is an Indian application, two of which are Japanese applications, one of which is a Korean application, one of which is a Mexican application, one of which is a New Zealander application, one of which is a Singaporean application, one of which is a Taiwanese application, and one of which is a South African application. These applications include claims directed to ORIC-101 as compositions of matter, pharmaceutical compositions, formulations, and related methods of use. Any patents that may issue from our pending patent applications related to ORIC-101 are expected to expire between 2036 and 2040, absent any patent term adjustments or extensions.

We also possess substantial know-how and trade secrets relating to the development and commercialization of our product candidates, including related manufacturing processes and technology.

With respect to our product candidates and processes we intend to develop and commercialize in the normal course of business, we intend to pursue patent protection covering, when possible, compositions, methods of use, dosing and formulations. We may also pursue patent protection with respect to manufacturing and drug development processes and technologies.

Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the United States can provide exclusionary rights for 20 years from the earliest effective filing date. In addition, in certain instances, the term of an issued U.S. patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The

restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the United States varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of oncology has emerged in the United States. The relevant patent laws and their interpretation outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our technology or product candidates and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. We cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, even our issued patents may not guarantee us the right to practice our technology in relation to the commercialization of our products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology, and our issued patents may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

Government regulation

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. drug development

In the United States, the FDA regulates drugs under the Food, Drug, and Cosmetic Act (FDCA). Drugs also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations

requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates are considered small molecule drugs and must be approved by the FDA through the NDA process before they may be legally marketed in the United States. The process generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with GLP;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practice (GCP) requirements and other clinical trial-related regulations to establish substantial evidence of the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to accept the filing for review;
- satisfactory completion of a FDA pre-approval inspection of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the preclinical study and/or clinical trial sites that generated the data in support of the NDA filing;
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy (REMS), and the potential requirement to conduct post-approval studies.

The data required to support an NDA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any current and future product candidates will be granted on a timely basis, or at all.

Preclinical studies and IND

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical

data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB must also approve the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA. The FDA will generally accept a well-designed and well-conducted foreign clinical trial not conducted under an IND if the trial was conducted in accordance with the ethical principles contained in the Declaration of Helsinki pursuant to 21 CFR 312.120(c)(4), incorporating the 1989 version of the Declaration, or with the laws and regulations of the foreign regulatory authority where the trial was conducted, such as the European Medicines Agency (EMA), whichever provides greater protection of the human subjects, and with GCP and GMP requirements, and the FDA is able to validate the data through an onsite inspection, if deemed necessary, and the practice of medicine in the foreign country is consistent with the United States.

Clinical trials in the United States generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, tolerability and safety of the drug.

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- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose and dosing schedule required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, are conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Sponsor is also responsible for submitting written IND safety reports, including reports of serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or *in vitro* testing that suggest a significant risk for human subjects, and any clinically significant increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check-points based on access to certain data from the trial.

Concurrent with clinical trials, companies usually complete additional animal safety studies and also must develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process, as performed by the manufacturing facility, must be capable of consistently producing quality batches of our product candidates. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their labeled shelf life.

NDA review process

Following completion of the clinical trials, data is analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. In short, the NDA is a request for approval to market the drug in the United States for one or more specified indications and must contain proof of safety and efficacy for a drug.

The application must include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA must be obtained before a drug may be legally marketed in the United States.

Under the Prescription Drug User Fee Act (PDUFA), as amended, each NDA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual program fee for each marketed human drug. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs before it accepts them for filing, and may request additional information rather than accepting the NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months, from the filing date, in which to complete its initial review of a new molecular-entity NDA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies and/or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. However, competitors may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if a product candidate is determined to be contained within the scope of the competitor's product for the same indication. If one of our products designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited development and review programs

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA approval, but ideally no later than the pre-NDA meeting with the FDA.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM), which is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. FDA may withdraw drug approval or require changes to the labeled indication of the drug if confirmatory post-market

trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it may require such post-marketing restrictions as it deems necessary to assure safe use of the product.

Additionally, a drug may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

Post-approval requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping requirements, requirements to report adverse events and comply with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations, known as “off-label promotion,” and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for REMS, to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market, or product recalls;
- fines, warning letters, or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications;
- suspension or revocation of product approvals;
- product seizure or detention;

- refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

FDA regulation of companion diagnostics

A therapeutic product may rely upon an *in vitro* companion diagnostic for use in selecting the patients that will be more likely to respond to that therapy. If an *in vitro* diagnostic is essential to the safe and effective use of the therapeutic product and if the manufacturer wishes to market or distribute such diagnostic for use as a companion diagnostic, then the FDA will require separate approval or clearance of the diagnostic as a companion diagnostic to the therapeutic product. According to FDA guidance, an unapproved or uncleared companion diagnostic device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational medical device unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. The sponsor of the diagnostic device will be required to comply with the IDE regulations for clinical studies involving the investigational diagnostic device. According to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products can be studied in the same clinical trial, if the trial meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the clinical trial protocol, the investigational product(s), and subjects involved, a sponsor may seek to submit an IDE alone (e.g., if the drug has already been approved by FDA and is used consistent with its approved labeling), or both an IND and an IDE.

Pursuing FDA approval/clearance of an *in vitro* companion diagnostic would require either a pre-market notification, also called 510(k) clearance, or a pre-market approval, or PMA, or a de novo classification for that diagnostic. The review of companion diagnostics involves coordination of review with the FDA's Center for Devices and Radiological Health.

510(k) clearance process

To obtain 510(k) clearance, a pre-market notification is submitted to the FDA demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or a device that was in commercial distribution before May 28, 1976 for which the FDA has not yet required the submission of a PMA application. The FDA's 510(k) clearance process may take three to 12 months from the date the application is submitted and filed with the FDA, but may take longer if FDA requests additional information, among other reasons. In some cases, the FDA may require clinical data to support substantial equivalence. In reviewing a pre-market notification submission, the FDA may request additional information, which may significantly prolong the review process. Notwithstanding compliance with all these requirements, clearance is never assured.

After a device receives 510(k) clearance, any subsequent modification of the device that could significantly affect its safety or effectiveness, or that would constitute a major change in its intended use, will require a new 510(k) clearance or require a PMA. In addition, the FDA may make substantial changes to industry requirements, including which devices are eligible for 510(k) clearance, which may significantly affect the process.

De novo classification process

If a new medical device does not qualify for the 510(k) pre-market notification process because no predicate device to which it is substantially equivalent can be identified, the device is automatically classified into Class III. The Food and Drug Administration Modernization Act of 1997 established a different route to market for low to moderate risk medical devices that are automatically placed into Class III due to the absence of a predicate device, called the "Request for Evaluation of Automatic Class III Designation," or the de novo classification process. This process allows a manufacturer whose novel device is automatically classified into Class III to request down-classification of its medical device into Class I or Class II on the basis that the device presents low or moderate risk, rather than requiring the submission and approval of a PMA. If the manufacturer seeks reclassification into Class II, the manufacturer must include a draft proposal for special controls that are necessary to provide a reasonable assurance of the safety and effectiveness of the medical device. The FDA may reject the reclassification petition if it identifies a legally marketed predicate device that would be appropriate for a 510(k) or determines that the device is not low to moderate risk and requires PMA or that general controls would be inadequate to control the risks and special controls cannot be developed.

Obtaining FDA marketing authorization, de novo down-classification, or approval for medical devices is expensive and uncertain, and may take several years, and generally requires significant scientific and clinical data.

PMA process

The PMA process, including the gathering of clinical and nonclinical data and the submission to and review by the FDA, can take several years or longer. The applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness, including information about the device and its components regarding, among other things, device design, manufacturing, and labeling. PMA applications are subject to an application fee. In addition, PMAs for medical devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes extensive testing, control, documentation, and other quality assurance and GMP requirements.

Other U.S. regulatory matters

- Our current and future arrangements with healthcare providers, third-party payors, customers, and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which we research, as well as, sell, market, and distribute any products for which we obtain marketing approval. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to: the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug or medical device manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the federal false claims, including the civil False Claims Act that can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalties prohibit individuals or entities from,

among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, and/or impose exclusions from federal health care programs and/or penalties for parties who engage in such prohibited conduct;

- the Federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations also impose obligations on covered entities such as health insurance plans, healthcare clearinghouses, and certain health care providers and their respective business associates, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to Centers for Medicare & Medicaid Services (CMS) information regarding certain payments and other transfers of value to physicians and teaching hospitals as well as information regarding ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, state laws that require biotechnology companies to comply with the biotechnology industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and require the registration of their sales representatives, state laws that require biotechnology companies to report information on the pricing of certain drug products, and state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pricing and rebate programs must also comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws. In addition, the distribution of pharmaceutical and/or medical device products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical and/or medical device products. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act as well as other applicable consumer safety requirements.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant civil, criminal and administrative penalties, including damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished

profits and future earnings, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts.

U.S. patent-term restoration and marketing exclusivity

Depending upon the timing, duration and specifics of FDA approval of any future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent-term restoration period is generally one-half the time between the effective date of an IND or the issue date of the patent, whichever is later, and the submission date of an NDA plus the time between the submission date of an NDA or the issue date of the patent, whichever is later, and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of a NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA), or a 505(b)(2) NDA submitted by another company for a generic version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for a NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness or generate such data themselves.

European Union drug development

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated, it must be approved in each of the EU countries where the trial is

to be conducted by two distinct bodies: the National Competent Authority (NCA), and one or more Ethics Committees (ECs). Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Recently enacted Clinical Trials Regulation EU No 536/2014 ensures that the rules for conducting clinical trials in the EU will be identical. In the meantime, Clinical Trials Directive 2001/20/EC continues to govern all clinical trials performed in the EU.

European Union drug review and approval

In the European Economic Area (EEA), which is comprised of the 28 Member States of the European Union and three European Free Trade Association States (Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization (MA). There are two types of marketing authorizations.

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use (CHMP), of the EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State (RMS). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics (SOPC), and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SOPC, labeling or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. Similar to the U.S. patent term-restoration, Supplementary Protection Certificates (SPCs) serve as an extension to a patent right in Europe for up to five years. SPCs apply to specific pharmaceutical products to offset the loss of patent protection due to the lengthy testing and clinical trials these products require prior to obtaining regulatory marketing approval.

Coverage and reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, for example, principal decisions about reimbursement for new products are typically made by CMS. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Healthcare reform

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not

necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private third-party payors often follow Medicare coverage policy and payment limitations in setting their own payment rates.

The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), was passed which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the HHS Secretary as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price (AMP), to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. Additionally, for a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have passed. On December 22, 2017, President Trump signed into law new federal tax legislation commonly referred to as the Tax Cuts and Jobs Act (the Tax Act) which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018 (the BBA), among other things, amended the ACA, effective January 1, 2019, to close the coverage gap

in most Medicare Part D drug plans. In December 2018, CMS published a new final rule permitting further collections and payments to and from certain ACA-qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are valid as well. It is unclear how this decision, future decisions, subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2029 unless additional congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Additionally, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drug products. For example, at the federal level, the Trump administration’s budget proposals for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump Administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. Although a number of these and other measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Facilities

Our corporate headquarters are located in South San Francisco, California, where we lease 33,322 square feet of office, research and laboratory space, under a non-cancelable lease that expires in May 2022 with an option to renew for an additional five-year term. We also lease office space and research and development space in San Diego, California under a short-term lease arrangement. We believe that these existing facilities will be

adequate for our near-term needs. If required, we believe that suitable additional or alternative space would be available in the future on commercially reasonable terms.

Employees

As of December 31, 2019, we had 57 full-time employees, more than half of whom hold doctorate degrees. Of these employees, 46 were engaged in research and development activities, and 11 were engaged in general and administrative activities. Substantially all of our employees are located in South San Francisco, California and San Diego, California. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Legal proceedings

From time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not currently a party to any material legal proceedings. Regardless of outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Management

Executive officers, key employees and directors

The following table sets forth the names and positions of our executive officers, key employees and directors and their ages as of December 31, 2019:

Name	Age	Position
Executive officers:		
Jacob Chacko, M.D.	41	President, Chief Executive Officer and Director
Dominic Piscitelli	45	Chief Financial Officer
Pratik Multani, M.D.	53	Chief Medical Officer
Key employees:		
Edna Chow Maneval, Ph.D.	59	SVP, Clinical Development
Lori Friedman, Ph.D.	55	Chief Scientific Officer
Matthew Panuwat	42	Chief Business Officer
Non-employee directors:		
Richard Heyman, Ph.D.	62	Chairman and Director
Carl Gordon, Ph.D., C.F.A.	55	Director
Leo Guthart, D.B.A.	82	Director
Richard Scheller, Ph.D.	66	Director
Peter Svernilson	58	Director

(1) Member of the audit committee

(2) Member of the compensation committee

(3) Member of the corporate governance and nominating committee

Executive officers

Jacob Chacko, M.D. has served as our Chief Executive Officer and as a member of our board of directors since May 2018 and as our President since May 2019. From May 2014 to February 2018, he served as Chief Financial Officer of Ignyta, Inc., a precision oncology company that was acquired in February 2018 by Roche Holding AG, a pharmaceuticals and diagnostics company. From August 2008 to May 2014, Dr. Chacko served as Vice President at TPG Capital, a private equity investment firm. Prior to that, Dr. Chacko was a consultant to healthcare clients at McKinsey & Company, a management consulting firm. He currently serves on the board of directors of Turning Point Therapeutics, Inc., a pharmaceutical company, and 4D Molecular Therapeutics, Inc., a pharmaceutical company. Dr. Chacko received an M.D. from UCLA, an M.B.A. from Harvard Business School, an M.Sc. from Oxford University and a B.A. in biology and B.S. in gerontology from the University of Southern California.

We believe that Dr. Chacko is qualified to serve on our board of directors because of the perspective and experience he provides as our President and Chief Executive Officer, as well as his broad experience within the biotechnology industry, particularly his experience with financial and corporate governance matters.

Dominic Piscitelli has served as our Chief Financial Officer since September 2019. From January 2017 to September 2019, he served as Chief Financial Officer of AnaptysBio, Inc., a biotechnology company. From September 2012 to January 2017, Mr. Piscitelli served as the Vice President of Finance at Medivation, Inc., a biopharmaceutical company. Prior to that, Mr. Piscitelli held various positions at Astellas Pharma US, a pharmaceutical company, and OSI Pharmaceuticals, Inc., a pharmaceutical company acquired by Astellas Pharma US. Mr. Piscitelli received an M.B.A. and B.S. in accounting and finance from Hofstra University.

Pratik Multani, M.D. has served as our Chief Medical Officer since September 2018. From February 2015 to February 2018, he served as the Chief Medical Officer of Ignyta, that was acquired by Roche in February 2018. From April 2009 to January 2015, Dr. Multani was Chief Medical Officer at Fate Therapeutics, Inc., a biopharmaceutical company. Prior to that, Dr. Multani was Vice President of Clinical Development at Kalypsys, Inc. and Senior Vice President of Clinical Development and Chief Medical Officer at Kanisa Pharmaceuticals, Inc. Dr. Multani received an M.D. from Harvard Medical School, an M.S. in epidemiology from Harvard School of Public Health and a B.S. in chemistry and biology from Yale University.

Key employees

Edna Chow Maneval, Ph.D. has served as our Senior Vice President, Clinical Development since March 2019. From March 2015 to January 2019, she served in multiple roles, including most recently as Senior Vice President, Clinical Development at Ignyta, which was acquired by Roche in February 2018. From August 2013 to February 2015, Dr. Chow Maneval served as Vice President, Clinical Development at Seragon Pharmaceuticals, a biotechnology company that was acquired by Genentech, Inc., a biotechnology company, in 2014. From March 2011 to August 2013, Dr. Chow Maneval served as Vice President, Clinical Development at Aragon Pharmaceuticals, a biotechnology company that was acquired by Johnson & Johnson, a medical device, pharmaceutical and consumer packaged goods company, in 2013. Prior to that, Dr. Chow Maneval held various positions at Pfizer from 1998 to 2011. Dr. Chow Maneval received a Ph.D. in biomedical engineering from University of Southern California and a B.S. in Physiology and Biophysics from UNISA, Sao Paulo, Brazil.

Lori Friedman, Ph.D. has served as our Chief Scientific Officer since July 2019. From July 2004 to July 2019, she served in various positions at Genentech, including as Senior Director of Translational Oncology from February 2011 to July 2019, Director, Cancer Signaling and Translational Oncology from June 2007 to February 2011, and Associate Director, Cancer Signaling, from July 2004 to May 2007. Prior to that, Dr. Friedman held various scientific leadership roles at Exelixis, Inc., an oncology-focused biotechnology company. Dr. Friedman received a Ph.D. in molecular and cell biology from UC Berkeley and a B.S. in microbiology from the University of Iowa.

Matthew Panuwat has served as our Chief Business Officer since November 2018. From January 2017 to November 2018, he served in multiple positions at Prothena Corporation plc, a biotechnology company, most recently as Senior Vice President of Business Development. From September 2014 to January 2017, Mr. Panuwat was Head of Business Development at Medivation, Inc., a biopharmaceutical company that was acquired by Pfizer Inc. in September 2016. From March 2014 to August 2014, he served in the Corporate Strategic Development department of Questcor Pharmaceuticals, Inc., a biopharmaceutical company that merged with Mallinckrodt plc in August 2014. Prior to that, Mr. Panuwat served in the Global Healthcare Investment Banking department of Merrill Lynch. Mr. Panuwat received an M.B.A. from UCLA, an M.S. in physiology and biophysics from Georgetown University and a B.S. in biology from Santa Clara University.

Non-employee directors

Richard Heyman, Ph.D. has served as a member of our board of directors since March 2015 and as Chairman of our board of directors since May 2018. Dr. Heyman also served as our President and Chief Executive Officer from November 2015 to May 2016 and as our Acting President and Chief Executive Officer from November 2017 to May 2018. Since June 2015, he has served as the Executive Chairman and Co-Founder of Metacrine, Inc., a private biotechnology company. Since 2019, Dr. Heyman has also served as a venture partner for Arch Ventures, a venture capital firm. From August 2013 to April 2015, Dr. Heyman served as President and Chief Executive Officer of Seragon, which was acquired by Genentech in 2014. Prior to that, he served as Co-Founder, President and Chief Executive Officer of Aragon Pharmaceuticals, Inc., a biotechnology company that was acquired by Johnson & Johnson, a medical device, pharmaceutical and consumer packaged goods company, in

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2013. Dr. Heyman currently serves on the board of directors of Gritstone Oncology, Inc., an oncology company. He is Vice Chair of the Board of Trustees at the Salk Institute, on the Board Foundation for the American Association for Cancer Research and on the executive committee at the University of California at San Diego Moores Cancer Center. Dr. Heyman received a Ph.D. in pharmacology from the University of Minnesota and a B.S. in chemistry from the University of Connecticut.

We believe that Dr. Heyman is qualified to serve on our board of directors because of his perspective having previously served as our President and Chief Executive Officer and more recently as our Acting President and Chief Executive Officer, his scientific background and his extensive career in the biotechnology industry.

Carl Gordon, CFA, Ph.D. has served as a member of our board of directors since November 2015. Dr. Gordon is also a member at OrbiMed Advisors, LLC, an investment firm, which he cofounded in January 1998. Prior to OrbiMed, Dr. Gordon served as a senior biotechnology analyst at Mehta and Isaly Assets Management, Inc. Dr. Gordon currently serves on the boards of directors of Turning Point Therapeutics, Inc., a pharmaceutical company, and Prevail Therapeutics, Inc., a biotechnology company, as well as several private companies. Dr. Gordon previously served on the boards of directors of several biopharmaceutical companies, including Alector Inc., a biotechnology company, from 2013 until June 2019, X4 Pharmaceuticals, Inc., a pharmaceutical company (formerly Arsanis, Inc.), from 2013 to March 2019, Acceleron Pharma Inc., a biopharmaceutical company, from 2006 to 2013, ARMO Biosciences, Inc., a biotechnology company, from 2013 until 2018, Intellia Therapeutics, Inc., a biotechnology company, from 2015 until 2017 and Selecta Biosciences, Inc., a biotechnology company, from 2010 to June 2017. Additionally, Dr. Gordon was a Fellow at The Rockefeller University from 1993 to 1995. Dr. Gordon received a B.A. in Chemistry from Harvard College and a Ph.D. in Molecular Biology from the Massachusetts Institute of Technology.

We believe that Dr. Gordon is qualified to serve on our board of directors due to his extensive business experience, experience in venture capital and the life science industry, and medical expertise.

Leo A. Guthart, D.B.A. has served as a member of our board of directors since November 2015. Since 2000, he has served as a founder of Topspin, a venture capital fund, and currently serves as its Managing Partner. Prior to that, Dr. Guthart served as Chairman and Chief Executive Officer of the security group of Pittway Corporation, a security company. Dr. Guthart served on the board of directors of AptarGroup Inc., a packaging supply company until 2015. Dr. Guthart received a D.B.A and M.B.A. from Harvard Business School and a B.A. in physics from Harvard College.

We believe that Dr. Guthart is qualified to serve on our board of directors because of his experience as a board member and his depth of experience in the biotechnology and venture capital industries.

Richard Scheller, Ph.D. has served as a member of our board of directors since March 2015. Since January 2019, Dr. Scheller has been the Chairman of Research & Development of BridgeBio Inc., a biopharmaceutical company. From 2015 until July 2019, he was the Chief Scientific Officer and Head of Therapeutic Development at 23andMe, Inc., a personal genetics company. From February 2001 to December 2014, Dr. Scheller was the Chief Scientific Officer at Genentech, a biotechnology company. Following Genentech's merger with Roche Holding AG, a pharmaceutical and diagnostics company, he was named Executive Vice President of Research and Early Development and a member of the Executive Committee. Prior to that, Dr. Scheller was a professor at Stanford University and an investigator with the Howard Hughes Medical Institute at Stanford University Medical Center. He currently serves on the board of directors of BridgeBio, Alector, Inc., a biotechnology company, Xenon Pharmaceuticals, Inc., a biopharmaceutical company, DiCE Molecules and Maze Therapeutics. Dr. Scheller received a Ph.D. in chemistry from the California Institute of Technology and a B.Sc. in biochemistry from the University of Wisconsin-Madison.

We believe Dr. Scheller is qualified to serve on our board of directors because of his experience as a board member, his scientific background, and his senior management experience in the biotechnology industry.

Peter Svenilsson has served as a member of our board of directors since August 2014. Mr. Svenilsson also served as our President and Chief Executive Officer from June 2015 to November 2015. In February 2007, Mr. Svenilsson founded The Column Group, a San Francisco-based biotechnology venture capital firm, and has grown the firm to include four additional funds with a total of \$1.4B in fund size. He currently serves as its managing partner. In addition, Mr. Svenilsson serves on the board of Ribon Therapeutics, a private biotech company and on the board of NGM Biopharmaceuticals, a publicly traded biotech company. Previously, he served as chairman of the board of Seragon from January 2013 until it was acquired by Genentech in August 2014. He was the chairman of the board of Aragon from May 2009 until it was acquired by Johnson & Johnson in August 2013. Mr. Svenilsson was also a board member of PTC Therapeutics, Inc. from 2012 until 2014, Immune Design from 2014 until 2018, Gritstone from 2015 until 2019 and Constellation Pharmaceuticals from 2016 until 2019. Prior to founding The Column Group, he founded Three Crowns Capital, where he served as its managing partner from June 1996 to February 2007. Prior to founding Three Crowns Capital, from 1987 to 1993 he was the associate managing director in charge of European Investment Banking Origination at Nomura Securities in London. Mr. Svenilsson is currently a trustee for the Institute for Advanced Study in Princeton, New Jersey. Mr. Svenilsson received a B.S. and an M.B.A. from the Stockholm School of Economics and Finance.

We believe Mr. Svenilsson is qualified to serve on our board of directors because of his experience working in the venture capital industry, leadership skills and life sciences public company experience.

Family relationships

There are no family relationships among any of our executive officers or directors.

Board composition

Our board of directors currently consists of six members. After the completion of this offering, the number of directors will be fixed from time to time by our board of directors, subject to the terms of our amended and restated certificate of incorporation and amended and restated bylaws. Each of our current directors will continue to serve as a director until the election and qualification of his or her successor, or until his or her earlier death, resignation or removal.

Our amended and restated certificate of incorporation will provide that our board of directors will be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our current directors will be divided among the three classes as follows:

- the Class I directors will be _____, and their terms will expire at the annual meeting of stockholders to be held in 2020;
- the Class II directors will be _____, and their terms will expire at the annual meeting of stockholders to be held in 2021; and
- the Class III directors will be _____, and their terms will expire at the annual meeting of stockholders to be held in 2022.

At each annual meeting of stockholders, upon the expiration of the term of a class of directors, the successor to each such director in the class will be elected to serve from the time of election and qualification until the third annual meeting following his or her election and until his or her successor is duly elected and qualified, in

accordance with our amended and restated certificate of incorporation. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one third of our directors.

This classification of our board of directors may have the effect of delaying or preventing changes in control of our company.

Director independence

Upon the completion of this offering, we anticipate that our common stock will be listed on the . Under the rules of , independent directors must comprise a majority of a listed company's board of directors within one year of the completion of this offering. In addition, the rules of require that, subject to specified exceptions, each member of a listed company's audit, compensation and corporate governance and nominating committees be independent. Audit committee members and compensation committee members must also satisfy the independence criteria set forth in Rule 10A-3 and Rule 10C-1, respectively, under the Securities Exchange Act of 1934, as amended (the Exchange Act). Under the rules of , a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

To be considered to be independent for purposes of Rule 10A-3 and under the rules of , a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee: (1) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries or (2) be an affiliated person of the listed company or any of its subsidiaries.

To be considered independent for purposes of Rule 10C-1 and under the rules of , the board of directors must affirmatively determine that each member of the compensation committee is independent, including a consideration of all factors specifically relevant to determining whether the director has a relationship to the company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including: (1) the source of compensation of such director, including any consulting, advisory or other compensatory fee paid by the company to such director and (2) whether such director is affiliated with the company, a subsidiary of the company or an affiliate of a subsidiary of the company.

Our board of directors undertook a review of its composition, the composition of its committees and the independence of our directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that , representing of our directors, do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of .

In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in the section titled "Certain relationships and related party transactions."

Board leadership structure

Our board of directors is currently chaired by Dr. Heyman. As a general policy, our board of directors believes that separation of the positions of Chair of our board of directors and Chief Executive Officer reinforces the independence of our board of directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of our board of directors as a whole. As such, Dr. Chacko serves as our President and Chief Executive Officer while Dr. Heyman serves as the Chair of our board of directors but is not an officer. We currently expect and intend the positions of Chair of our board of directors and Chief Executive Officer to continue to be held by two individuals in the future.

Role of the board in risk oversight

Our board of directors has an active role, as a whole and also at the committee level, in overseeing the management of our risks. Our board of directors is responsible for general oversight of risks and regular review of information regarding our risks, including credit risks, liquidity risks and operational risks. The compensation committee is responsible for overseeing the management of risks relating to our executive compensation plans and arrangements. The audit committee is responsible for overseeing the management of risks relating to accounting matters and financial reporting. The corporate governance and nominating committee is responsible for overseeing the management of risks associated with the independence of our board of directors and potential conflicts of interest. Although each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through discussions from committee members about such risks.

Board committees

Prior to the completion of this offering, our board of directors will have an audit committee, a compensation committee and a corporate governance and nominating committee, each of which will have the composition and the responsibilities described below.

Audit committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, the members of our audit committee will be . . . will be the chair of our audit committee and is an audit committee financial expert, as that term is defined under the SEC rules implementing Section 407 of the Sarbanes-Oxley Act of 2002, and possesses financial sophistication, as defined under the rules of . . . Our audit committee will oversee our corporate accounting and financial reporting process and assist our board of directors in monitoring our financial systems. Our audit committee will also:

- select and hire the independent registered public accounting firm to audit our financial statements;
- help to ensure the independence and performance of the independent registered public accounting firm;
- approve audit and non-audit services and fees;
- review financial statements and discuss with management and the independent registered public accounting firm our annual audited and quarterly financial statements, the results of the independent audit and the quarterly reviews and the reports and certifications regarding internal controls over financial reporting and disclosure controls;
- prepare the audit committee report that the SEC requires to be included in our annual proxy statement;
- review reports and communications from the independent registered public accounting firm;

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- review the adequacy and effectiveness of our internal controls and disclosure controls and procedure;
- review our policies on risk assessment and risk management;
- review and monitor conflicts of interest situations, and approve or prohibit any involvement in matters that may involve a conflict of interest or taking of a corporate opportunity;
- review related party transactions; and
- establish and oversee procedures for the receipt, retention and treatment of accounting related complaints and the confidential submission by our employees of concerns regarding questionable accounting or auditing matters.

Our audit committee will operate under a written charter, to be effective upon the effectiveness of the registration statement of which this prospectus forms a part, which will satisfy the applicable rules of the SEC and the listing standards of _____.

Compensation committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, the members of our compensation committee will be _____ will be the chair of our compensation committee. Our compensation committee will oversee our compensation policies, plans and benefits programs. The compensation committee will also:

- oversee our overall compensation philosophy and compensation policies, plans and benefit programs;
- review and approve compensation for our executive officers and directors;
- prepare the compensation committee report that the SEC will require to be included in our annual proxy statement; and
- administer our equity compensation plans.

Our compensation committee will operate under a written charter, to be effective upon the effectiveness of the registration statement of which this prospectus forms a part, which will satisfy the applicable rules of the SEC and the listing standards of _____.

Corporate governance and nominating committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, the members of our corporate governance and nominating committee will be _____ will be the chair of our corporate governance and nominating committee. Our corporate governance and nominating committee will oversee and assist our board of directors in reviewing and recommending nominees for election as directors. Specifically, the corporate governance and nominating committee will:

- identify, evaluate and make recommendations to our board of directors regarding nominees for election to our board of directors and its committees;
- consider and make recommendations to our board of directors regarding the composition of our board of directors and its committees;
- review developments in corporate governance practices;

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- evaluate the adequacy of our corporate governance practices and reporting; and
- evaluate the performance of our board of directors and of individual directors.

Our corporate governance and nominating committee will operate under a written charter, to be effective upon the effectiveness of the registration statement of which this prospectus forms a part, which will satisfy the applicable rules of the SEC and the listing standards of

Scientific advisory board compensation

We provide cash compensation annually to certain members of our scientific advisory board for service as a member of our scientific advisory board. We also reimburse each member of our scientific advisory board for all reasonable and necessary travel expenses in connection with the performance of his or her services. From time to time, we have also granted certain members of our scientific advisory board options to purchase shares of our common stock.

Director compensation

Prior to this offering, we have not implemented a formal policy with respect to compensation payable to our non-employee directors. Other than compensation paid to Dr. Heyman, as detailed below, we did not pay any compensation, including equity awards, to any of our non-employee directors in 2019. We reimburse our directors for expenses associated with attending meetings of our board of directors and its committees. Following the completion of this offering, we expect to implement an annual cash and equity compensation program for our non-employee directors.

Dr. Chacko was our only employee who served as a director during 2019. See the section titled “Executive compensation” for information about Dr. Chacko’s compensation.

The following table presents the total compensation each of our non-employee directors received during the year ended December 31, 2019.

Name	Fees Earned or Paid in Cash (\$)	Total (\$)
Richard Heyman, Ph.D. ⁽¹⁾⁽²⁾	75,000	75,000
Carl L. Gordon, Ph.D., CFA	—	—
Leo A. Guthart, Ph.D.	—	—
Richard Scheller, Ph.D.	—	—
Peter Svennilson	—	—

(1) In 2019, Dr. Heyman received \$6,250 per month for his service as Chairman and as a member of our board of directors.

(2) As of December 31, 2019, Dr. Heyman held outstanding option awards covering 260,213 shares. None of our other non-employee directors held outstanding option awards or unvested stock awards as of December 31, 2019.

Compensation committee interlocks and inside participation

None of the members of our compensation committee is or has been an officer or employee of our company. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee (or other board committee performing equivalent functions or, in the absence of any such committee, the entire board of directors) of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Code of business conduct and ethics

Prior to the effectiveness of the registration statement of which this prospectus forms a part, we intend to adopt a written code of business conduct and ethics that will apply to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions. Following this offering, the code of business conduct and ethics will be available on our website at www.oricpharma.com. We intend to disclose future amendments to such code, or any waivers of its requirements, applicable to any principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions or our directors on our website identified above or in a current report on Form 8-K. Information contained on the website is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus.

Executive compensation

Our named executive officers for 2019, which consist of each person who served as our principal executive officer during 2019 and our next two most highly compensated executive officers during 2019, are:

- Jacob Chacko, M.D., our President and Chief Executive Officer;
- Dominic Piscitelli, our Chief Financial Officer; and
- Pratik Multani, M.D., our Chief Medical Officer.

Summary compensation table

The following table sets forth information regarding the compensation of our named executive officers for the years ended December 31, 2018 and December 31, 2019:

Name and principal position	Year	Salary (\$)	Option awards (\$) ⁽¹⁾	Non-equity incentive plan compensation (\$) ⁽²⁾	All other compensation (\$)	Total (\$)
Jacob Chacko, M.D.	2019	455,833	—	205,100	21,396 ⁽³⁾	682,329
<i>President and Chief Executive Officer</i>	2018	290,000 ⁽⁴⁾	1,194,442	92,800 ⁽⁵⁾	57,897 ⁽⁶⁾	1,635,139
Dominic Piscitelli	2019	115,144 ⁽⁷⁾	1,083,150	40,300	111 ⁽⁸⁾	1,238,705
<i>Chief Financial Officer</i>						
Pratik Multani, M.D.	2019	398,333	—	139,400	4,423 ⁽⁸⁾	542,156
<i>Chief Medical Officer</i>	2018	112,500 ⁽⁹⁾	324,768	27,000 ⁽¹⁰⁾	25,876 ⁽¹¹⁾	490,144

(1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in Note 2(m) to our audited financial statements included elsewhere in this prospectus. These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting of the applicable awards.

(2) The 2018 amounts reported represent cash bonuses earned under our 2018 bonus plan based upon the achievement of company objectives for the year ended December 31, 2018, which were paid in 2019. The 2019 amounts reported represent estimated cash bonuses under our 2019 bonus plan based upon 100% achievement of company objectives for the year ended December 31, 2019. Such amounts will be updated to reflect actual achievement upon board determination in early 2020. The 2019 bonus amounts will be paid in 2020. Our bonus plans are more fully described below under the section titled “—Non-equity incentive plan compensation.”

(3) The amounts reported represent \$20,765 for commuting expenses and \$631 for life insurance premiums.

(4) Dr. Chacko joined as Chief Executive Officer in May 2018 and therefore the base salary amount set forth in the table above reflects the amount earned for the portion of 2018 in which he was employed by us. Dr. Chacko had an annual base salary rate of \$435,000 in 2018.

(5) Dr. Chacko joined as Chief Executive Officer in May 2018 and therefore the bonus amount set forth in the table above reflects the amount earned for the portion of 2018 in which he was employed by us. Dr. Chacko had a bonus target of 40% of his annualized base salary in 2018 under our 2018 bonus plan.

(6) The amounts reported represent \$57,161 for commuting expenses and \$736 in life insurance premiums.

(7) Mr. Piscitelli joined as Chief Financial Officer in September 2019 and therefore the base salary amount set forth in the table above reflects the amount earned for the portion of 2019 in which he was employed by us. Mr. Piscitelli had an annual base salary rate of \$375,000 in 2019.

(8) The amounts reported represent life insurance premiums.

(9) Dr. Multani joined as Chief Medical Officer in September 2018, and therefore the base salary amount set forth in the table above reflects the amount earned for the portion of 2018 in which he was employed by us. Dr. Multani had an annual base salary rate of \$390,000 in 2018.

(10) Dr. Multani joined as Chief Medical Officer in September 2018, and therefore the bonus amount set forth in the table above reflects the amount earned for the portion of 2018 in which he was employed by us. Dr. Multani had a bonus target of 30% of his annualized base salary in 2018 under our 2018 bonus plan.

(11) The amounts reported represent \$276 in life insurance premiums and \$25,600 for pre-employment consulting services.

Non-equity incentive plan compensation

At the beginning of each of 2018 and 2019, we adopted a bonus plan for our executive and non-executive employees that provides for cash incentives for performance in the year. Each of the 2018 and 2019 bonus opportunities for our executives was based on the assessment of our board of directors of the achievement of company objectives that were established by our board of directors at the beginning of the applicable year as well as other achievements which occurred during the year. The company objectives for each of 2018 and 2019 consisted of product development and pipeline goals as well as corporate development goals.

Based on our performance against the company objectives, our board of directors determined to fund the 2018 bonus plan at 80% of the target level and determined to fund the 2019 bonus plan at % of the target level.

The amounts in the Summary Compensation Table under the column “Non-equity incentive plan compensation” are based on the named executive officer’s target bonus amount multiplied by the achievement percentage set by our board of directors consistent with its determinations under the applicable year’s bonus plan (and further pro-rated based on the period of time during which they were employed with us during the year).

Outstanding equity awards at fiscal year-end

The following table sets forth information concerning outstanding equity awards held by each of our named executive officers as of December 31, 2019:

Name	Grant date ⁽¹⁾	Number of securities underlying unexercised options exercisable (#)	Option awards		
			Number of securities underlying unexercised options unexercisable (#)	Option exercise price (\$) ⁽²⁾	Option expiration date
Jacob Chacko, M.D.	5/10/2018	3,402,000 ⁽³⁾	—	0.40	5/10/2028
Dominic Piscitelli	9/11/2019	830,000 ⁽⁴⁾	—	1.61	9/11/2029
Pratik Multani, M.D.	9/20/2018	925,000 ⁽⁵⁾	—	0.40	9/20/2028

(1) Each of the outstanding equity awards was granted pursuant to our 2014 Plan.

(2) This column represents the fair market value of a share of our common stock on the date of grant, as determined by our board of directors.

(3) This option award is subject to an early exercise provision and is immediately exercisable as of the date of grant. One fourth of the total number of shares subject to the option vested on April 30, 2019, and one forty-eighth of the shares subject to the option vested, and continue to vest, monthly thereafter, subject to continued service to us through each such vesting date. The award also is subject to vesting acceleration under certain circumstances as more fully described in the section titled “—Potential payments upon termination or change in control.”

(4) This option award is subject to an early exercise provision and is immediately exercisable as of the date of grant. One fourth of the total number of shares subject to the option will vest on September 10, 2020, and one forty-eighth of the shares subject to the option will vest monthly thereafter, subject to continued service to us through each such vesting date. The award also is subject to vesting acceleration under certain circumstances as more fully described in the section titled “—Potential payments upon termination or change in control.”

(5) This option award is subject to an early exercise provision and is immediately exercisable as of the date of grant. One fourth of the total number of shares subject to the option vested on September 17, 2019, and one forty-eighth of the shares subject to the option vested, and continue to vest, monthly thereafter, subject to continued service to us through each such vesting date. The award also is subject to vesting acceleration under certain circumstances as more fully described in the section titled “—Potential payments upon termination or change in control.”

Employment arrangements with our named executive officers

We have entered into an employment offer letter agreement with each of our named executive officers in connection with his employment with us. These offer letters provide for “at will” employment.

Jacob Chacko, M.D.

We currently expect that, prior to the completion of this offering, we will enter into a confirmatory employment letter with Dr. Chacko, our President and Chief Executive Officer. The confirmatory employment letter currently is expected to have no specific term and will provide for at-will employment. Dr. Chacko’s current annual base salary is \$460,000, and Dr. Chacko’s current annual target bonus is 45% of his annual base salary.

Dominic Piscitelli

We currently expect that, prior to the completion of this offering, we will enter into a confirmatory employment letter with Mr. Piscitelli, our Chief Financial Officer. The confirmatory employment letter currently is expected to have no specific term and will provide for at-will employment. Mr. Piscitelli’s current annual base salary is \$375,000, and Mr. Piscitelli’s current annual target bonus is 35% of his annual base salary.

Pratik Multani, M.D.

We currently expect that, prior to the completion of this offering, we will enter into a confirmatory employment letter with Dr. Multani, our Chief Medical Officer. The confirmatory employment letter currently is expected to have no specific term and will provide for at-will employment. Dr. Multani’s current annual base salary is \$400,000, and Dr. Multani’s current annual target bonus is 35% of his annual base salary.

Potential payments upon termination or change in control

We currently expect that, prior to the completion of this offering, we will adopt arrangements for our executive officers that provide for payments and benefits on termination or change of control, which arrangements may be included in the anticipated confirmatory offer letters or separate plans or agreements.

Employee benefit and stock plans

2020 Equity Incentive Plan

Prior to the effectiveness of this offering, we expect that our board of directors will adopt, and our stockholders will approve, our 2020 Equity Incentive Plan (the 2020 Plan). The 2020 Plan will be effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. Our 2020 Plan will provide for the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and any of our parent and subsidiary corporations’ employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units, and performance shares to our employees, directors, and consultants and our subsidiary corporations’ employees and consultants.

Authorized shares. A total of _____ shares of our common stock are reserved for issuance pursuant to our 2020 Plan. In addition, the shares reserved for issuance under our 2020 Plan will also include (1) those shares reserved but unissued under our 2014 Plan as of the date of stockholder approval of the 2020 Plan and (2) shares of our common stock subject to or issued pursuant to awards granted under our 2014 Plan that, after the date of stockholder approval of the 2020 Plan, expire or otherwise terminate without having been exercised in full or are forfeited to or repurchased by us due to failure to vest (provided that the maximum number of

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shares that may be added to the 2020 Plan pursuant to (1) and (2) is _____ shares). The number of shares available for issuance under our 2020 Plan will also include an annual increase on the first day of each fiscal year beginning with our 2021 fiscal year, equal to the least of:

- _____ shares;
- _____ percent (_____ %) of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or
- such other amount as our board of directors may determine.

If an award expires or becomes unexercisable without having been exercised in full, is surrendered pursuant to an exchange program, or, with respect to restricted stock, restricted stock units, performance units or performance shares, is forfeited to or repurchased by us due to failure to vest, the unpurchased shares (or for awards other than stock options or stock appreciation rights, the forfeited or repurchased shares) will become available for future grant or sale under the 2020 Plan (unless the 2020 Plan has terminated). With respect to stock appreciation rights, only the net shares actually issued will cease to be available under the 2020 Plan and all remaining shares under stock appreciation rights will remain available for future grant or sale under the 2020 Plan (unless the 2020 Plan has terminated). Shares that have actually been issued under the 2020 Plan will not be returned to the 2020 Plan except if shares issued pursuant to awards of restricted stock, restricted stock units, performance shares, or performance units are repurchased by or forfeited to us due to failure to vest, such shares will become available for future grant under the 2020 Plan. Shares used to pay the exercise price of an award or satisfy the tax withholding obligations related to an award will become available for future grant or sale under the 2020 Plan. To the extent an award is paid out in cash rather than shares, such cash payment will not result in a reduction in the number of shares available for issuance under the 2020 Plan.

Plan administration. Our board of directors or one or more committees appointed by our board of directors will administer our 2020 Plan. The compensation committee of our board of directors will initially administer our 2020 Plan. In addition, if we determine it is desirable to qualify transactions under our 2020 Plan as exempt under Rule 16b-3 of the Exchange Act, such transactions will be structured to satisfy the requirements for exemption under Rule 16b-3. Subject to the provisions of our 2020 Plan, the administrator has the power to administer our 2020 Plan and make all determinations deemed necessary or advisable for administering the 2020 Plan, including but not limited to, the power to determine the fair market value of our common stock, select the service providers to whom awards may be granted, determine the number of shares covered by each award, approve forms of award agreements for use under the 2020 Plan, determine the terms and conditions of awards (including, but not limited to, the exercise price, the time or times at which awards may be exercised, any vesting acceleration or waiver or forfeiture restrictions and any restriction or limitation regarding any award or the shares relating thereto), construe and interpret the terms of our 2020 Plan and awards granted under it, prescribe, amend and rescind rules relating to our 2020 Plan, including creating sub-plans, modify or amend each award, including but not limited to the discretionary authority to extend the post-termination exercisability period of awards (except no option or stock appreciation right will be extended past its original maximum term), and allow a participant to defer the receipt of payment of cash or the delivery of shares that would otherwise be due to such participant under an award. The administrator also has the authority to allow participants the opportunity to transfer outstanding awards to a financial institution or other person or entity selected by the administrator and to institute an exchange program by which outstanding awards may be surrendered or cancelled in exchange for awards of the same type, which may have a higher or lower exercise price and/or different terms, awards of a different type, and/or cash or by which the exercise price of an outstanding award is increased or reduced. The administrator's decisions, interpretations, and other actions are final and binding on all participants.

Stock options. Stock options may be granted under our 2020 Plan. The exercise price of options granted under our 2020 Plan must at least be equal to the fair market value of our common stock on the date of grant. The term of an option may not exceed ten years. With respect to any participant who owns more than 10% of the voting power of all classes of our (or any parent or subsidiary of ours) outstanding stock, the term of an incentive stock option granted to such participant must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other property acceptable to the administrator, as well as other types of consideration permitted by applicable law. After the termination of service of an employee, director, or consultant, he or she may exercise his or her option for the period of time stated in his or her option agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the option will remain exercisable for 12 months following the termination of service. In all other cases, in the absence of a specified time in an award agreement, the option will remain exercisable for three months following the termination of service. An option, however, may not be exercised later than the expiration of its term. Subject to the provisions of our 2020 Plan, the administrator determines the other terms of options.

Stock appreciation rights. Stock appreciation rights may be granted under our 2020 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the exercise date and the date of grant. Stock appreciation rights may not have a term exceeding ten years. After the termination of service of an employee, director, or consultant, he or she may exercise his or her stock appreciation right for the period of time stated in his or her stock appreciation rights agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the stock appreciation rights will remain exercisable for 12 months following the termination of service. In all other cases, in the absence of a specified time in an award agreement, the stock appreciation rights will remain exercisable for three months following the termination of service. However, in no event may a stock appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2020 Plan, the administrator determines the other terms of stock appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with shares of our common stock, or a combination thereof, except that the per share exercise price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted stock. Restricted stock may be granted under our 2020 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of shares of restricted stock granted to any employee, director, or consultant and, subject to the provisions of our 2020 Plan, will determine the terms and conditions of such awards. The administrator may impose whatever vesting conditions it determines to be appropriate (for example, the administrator may set restrictions based on the achievement of specific performance goals or continued service to us), except the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally will have voting and dividend rights with respect to such shares upon grant without regard to vesting, unless the administrator provides otherwise. Shares of restricted stock that do not vest are subject to our right of repurchase or forfeiture.

Restricted stock units. Restricted stock units may be granted under our 2020 Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one share of our common stock. Subject to the provisions of our 2020 Plan, the administrator determines the terms and conditions of RSUs, including the vesting criteria and the form and timing of payment. The administrator may set vesting criteria based upon the achievement of company-wide, divisional, business unit or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis

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determined by the administrator in its discretion. The administrator, in its sole discretion, may pay earned restricted stock units in the form of cash, in shares or in some combination thereof. In addition, the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed.

Performance units and performance shares. Performance units and performance shares may be granted under our 2020 Plan. Performance units and performance shares are awards that will result in a payment to a participant only if performance objectives established by the administrator are achieved or the awards otherwise vest. The administrator will establish performance objectives or other vesting criteria in its discretion, which, depending on the extent to which they are met, will determine the number or the value of performance units and performance shares to be paid out to participants. The administrator may set performance objectives based on the achievement of company-wide, divisional, business unit, or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. After the grant of a performance unit or performance share, the administrator, in its sole discretion, may reduce or waive any performance objectives or other vesting provisions for such performance units or performance shares. Performance units will have an initial value established by the administrator on or prior to the grant date. Performance shares will have an initial value equal to the fair market value of our common stock on the grant date. The administrator, in its sole discretion, may pay out earned performance units or performance shares in cash, shares, or in some combination thereof.

Outside directors. All outside (non-employee) directors will be eligible to receive all types of awards (except for incentive stock options) under our 2020 Plan. To provide a maximum limit on the cash compensation and equity awards that can be made to our outside directors, our 2020 Plan provides that in any given fiscal year, an outside director will not be granted cash compensation and equity awards with an aggregate value greater than \$ _____, with the value of each equity award based on its grant date fair value as determined according to GAAP for purposes of this limit. Any cash compensation paid or awards granted to an individual for his or her services as an employee or consultant (other than as an outside director) will not count toward this limit.

Non-transferability of awards. Unless the administrator provides otherwise, our 2020 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime. If the administrator makes an award transferrable, such award will contain such additional terms and conditions as the administrator deems appropriate.

Certain adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under our 2020 Plan, the administrator will adjust the number and class of shares that may be delivered under our 2020 Plan and/or the number, class, and price of shares covered by each outstanding award and the numerical share limits set forth in our 2020 Plan.

Dissolution or liquidation. In the event of our proposed liquidation or dissolution, the administrator will notify participants as soon as practicable and, to the extent not exercised, all awards will terminate immediately prior to the consummation of such proposed transaction.

Merger or change in control. Our 2020 Plan provides that in the event of a merger or change in control, as defined under our 2020 Plan, each outstanding award will be treated as the administrator determines, without a participant's consent. The administrator is not required to treat all awards, all awards held by a participant or all awards of the same type similarly.

If a successor corporation does not assume or substitute for any outstanding award, then the participant will fully vest in and have the right to exercise all of his or her outstanding options and stock appreciation rights, all restrictions on restricted stock and restricted stock units will lapse, and for awards with performance-based

vesting, unless specifically provided for otherwise under the applicable award agreement or other agreement or policy applicable to the participant, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met. If an option or stock appreciation right is not assumed or substituted in the event of a change in control, the administrator will notify the participant in writing or electronically that such option or stock appreciation right will be exercisable for a period of time determined by the administrator in its sole discretion and the option or stock appreciation right will terminate upon the expiration of such period.

For awards granted to an outside director, in the event of a change in control, the outside director will fully vest in and have the right to exercise all of his or her outstanding options and stock appreciation rights, all restrictions on restricted stock and restricted stock units will lapse and, for awards with performance-based vesting, unless specifically provided for otherwise under the applicable award agreement or other agreement or policy applicable to the participant, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met.

Clawback. Awards will be subject to any clawback policy of ours, and the administrator also may specify in an award agreement that the participant's rights, payments, and/or benefits with respect to an award will be subject to reduction, cancellation, forfeiture, and/or recoupment upon the occurrence of certain specified events. Our board of directors may require a participant to forfeit, return, or reimburse us all or a portion of the award and/or shares issued under the award, any amounts paid under the award, and any payments or proceeds paid or provided upon disposition of the shares issued under the award in order to comply with such clawback policy or applicable laws.

Amendment; termination. The administrator has the authority to amend, alter, suspend or terminate our 2020 Plan, provided such action does not materially impair the rights of any participant. Our 2020 Plan automatically will terminate in 2030, unless we terminate it sooner.

2020 Employee Stock Purchase Plan

Prior to the effectiveness of this offering, we expect that our board of directors will adopt, and our stockholders will approve, our 2020 Employee Stock Purchase Plan (ESPP). We expect that our ESPP will be effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. However, no offering period or purchase period under the ESPP will begin unless and until otherwise determined by our board of directors.

Authorized shares. A total of _____ shares of our common stock will be available for sale under our ESPP. The number of shares of our common stock that will be available for sale under our ESPP also includes an annual increase on the first day of each fiscal year following the fiscal year in which the first offering period under the ESPP commences, equal to the least of:

- _____ shares;
- _____ percent (_____ %) of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or
- such other amount as the administrator may determine.

ESPP administration. We expect that the compensation committee of our board of directors will administer our ESPP and will have full and exclusive discretionary authority to construe, interpret, and apply the terms of the ESPP, delegate ministerial duties to any of our employees, designate separate offerings under the ESPP, designate our subsidiaries and affiliates as participating in the ESPP, determine eligibility, adjudicate all

disputed claims filed under the ESPP, and establish procedures that it deems necessary for the administration of the ESPP, including, but not limited to, adopting such procedures and sub-plans as are necessary or appropriate to permit participation in the ESPP by employees who are foreign nationals or employed outside the United States. The administrator's findings, decisions and determinations are final and binding on all participants to the full extent permitted by law.

Eligibility. Generally, all of our employees will be eligible to participate if they are customarily employed by us, or any participating subsidiary or affiliate, for at least 20 hours per week and more than five months in any calendar year. The administrator, in its discretion, may, prior to an enrollment date, for all options to be granted on such enrollment date in an offering, determine that an employee who (1) has not completed at least two years of service (or a lesser period of time determined by the administrator) since his or her last hire date, (2) customarily works not more than 20 hours per week (or a lesser period of time determined by the administrator), (3) customarily works not more than five months per calendar year (or a lesser period of time determined by the administrator), (4) is a highly compensated employee within the meaning of Section 414(q) of the Code, or (5) is a highly compensated employee within the meaning of Section 414(q) of the Code with compensation above a certain level or is an officer or subject to disclosure requirements under Section 16(a) of the Exchange Act, is or is not eligible to participate in such offering period.

However, an employee may not be granted rights to purchase shares of our common stock under our ESPP if such employee:

- immediately after the grant would own capital stock and/or hold outstanding options to purchase such stock possessing 5% or more of the total combined voting power or value of all classes of capital stock of ours or of any parent or subsidiary of ours; or
- holds rights to purchase shares of our common stock under all employee stock purchase plans of ours or any parent or subsidiary of ours that accrue at a rate that exceeds \$25,000 worth of shares of our common stock for each calendar year in which such rights are outstanding at any time.

Offering periods. Our ESPP will include a component that allows us to make offerings intended to qualify under Section 423 of the Code and a component that allows us to make offerings not intended to qualify under Section 423 of the Code to designated companies, as described in our ESPP. No offering is expected to be authorized to date by our board of directors under the ESPP prior to the completion of this offering. If our board of directors authorizes an offering period under the ESPP, our board of directors is authorized to establish the duration of offering periods and purchase periods, including the starting and ending dates of offering periods and purchase periods, provided that no offering period may have a duration exceeding 27 months.

Contributions. Our ESPP will permit participants to purchase shares of our common stock through contributions (in the form of payroll deductions or otherwise to the extent permitted by the administrator) of up to % of their eligible compensation. A participant may purchase a maximum of shares of our common stock during a purchase period.

Exercise of purchase right. If our board of directors authorizes an offering and purchase period under the ESPP, amounts contributed and accumulated by the participant during any offering period will be used to purchase shares of our common stock at the end of each purchase period. The purchase price of the shares will be % of the lower of the fair market value of our common stock on the first trading day of the offering period or on the exercise date. Participants may end their participation at any time during an offering period and will be paid their accrued contributions that have not yet been used to purchase shares of our common stock. Participation ends automatically upon termination of employment with us.

Non-transferability. A participant may not transfer rights granted under our ESPP (other than by will, the laws of descent and distribution or as otherwise provided under our ESPP).

Merger or change in control. Our ESPP will provide that in the event of a merger or change in control, as defined under our ESPP, a successor corporation may assume or substitute each outstanding purchase right. If the successor corporation refuses to assume or substitute for the outstanding purchase right, the offering period then in progress will be shortened, and a new exercise date will be set that will be before the date of the proposed merger or change in control. The administrator will notify each participant that the exercise date has been changed and that the participant's option will be exercised automatically on the new exercise date unless prior to such date the participant has withdrawn from the offering period.

Amendment; termination. The board will have the authority suspend or terminate our ESPP and the administrator will have the authority to amend the ESPP, except that, subject to certain exceptions described in our ESPP, no such action may adversely affect any outstanding rights to purchase shares of our common stock under our ESPP. Our ESPP automatically will terminate in 2040, unless we terminate it sooner.

2014 Equity Incentive Plan, as amended

Our 2014 Equity Incentive Plan (the 2014 Plan) allows us to provide incentive stock options, within the meaning of Section 422 of the Code, nonstatutory stock options, stock appreciation rights, restricted stock awards and restricted stock units (each, an "award" and the recipient of such award, a participant) to eligible employees, directors and consultants, including employees and consultants of any of our parent or subsidiary companies. It is expected that as of one business day prior to the effectiveness of the registration statement of which this prospectus forms a part, our 2014 Plan will terminate and we will not grant any additional awards under our 2014 Plan thereafter. However, our 2014 Plan will continue to govern the terms and conditions of the outstanding awards previously granted under our 2014 Plan.

As of December 31, 2019, stock options covering 10,615,463 shares of our common stock were outstanding under our 2014 Plan and there were no stock appreciation rights, restricted stock awards or restricted stock units outstanding under our 2014 Plan.

Plan administration. Our compensation committee has the authority, concurrent with our board of directors to administer our 2014 Plan. Different committees may administer our 2014 Plan with respect to different service providers. The administrator has all authority and discretion necessary or appropriate to administer our 2014 Plan and to control its operation, including the authority to construe and interpret the terms of our 2014 Plan and the awards granted under our 2014 Plan. The administrator's decisions are final and binding on all participants and any other persons holding awards.

The administrator's powers include the power to institute an exchange program (without stockholder approval) under which (1) outstanding awards are surrendered or cancelled in exchange for awards of the same type (which may have higher or lower exercise prices and different terms), awards of a different type and/or cash, (2) participants would have the opportunity to transfer any outstanding awards to a financial institution or other person or entity selected by the administrator and/or (3) the exercise price of an outstanding award is increased or reduced. The administrator's powers also include the power to prescribe, amend and rescind rules and regulations relating to our 2014 Plan, to modify or amend each award and to make all other determinations deemed necessary or advisable for administering our 2014 Plan.

Eligibility. Employees, directors and consultants, including employees and consultants of any of our parent or subsidiary companies, are eligible to receive awards, provided such consultants render bona fide services not in connection with the offer or sale of securities in a capital-raising transaction and do not directly promote or

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maintain a market for our securities. Only our employees or employees of our parent or subsidiary companies are eligible to receive incentive stock options. *Stock options.* Stock options have been granted under our 2014 Plan. Subject to the provisions of our 2014 Plan, the administrator determines the term of an option, the number of shares subject to an option, and the time period in which an option may be exercised.

The term of an option is stated in the applicable award agreement, but the term of an option may not exceed 10 years from the grant date. The administrator determines the exercise price of options, which generally may not be less than 100% of the fair market value of our common stock on the grant date, except as provided for in the 2014 Plan. However, an incentive stock option granted to an individual who directly or by attribution owns more than 10% of the total combined voting power of all of our classes of stock or of any our parent or subsidiary companies will have a term of no longer than five years from the grant date and will have an exercise price of at least 110% of the fair market value of our common stock on the grant date. In addition, to the extent that the aggregate fair market value of the shares with respect to which incentive stock options are exercisable for the first time by an employee during any calendar year (under all plans of ours and any of our parent or subsidiary companies) exceeds \$100,000, such options will be treated as nonstatutory stock options.

The administrator determines how a participant may pay the exercise price of an option, and the permissible methods are generally set forth in the applicable award agreement. If a participant's status as a "service provider" (as defined in our 2014 Plan) terminates, that participant may exercise the vested portion of his or her option for the period of time stated in the applicable award agreement. Vested options generally will remain exercisable for 30 days or such longer period of time as set forth in the applicable award agreement if a participant's status as a service provider terminates for a reason other than death or disability. If a participant's status as a service provider terminates due to death or disability, vested options generally will remain exercisable for six months from the date of termination (or such other longer period as set forth in the applicable award agreement). In no event will an option remain exercisable beyond its original term. If a participant does not exercise his or her option within the time specified in the award agreement, the option will terminate. Except as described above, the administrator has the discretion to determine the post-termination exercisability periods for an option.

Non-transferability of awards. Unless determined otherwise by the administrator, awards may not be sold, transferred, pledged, assigned or otherwise alienated or hypothecated in any manner other than by will or by the laws of descent and distribution. In addition, during an applicable participant's lifetime, only that participant may exercise their award. If the administrator makes an award transferable, such award may only be transferred (1) by will, (2) by the laws of descent and distribution or (3) as permitted by Rule 701 of the Securities Act of 1933, as amended (the Securities Act).

Certain adjustments. If there is a dividend or other distribution (whether in the form of cash, shares, other securities or other property), recapitalization, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, repurchase, exchange of shares or our other securities or other change in our corporate structure affecting the shares, the administrator will make proportionate adjustments to the number and class of shares that may be delivered under our 2014 Plan or the number, class and price of shares covered by each outstanding award. The administrator's determination regarding such adjustments will be final, binding and conclusive.

Dissolution or liquidation. In the event of our proposed dissolution or liquidation, the administrator will notify each participant as soon as practicable prior to the effective date of such proposed transaction. To the extent it has not been previously exercised, an award will terminate immediately prior to the consummation of such proposed action.

Merger and change in control. In the event of our merger with or into another corporation or entity or a "change in control" (as defined in our 2014 Plan), each outstanding award will be treated as the administrator

determines, including, without limitation, that (1) awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof) with appropriate adjustments as to the number and kind of shares and prices; (2) upon written notice to a participant, the participant's awards will terminate upon or immediately prior to the consummation of such merger or change in control; (3) outstanding awards will vest and become exercisable, realizable or payable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon consummation of such merger or change in control, and, to the extent the administrator determines, terminate upon or immediately prior to the effectiveness of such merger or change in control; (4) (a) the termination of an award in exchange for an amount of cash or property, if any, equal to the amount that would have been attained upon the exercise of such award or realization of the participant's rights as of the date of the occurrence of the transaction (and, for the avoidance of doubt, if as of the date of the occurrence of the transaction the administrator determines in good faith that no amount would have been attained upon the exercise of such award or realization of the participant's rights, then such award may be terminated by us without payment) or (b) the replacement of such award with other rights or property selected by the administrator in its sole discretion; or (5) any combination of the foregoing. The administrator will not be obligated to treat all awards, all awards a participant holds or all awards of the same type, similarly.

In the event that the successor corporation does not assume or substitute for an award (or portion thereof), the participant will fully vest in and have the right to exercise all of his or her outstanding options and stock appreciation rights, including shares as to which such awards would not otherwise be vested or exercisable, all restrictions on restricted stock and restricted stock units will lapse, and, with respect to awards with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met. In addition, if an option or stock appreciation right is not assumed or substituted in the event of a merger or change in control, the administrator will notify the participant in writing or electronically that the option or stock appreciation right will be exercisable for a period of time determined by the administrator in its sole discretion, and the option or stock appreciation right will terminate upon the expiration of such period.

Amendment and termination. Our board of directors may, at any time, amend, alter, suspend or terminate our 2014 Plan in any respect, including, without limitation, amendment of any form of award agreement or instrument to be executed pursuant to our 2014 Plan. To the extent necessary and desirable to comply with applicable laws, we will obtain stockholder approval of any amendment to our 2014 Plan. No amendment, alteration, suspension or termination of our 2014 Plan will impair the rights of a participant, unless mutually agreed otherwise between the participant and the administrator in writing. As noted above, it is expected that as of one business day prior to the effectiveness of the registration statement of which this prospectus forms a part, our 2014 Plan will be terminated, and we will not grant any additional awards under our 2014 Plan thereafter.

Executive Incentive Compensation Plan

Prior to the effectiveness of this offering, we expect that our board of directors will adopt the Executive Incentive Compensation Plan (Incentive Compensation Plan). We expect that our Incentive Compensation Plan will be effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. Our Incentive Compensation Plan will allow our compensation committee to grant incentive awards, generally payable in cash, to employees selected by our compensation committee, including our named executive officers, based upon performance goals established by our compensation committee.

Under our Incentive Compensation Plan, our compensation committee will determine the performance goals applicable to any award, which goals may include, without limitation, goals related to research and

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development, regulatory milestones or regulatory-related goals, gross margin, financial milestones, new product or business development, operating margin, product release timelines or other product release milestones, publications, cash flow, procurement, savings, internal structure, leadership development, project, function or portfolio-specific milestones, license or research collaboration agreements, capital raising, initial public offering preparations, patentability and individual objectives such as peer reviews or other subjective or objective criteria. The performance goals may differ from participant to participant and from award to award.

We expect that the compensation committee of our board of directors will administer our Incentive Compensation Plan and will, in its sole discretion and at any time, increase, reduce or eliminate a participant's actual award, and/or increase, reduce or eliminate the amount allocated to the bonus pool for a particular performance period. The actual award may be below, at or above a participant's target award, in the discretion of the administrator. The administrator may determine the amount of any increase, reduction or elimination on the basis of such factors as it deems relevant, and it will not be required to establish any allocation or weighting with respect to the factors it considers.

Actual awards generally will be paid in cash (or its equivalent) only after they are earned, and, unless otherwise determined by the administrator, to earn an actual award a participant must be employed by us through the date the actual award is paid. The compensation committee may reserve the right to settle an actual award with a grant of an equity award under our then-current equity compensation plan, which equity award may have such terms and conditions, including vesting, as the compensation committee determines. Payment of awards will occur as soon as practicable after they are earned, but no later than the dates set forth in our Incentive Compensation Plan.

Our board of directors and our compensation committee will have the authority to amend, suspend or terminate our Incentive Compensation Plan, provided such action does not impair the existing rights of any participant with respect to any earned awards.

401(k) plan

We maintain a 401(k) retirement savings plan for the benefit of our employees, including our named executive officers who remain employed with us, and who satisfy certain eligibility requirements. Under the 401(k) plan, eligible employees may elect to defer a portion of their compensation, within the limits prescribed by the Code, on a pre-tax or after-tax (Roth) basis, through contributions to the 401(k) plan. The 401(k) plan authorizes employer safe harbor contributions. The 401(k) plan is intended to qualify under Sections 401(a) and 501(a) of the Code. As a tax-qualified retirement plan, pre-tax contributions to the 401(k) plan and earnings on those pre-tax contributions are not taxable to the employees until distributed from the 401(k) plan, and earnings on Roth contributions are not taxable when distributed from the 401(k) plan.

Limitation of liability and indemnification

Our amended and restated certificate of incorporation and amended and restated bylaws, each to be effective upon the completion of this offering, will provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by Delaware law. Delaware law prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to us or to our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

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- unlawful payment of dividends or unlawful stock repurchases or redemptions; and
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director's duty of care and, in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director's responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we will also be empowered to purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we intend to enter into an indemnification agreement with each member of our board of directors and each of our officers prior to the completion of the offering. These agreements provide for the indemnification of our directors and officers for certain expenses and liabilities incurred in connection with any action, suit, proceeding or alternative dispute resolution mechanism or hearing, inquiry or investigation that may lead to the foregoing, to which they are a party, or are threatened to be made a party, by reason of the fact that they are or were a director, officer, employee, agent or fiduciary of our company, or any of our subsidiaries, by reason of any action or inaction by them while serving as an officer, director, agent or fiduciary, or by reason of the fact that they were serving at our request as a director, officer, employee, agent or fiduciary of another entity. In the case of an action or proceeding by or in the right of our company or any of our subsidiaries, no indemnification will be provided for any claim where a court determines that the indemnified party is prohibited from receiving indemnification. We believe that these charter and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. Moreover, a stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

Certain relationships and related party transactions

Other than compensation arrangements, including employment, termination of employment and change in control arrangements, with our directors and executive officers, including those discussed in the sections titled “Management” and “Executive compensation” and the registration rights described in the section titled “Description of capital stock—Registration rights,” the following is a description of each transaction since January 1, 2017 and each currently proposed transaction in which:

- we have been or are to be a participant;
- the amount involved exceeded or exceeds \$120,000; and
- any of our directors, executive officers or holders of more than 5% of our outstanding capital stock, or any immediate family member of, or person sharing the household with, any of these individuals or entities, had or will have a direct or indirect material interest.

Convertible preferred stock financings

In February 2018, May 2018 and February 2019, we issued and sold an aggregate of 17,795,153 shares of our Series C convertible preferred stock at a purchase price of \$3.00 per share for an aggregate purchase price of approximately \$53.4 million.

In June 2019 and July 2019, we issued and sold an aggregate of 16,869,345 shares of our Series D convertible preferred stock at a purchase price of \$3.30 per share for an aggregate purchase price of approximately \$55.7 million.

Purchasers of our Series C and Series D convertible preferred stock include our officers, directors and venture capital funds that beneficially own more than 5% of our outstanding capital stock and/or are represented on our board of directors. The following tables present the number of shares and the total purchase price paid by these entities.

Series C convertible preferred stock

Investor	Shares of Series C convertible preferred stock	Total Series C purchase price
The Column Group II, LP ⁽¹⁾	1,666,667	\$ 5,000,001
Entities affiliated with Topspin Fund, LP ⁽²⁾	1,991,239	\$ 5,973,717
OrbiMed Private Investments VI, LP ⁽³⁾	1,493,429	\$ 4,480,287
Entities affiliated with EcoR1 Capital LLC ⁽⁴⁾	746,666	\$ 2,239,998

(1) Peter Svenilson, a member of our board of directors, is a Managing Partner at The Column Group, LP.

(2) Topspin Biotech Fund II, L.P is affiliated with Topspin Fund, LP. The shares of these entities are aggregated for purposes of reporting share ownership. Leo Guthart, D.B.A., a member of our board of directors, is a Founder and Managing Partner of Topspin Fund, LP.

(3) Carl Gordon, Ph.D., a member of our board of directors, is a Founding Partner and Co-Head of Global Private Equity at OrbiMed Advisors, LLC.

(4) EcoR1 Capital Fund, L.P., EcoR1 Capital Fund Qualified, L.P. and EcoR1 Special Opportunity Fund II, L.P. are affiliated with EcoR1 Capital LLC. The shares of these entities are aggregated for purposes of reporting share ownership.

Series D convertible preferred stock

Investor	Shares of Series D convertible preferred stock	Total Series D purchase price
The Column Group II, LP ⁽¹⁾	606,061	\$ 2,000,001
Entities affiliated with Topspin Fund, LP ⁽²⁾	1,259,260	\$ 4,155,558
OrbiMed Private Investments VI, LP ⁽³⁾	944,445	\$ 3,116,669
Entities affiliated with EcoR1 Capital LLC ⁽⁴⁾	472,217	\$ 1,558,316

(1) Peter Svennilson, a member of our board of directors, is a Managing Partner at The Column Group, LP.

(2) Topspin Biotech Fund II, L.P is affiliated with Topspin Fund, LP. The shares of these entities are aggregated for purposes of reporting share ownership. Leo Guthart, D.B.A., a member of our board of directors, is a Founder and Managing Partner of Topspin Fund, LP.

(3) Carl Gordon, Ph.D., a member of our board of directors, is a Founding Partner and Co-Head of Global Private Equity at OrbiMed Advisors, LLC.

(4) EcoR1 Capital Fund, L.P., EcoR1 Capital Fund Qualified, L.P. and EcoR1 Special Opportunity Fund II, L.P. are affiliated with EcoR1 Capital LLC. The shares of these entities are aggregated for purposes of reporting share ownership.

Partial recourse note

On May 27, 2016, we entered into a partial recourse note (the Note) with Ashraf Hanna, our prior Chief Executive Officer, pursuant to which we loaned \$397,600 to cover the aggregate exercise price of Mr. Hanna's early exercise options. On October 31, 2017, upon Mr. Hanna's termination of employment, we exercised our repurchase right with respect to the unvested portion of the shares through partial cancellation of the Note. As of December 31, 2019, the amount of the Note outstanding was \$192,723.

Investors' rights agreement

We are party to an investors' rights agreement, as amended, with certain holders of our capital stock, including entities affiliated with The Column Group II, LP, Topspin Fund, LP, OrbiMed Private Investments VI, LP and EcoR1 Capital LLC. Under our investors' rights agreement, certain holders of our capital stock have the right to demand that we file a registration statement or request that their shares of our capital stock be covered by a registration statement that we are otherwise filing. See the section titled "Description of capital stock—Registration rights" for additional information regarding these registration rights.

Voting agreement

We are party to a voting agreement, as amended, with certain holders of our capital stock, including entities affiliated with The Column Group II, LP, Topspin Fund, LP, OrbiMed Private Investments VI, LP, EcoR1 Capital LLC, Richard Heyman, a member of the board directors, and Jacob Chacko, our President, Chief Executive Officer and a member of our board of directors. The parties to the voting agreement have agreed, subject to certain conditions, to vote the shares of our capital stock held by them so as to elect the following individuals as directors: (1) one nominee designated by Topspin Biotech Fund II, LP, currently Leo Guthart, (2) one individual designated by OrbiMed Private Investments VI, LP, currently Carl Gordon, (3) two individuals designated by The Column Group II, LP, currently Peter Svennilson and one vacancy, (4) our chief executive officer, currently Jacob Chacko, and (5) two individuals designated by the holders of a majority the outstanding shares of common stock and preferred stock (on an as-converted basis), currently Richard Heyman and Richard Scheller. Upon the consummation of this offering, the obligations of the parties to the voting agreement to vote their shares so as to elect these nominees, as well as the other rights and obligations under this agreement, will terminate and none of our stockholders will have any special rights regarding the nomination, election or designation of members of our board of directors. Our existing certificate of incorporation contains provisions regarding election of members of the board of directors that correspond to the voting agreement; however, such

provisions will be removed in the amended and restated certificate of incorporation that will be effective at the closing of this offering.

Indemnification agreements

We have entered into separate indemnification agreements with each of our directors and executive officers, in addition to the indemnification provided for in our amended and restated certificate of incorporation and bylaws. The indemnification agreements and our amended restated certificate of incorporation and bylaws that will be in effect upon the closing of this offering require us to indemnify our directors, executive officers and certain controlling persons to the fullest extent permitted by Delaware law. See the section titled “Executive compensation—Limitation of liability and indemnification” for additional information.

Related party transaction policy

Our audit committee will have the primary responsibility for reviewing and approving or disapproving “related party transactions,” which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed \$120,000 and in which a related person has or will have a direct or indirect material interest. The charter of our audit committee will provide that our audit committee shall review and approve in advance any related party transaction.

Prior to the effectiveness of the registration statement of which this prospectus forms a part, we intend to adopt a formal written policy providing that we are not permitted to enter into any transaction that exceeds \$120,000 and in which any related person has a direct or indirect material interest without the consent of our audit committee. In approving or rejecting any such transaction, our audit committee is to consider the relevant facts and circumstances available and deemed relevant to our audit committee, including whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person’s interest in the transaction.

Principal stockholders

The following table sets forth the beneficial ownership of our common stock as of December 31, 2019 by:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;
- each of the named executive officers;
- each of our directors; and
- all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with the rules of the SEC, and thus it represents sole or shared voting or investment power with respect to our securities. Unless otherwise indicated below, to our knowledge, the persons and entities named in the table have sole voting and sole investment power with respect to all shares that they beneficially owned, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Sections 13(d) and 13(g) of the Exchange Act.

We have based our calculation of the percentage of beneficial ownership prior to this offering on 85,169,744 shares of our common stock outstanding as of December 31, 2019, after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into 77,114,498 shares of our common stock immediately prior to the completion of this offering. We have based our calculation of the percentage of beneficial ownership after this offering on _____ shares of our common stock outstanding immediately after the completion of this offering, assuming no exercise by the underwriters of their option to purchase additional shares. We have deemed shares of our common stock subject to stock options that are currently exercisable or exercisable within 60 days of December 31, 2019, to be outstanding and to be beneficially owned by the person holding the stock option for the purpose of computing the percentage ownership of that person. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

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Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o ORIC Pharmaceuticals, Inc., 240 E. Grand Ave, 2nd Floor, South San Francisco, California 94080.

Name of beneficial owner	Shares beneficially owned prior to this offering		Shares beneficially owned after this offering	
	Shares	Percentage	Shares	Percentage
5% stockholders:				
The Column Group II, LP ⁽¹⁾	19,072,728	22.39%		
Entities affiliated with Topspin Fund, LP ⁽²⁾	13,250,499	15.55%		
OrbiMed Private Investments VI, LP ⁽³⁾	9,937,874	11.67%		
Entities affiliated with EcoR1 Capital LLC ⁽⁴⁾	4,968,883	5.83%		
Named executive officers and directors:				
Jacob Chacko, M.D. ⁽⁵⁾	3,652,000	4.12%		
Pratik Multani, M.D. ⁽⁶⁾	925,000	1.07%		
Dominic Piscitelli ⁽⁷⁾	830,000	*		
Richard Heyman, Ph.D. ⁽⁸⁾	1,220,213	1.43%		
Carl Gordon, Ph.D. ⁽⁹⁾	9,937,874	11.67%		
Leo Guthart, D.B.A. ⁽¹⁰⁾	13,250,499	15.55%		
Richard Scheller, Ph.D.	200,000	*		
Peter Svenilson ⁽¹¹⁾	19,072,728	22.39%		
All current executive officers and directors as a group (8 persons) ⁽¹²⁾	49,088,314	54.18%		

* Represents beneficial ownership of less than 1% of the outstanding shares of our common stock.

- (1) Consists of 19,072,728 shares held of record by The Column Group II, LP (Column II). The Column Group II GP, LP (Column II GP-LP) is the general partner of Column II. Peter Svenilson and David V. Goeddel, Ph.D. are the Managing Partners of Column II GP-LP and may be deemed to share voting and investment power with respect to the shares reported herein. Each of Mr. Svenilson and Dr. Goeddel disclaim beneficial ownership of such shares, except to the extent of his pecuniary interest therein, if any. The address of the entities listed herein is 1700 Owens Street, Suite 500, San Francisco, California 94158.
- (2) Consists of (a) 4,175,499 shares held of record by Topspin Fund, L.P. (Topspin) and (b) 9,075,000 shares held of record by Topspin Biotech Fund II, L.P. (Topspin II). LG Management, LLC is the general partner of Topspin and Topspin II. Leo Guthart is a Managing Partner of Topspin Management Company LLC, an affiliate of Topspin, Topspin II and LG Management LLC, and is also a member of our board of directors. Dr. Guthart may be deemed to share voting and investment power with respect to the shares reported herein and disclaims beneficial ownership over such shares, except to the extent of his pecuniary interest therein, if any. The address of the entities listed herein is 3 Expressway Plaza, Roslyn Heights, New York 11577.
- (3) These securities are held of record by OrbiMed Private Investments VI, LP (OPI VI). OrbiMed Capital GP VI LLC (GP VI) is the general partner of OPI VI, and OrbiMed Advisors LLC (Advisors) is the managing member of GP VI. By virtue of such relationships, GP VI and Advisors may be deemed to have voting power and investment power over the securities held by OPI VI and as a result, may be deemed to have beneficial ownership over such securities. Advisors exercises voting and investment power through a management committee comprised of Carl L. Gordon, Sven H. Borho, and Jonathan T. Silverstein, each of whom disclaims beneficial ownership of the shares held by OPI VI. The address of the entities listed herein is 601 Lexington Avenue, 54th Floor, New York, New York 10022.
- (4) Consists of (a) 793,201 shares held by EcoR1 Capital Fund, L.P. (or EcoR1 Capital), (b) 2,473,182 shares held by EcoR1 Capital Fund Qualified, L.P. (EcoR1 Qualified) and (c) 1,702,500 shares held by EcoR1 Special Opportunity Fund II, L.P. (EcoR1 Special Opportunity). Oleg Nodelman owns and controls EcoR1 Capital LLC, the general partner of EcoR1 Capital, EcoR1 Qualified and EcoR1 Special Opportunity, may be deemed to have voting and investment power with respect to the shares held by EcoR1 Capital, EcoR1 Qualified and EcoR1 Special Opportunity and, as a result, may be deemed to have beneficial ownership of these shares. The address of EcoR1 Capital, EcoR1 Qualified and EcoR1 Special Opportunity is 357 Tehama Street #3, San Francisco, California 94103.
- (5) Consists of (a) 250,000 shares held of record by Dr. Chacko and (b) 3,402,000 shares subject to options held by Dr. Chacko, all of which shares are exercisable and 1,559,250 shares of which are vested within 60 days of December 31, 2019.
- (6) Consists of 925,000 shares subject to options held by Dr. Multani, all of which shares are exercisable and 327,604 shares of which are vested within 60 days of December 31, 2019.
- (7) Consists of 830,000 shares subject to options held by Mr. Piscitelli, all of which shares are exercisable and none of which are vested within 60 days of December 31, 2019.
- (8) Consists of (a) 910,000 shares held of record by RAHD Capital, LLC, (b) 50,000 shares held of record by Dr. Heyman, and (c) 260,213 shares subject to options held by Dr. Heyman, all of which shares are exercisable and 219,431 shares of which are vested within 60 days of December 31, 2019. Dr. Heyman has voting and investment power with respect to the shares held of record by RAHD Capital, LLC.

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- (9) Consists of the shares described in footnote (3) above. Dr. Gordon is on the management committee of Advisors and may be deemed to have voting and investment power with respect to the shares held by OrbiMed VI. Dr. Gordon disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein.
- (10) Consists of the shares described in footnote (2) above. Dr. Guthart is a Managing Partner of Topspin Management Company LLC and may be deemed to have voting and investment power with respect to the shares held by Topspin and Topspin II. Dr. Guthart disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein.
- (11) Consists of the shares described in footnote (1) above. Mr. Svenilson is a member of our board of directors and a Managing Partner of Column II GP-LP and may be deemed to have voting and investment power with respect to the shares held by Column II. Mr. Svenilson disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein.
- (12) Consists of (a) 43,671,101 shares beneficially owned by our current executive officers and directors as of December 31, 2019 and (b) 5,417,213 shares subject to options exercisable within 60 days of December 31, 2019, of which 2,106,285 are vested as of such date.

Description of capital stock

The following descriptions of our capital stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws that will be in effect upon completion of this offering. Copies of these documents will be filed with the SEC as exhibits to our registration statement of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur upon the completion of this offering.

Immediately prior to the completion of this offering and the filing of our amended and restated certificate of incorporation to be effective upon completion of this offering, our authorized capital stock will consist of _____ shares of common stock, par value \$0.0001 per share, and _____ shares of preferred stock, par value \$0.0001 per share.

Immediately prior to the completion of this offering, all the outstanding shares of our convertible preferred stock will automatically convert into an aggregate of 77,114,498 shares of our common stock.

Based on 8,055,246 shares of common stock outstanding as of December 31, 2019, and after giving effect to the automatic conversion of all of our outstanding convertible preferred stock into an aggregate of 77,114,498 shares of common stock immediately prior to the completion of this offering and the issuance of _____ shares of common stock in this offering, there will be _____ shares of common stock outstanding upon the completion of this offering. As of December 31, 2019, we had 91 stockholders of record.

Common stock

Voting rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our amended and restated certificate of incorporation and amended and restated bylaws to be in effect upon the completion of this offering do not provide for cumulative voting rights. Because of this, the holders of a plurality of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. With respect to matters other than the election of directors, at any meeting of the stockholders at which a quorum is present or represented, the affirmative vote of a majority of the voting power of the shares present in person or represented by proxy at such meeting and entitled to vote on the subject matter shall be the act of the stockholders, except as otherwise required by law. The holders of a majority of the stock issued and outstanding and entitled to vote, present in person or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders.

Dividends

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

Rights and preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully paid and nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering, upon payment and delivery in accordance with the underwriting agreement, will be fully paid and nonassessable.

Preferred stock

Upon the completion of this offering, our board of directors will have the authority, without further action by the stockholders, to issue up to shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in our control or other corporate action. Upon the completion of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Options

As of December 31, 2019, we had outstanding options to purchase an aggregate of 10,615,463 shares of our common stock, with a weighted-average exercise price of \$0.94 per share, under our 2014 Plan.

Registration rights

After the completion of this offering, under our investors' rights agreement, as amended, the holders of 77,114,498 shares of common stock or their transferees, will have the right to require us to register the offer and sale of their shares or to include their shares in any registration statement we file, in each case as described below.

Demand registration rights

After the completion of this offering, the holders of up to 77,114,498 shares of our common stock will be entitled to certain demand registration rights. At any time beginning after 180 days following the date of effectiveness of the registration statement of which this prospectus forms a part, the holders of at least 50% of the shares having registration rights can request that we file a registration statement to register the offer and sale of their shares. We are only obligated to effect up to two such registrations. Each such request for registration must cover securities the anticipated aggregate gross proceeds of which, before deducting underwriting discounts and expenses, is at least \$10 million. These demand registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances. If we determine that it would be materially detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than once in any twelve month period, for a period of up to 90 days.

Form S-3 registration rights

After the completion of this offering, the holders of up to 77,114,498 shares of our common stock will be entitled to certain Form S-3 registration rights. At any time after the completion of this offering when we are eligible to file a registration statement on Form S-3, the holders of the shares having these rights can request that we register the offer and sale of their shares of our common stock on a registration statement on Form S-3 so long as the request covers securities the anticipated aggregate public offering price of which is at least \$1 million. These stockholders may make an unlimited number of requests for registration on a registration statement on Form S-3. However, we will not be required to effect a registration on Form S-3 if we have effected two such registrations within the twelve month period preceding the date of the request. These Form S-3 registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances. Additionally, if we determine that it would be seriously detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than once in any twelve month period, for a period of up to 90 days.

Piggyback registration rights

After the completion of this offering, the holders of up to 77,114,498 shares of our common stock will be entitled to certain “piggyback” registration rights. If we propose to register the offer and sale of shares of our common stock under the Securities Act, the holders of these shares can request that we include their shares in such registration, subject to certain marketing and other limitations, including the right of the underwriters to limit the number of shares included in any such registration statement under certain circumstances. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to (1) a registration related to any employee benefit plan or a corporate reorganization or other transaction covered by Rule 145 promulgated under the Securities Act, (2) a registration relating to the offer and sale of debt securities, (3) a registration on any registration form that does not permit secondary sales or (4) a registration pursuant to the demand or Form S-3 registration rights described in the preceding two paragraphs above, the holders of these shares are entitled to notice of the registration and have the right, subject to certain limitations, to include their shares in the registration.

Expenses of registration

We will pay all expenses relating to any demand registrations, Form S-3 registrations and piggyback registrations, subject to specified exceptions.

Termination

The registration rights terminate upon the earliest of (1) the date that is four years after the closing of this offering, (2) immediately prior to the closing of certain liquidation events and (3) as to a given holder of registration rights, the date after the closing of this offering when such holder of registration rights can sell all of such holder’s registrable securities during any 90-day period pursuant to Rule 144 promulgated under the Securities Act.

Anti-takeover effects of certain provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws

Certain provisions of Delaware law and certain provisions that will be included in our amended and restated certificate of incorporation and amended and restated bylaws summarized below may be deemed to have an

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anti-takeover effect and may delay, deter or prevent a tender offer or takeover attempt that a stockholder might consider to be in its best interests, including attempts that might result in a premium being paid over the market price for the shares held by stockholders.

Preferred stock

Our amended and restated certificate of incorporation will contain provisions that permit our board of directors to issue, without any further vote or action by the stockholders, shares of preferred stock in one or more series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting rights (if any) of the shares of the series and the powers, preferences or relative, participation, optional and other special rights, if any, and any qualifications, limitations or restrictions, of the shares of such series.

Classified board

Our amended and restated certificate of incorporation will provide that our board of directors is divided into three classes, designated Class I, Class II and Class III. Each class will be an equal number of directors, as nearly as possible, consisting of one third of the total number of directors constituting the entire board of directors. The term of initial Class I directors shall terminate on the date of the 2020 annual meeting, the term of the initial Class II directors shall terminate on the date of the 2021 annual meeting, and the term of the initial Class III directors shall terminate on the date of the 2022 annual meeting. At each annual meeting of stockholders beginning in 2020, the class of directors whose term expires at that annual meeting will be subject to reelection for a three-year term.

Removal of directors

Our amended and restated certificate of incorporation will provide that stockholders may only remove a director for cause by a vote of no less than a majority of the shares present in person or by proxy at the meeting and entitled to vote.

Director vacancies

Our amended and restated certificate of incorporation will authorize only our board of directors to fill vacant directorships.

No cumulative voting

Our amended and restated certificate of incorporation will provide that stockholders do not have the right to cumulate votes in the election of directors.

Special meetings of stockholders

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that, except as otherwise required by law, special meetings of the stockholders may be called only by an officer at the request of a majority of our board of directors, by the Chair of our board of directors or by our Chief Executive Officer.

Advance notice procedures for director nominations

Our amended and restated bylaws will provide that stockholders seeking to nominate candidates for election as directors at an annual or special meeting of stockholders must provide timely notice thereof in writing. To be

timely, a stockholder's notice generally will have to be delivered to and received at our principal executive offices before notice of the meeting is issued by the secretary of the company, with such notice being served not less than 90 nor more than 120 days before the meeting. Although the amended and restated bylaws will not give the board of directors the power to approve or disapprove stockholder nominations of candidates to be elected at an annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Action by written consent

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that any action to be taken by the stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by written consent.

Amending our certificate of incorporation and bylaws

Our amended and restated certificate of incorporation may be amended or altered in any manner provided by the Delaware General Corporation Law (DGCL). Our amended and restated bylaws may be adopted, amended, altered or repealed by stockholders only upon approval of at least majority of the voting power of all the then outstanding shares of the common stock, except for any amendment of the above provisions, which would require the approval of a two-thirds majority of our then outstanding common stock. Additionally, our amended and restated certificate of incorporation will provide that our bylaws may be amended, altered or repealed by the board of directors.

Authorized but unissued shares

Our authorized but unissued shares of common stock and preferred stock will be available for future issuances without stockholder approval, except as required by the listing standards of _____, and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of the company by means of a proxy contest, tender offer, merger or otherwise.

Exclusive jurisdiction

Our amended and restated bylaws will provide that, unless we consent to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim arising pursuant to the DGCL, any action regarding our amended and restated certificate of incorporation or amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to this provision. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against us or our directors and officers. Nothing in our amended and restated bylaws precludes stockholders that assert claims under the Securities Act or the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

Business combinations with interested stockholders

We are governed by Section 203 of the DGCL. Subject to certain exceptions, Section 203 of the DGCL prohibits a public Delaware corporation from engaging in a business combination (as defined in such section) with an “interested stockholder” (defined generally as any person who beneficially owns 15% or more of the outstanding voting stock of such corporation or any person affiliated with such person) for a period of three years following the time that such stockholder became an interested stockholder, unless (1) prior to such time the board of directors of such corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (2) upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of such corporation at the time the transaction commenced (excluding for purposes of determining the voting stock of such corporation outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (a) by persons who are directors and also officers of such corporation and (b) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer); or (3) at or subsequent to such time the business combination is approved by the board of directors of such corporation and authorized at a meeting of stockholders (and not by written consent) by the affirmative vote of at least 66 2/3% of the outstanding voting stock of such corporation not owned by the interested stockholder.

Our amended and restated certificate of incorporation and our amended and restated bylaws will provide that we must indemnify our directors and officers to the fullest extent authorized by the DGCL. We are expressly authorized to, and do, carry directors’ and officers’ insurance providing coverage for our directors, officers and certain employees for some liabilities. We believe that these indemnification provisions and insurance are useful to attract and retain qualified directors and executive officers.

The limitation on liability and indemnification provisions in our certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duty. These provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. In addition, your investment may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions.

Listing

We intend to apply to list our common stock on _____ under the symbol “ORIC.”

Transfer agent and registrar

Upon completion of this offering, the transfer agent and registrar for our common stock will be _____. The transfer agent and registrar’s address is _____.

Shares eligible for future sale

Prior to this offering, there has been no public market for our common stock, and although we expect that our common stock will be approved for listing on the _____, we cannot assure investors that there will be an active public market for our common stock following this offering. We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. Future sales of substantial amounts of common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, however, could adversely affect the market price of our common stock and also could adversely affect our future ability to raise capital through the sale of our common stock or other equity-related securities of ours at times and prices we believe appropriate.

Upon completion of this offering, based on our shares outstanding as of December 31, 2019 and after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock, _____ shares of our common stock will be outstanding, or _____ shares of common stock if the underwriters exercise their option to purchase additional shares in full. All of the shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act unless held by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining outstanding shares of our common stock will be deemed "restricted securities" as that term is defined under Rule 144. Restricted securities may be sold in the public market only if their offer and sale is registered under the Securities Act or if the offer and sale of those securities qualify for an exemption from registration, including exemptions provided by Rules 144 and 701 under the Securities Act, which are summarized below.

As a result of the lock-up agreements and market stand-off provisions described below and the provisions of Rules 144 or 701, the shares of our common stock that will be deemed "restricted securities" will be available for sale in the public market following the completion of this offering as follows:

- no shares will be eligible for sale on the date of this prospectus; and
- _____ shares will be eligible for sale upon expiration of the lock-up agreements and market stand-off provisions described below, following the date that is 180 days after the date of this prospectus.

Lock-up agreements and market stand-off agreements

Our officers, directors and the holders of substantially all of our capital stock and options have entered into market stand-off agreements with us and have entered into or will enter into lock-up agreements with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus, except with the prior consent of J.P. Morgan Securities LLC, Citigroup Global Markets Inc. and Jefferies LLC. See the section titled "Underwriting" for additional information.

Rule 144

Rule 144, as currently in effect, generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who is not deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our capital stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 without complying with the volume limitation, manner of sale or notice conditions of Rule 144. If such stockholder has beneficially owned the shares of our capital stock proposed to be

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sold for at least one year, then such person is entitled to sell such shares in reliance upon Rule 144 without complying with any of the other conditions of Rule 144.

Rule 144 also provides that a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our common stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 within any three month period beginning 90 days after the date of this prospectus a number of such shares that does not exceed the greater of the following:

- 1% of the number of shares of our capital stock then outstanding, which will equal _____ shares immediately after the completion of this offering, assuming no exercise by the underwriters of their option to purchase additional shares; or
- the average weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Sales of our capital stock made in reliance upon Rule 144 by a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days are also subject to the current public information, manner of sale and notice conditions of Rule 144.

Rule 701

Rule 701 generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is not deemed to have been one of our affiliates at any time during the preceding 90 days may sell such shares in reliance upon Rule 144 without complying with the current public information or holding period conditions of Rule 144. Rule 701 also provides that a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is deemed to have been one of our affiliates during the preceding 90 days may sell such shares under Rule 144 without complying with the holding period condition of Rule 144. However, all stockholders who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701.

Registration rights

After the completion of this offering, the holders of up to 77,114,498 shares of our common stock will be entitled to certain rights with respect to the registration of such shares under the Securities Act. The registration of these shares of our common stock under the Securities Act would result in these shares becoming eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration. See the section titled "Description of capital stock—Registration rights" for a description of these registration rights.

Registration statement

After the completion of this offering, we intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to equity awards outstanding or reserved for issuance under our equity compensation plans. The shares of our common stock covered by such registration statement will be eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration statement, subject to vesting restrictions, the conditions of Rule 144 applicable to affiliates, and any applicable market stand-off agreements and lock-up agreements. See the section titled “Executive compensation—Employee benefit and stock plans” for a description of our equity compensation plans.

Material U.S. federal income tax consideration for non-U.S. holders of our common stock

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock acquired in this offering by a “non-U.S. holder” (as defined below), but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended (the Code), Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought, and do not intend to seek, any ruling from the Internal Revenue Service (IRS), with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state or local jurisdiction or under U.S. federal gift and estate tax rules, and does not address tax considerations applicable to an investor’s particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies, regulated investment companies, real estate investment trusts or other financial institutions;
- tax-exempt organizations;
- pension plans and tax-qualified retirement plans;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- brokers or dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- partnerships (or entities or arrangements classified as such for U.S. federal income tax purposes), other pass-through entities, and investors therein;
- persons who hold our common stock as a position in a hedging transaction, “straddle,” “conversion transaction” or other risk reduction transaction;
- persons who hold or receive our common stock pursuant to the exercise of any option or otherwise as compensation;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to our common stock being taken into account in an “applicable financial statement” as defined in Section 451(b) of the Code;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

In addition, if a partnership, entity or arrangement classified as a partnership or flow-through entity for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner generally will depend on the status of the partner and upon the activities of the partnership or other entity. A partner in a partnership or other such entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other such entity, as applicable.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal gift or estate tax rules or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

Non-U.S. holder defined

For purposes of this discussion, you are a “non-U.S. holder” if you are a beneficial owner of our common stock that, for U.S. federal income tax purposes, is not a partnership (including any entity or arrangement treated as a partnership and the equity holders therein) or:

- an individual who is a citizen or resident of the United States;
- a corporation or other entity taxable as a corporation created or organized in the United States or under the laws of the United States or any political subdivision thereof, or otherwise treated as such for U.S. federal income tax purposes;
- an estate whose income is subject to U.S. federal income tax regardless of its source; or
- a trust (1) whose administration is subject to the primary supervision of a U.S. court and that has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (2) that has made a valid election under applicable Treasury Regulations to be treated as a U.S. person.

Distributions

As described in the section titled “Dividend policy,” we have never declared or paid cash dividends on our capital stock, and we do not anticipate paying any cash dividends following the completion of this offering. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Subject to the discussions below on effectively connected income and in the sections titled “—Backup withholding and information reporting” and “—Foreign Account Tax Compliance Act (FATCA),” any dividend paid to you generally will be subject to U.S. federal withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. In order to receive a reduced treaty rate, you must provide us with a properly executed IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate. If you are eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty, you may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS. If you hold our common stock through a financial institution or other agent acting on the non-U.S. holder’s behalf, you will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries.

Dividends received by you that are treated as effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, are attributable to a permanent establishment or fixed base maintained by you in the United States) are generally exempt from the 30% U.S. federal withholding tax, subject to the discussion below in the sections titled “—Backup withholding and information reporting” and “—Foreign Account Tax Compliance Act (FATCA).” In order to obtain this exemption, you must provide us with a properly executed IRS Form W-8ECI or applicable successor form properly certifying such exemption. Such effectively connected dividends, although not subject to U.S. federal withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. You should consult your tax advisor regarding the tax consequences of the ownership and disposition of our common stock, including any applicable tax treaties that may provide for different rules.

Gain on disposition of common stock

Subject to the discussion in the section titled “—Backup withholding and information reporting,” you generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with your conduct of a U.S. trade or business (and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by you in the United States);
- you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock constitutes a United States real property interest by reason of our status as a “United States real property holding corporation” (USRPHC), for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock, unless our common stock is regularly traded on an established securities market and you hold no more than 5% of our outstanding common stock, directly, indirectly and constructively, at all times, during the shorter of the five-year period ending on the date of the taxable disposition or your holding period for our common stock.

We believe that we are not currently and will not become a USRPHC for U.S. federal income tax purposes, and the remainder of this discussion so assumes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of our U.S. and worldwide real property plus our other business assets, there can be no assurance that we will not become a USRPHC in the future. If we are a USRPHC and either our common stock is not regularly traded on an established securities market or you hold, or are treated as holding, more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, you will generally be taxed on any gain in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. If we are a USRPHC and our common stock is not regularly traded on an established securities market, your proceeds received on the disposition of shares will also generally be subject to withholding at a rate of 15%. You are encouraged to consult your own tax advisors regarding the possible consequences to you if we are, or were to become, a USRPHC.

If you are a non-U.S. holder described in the first bullet above, you will be required to pay tax on the gain derived from the sale (net of certain deductions and credits) under regular graduated U.S. federal income tax rates, and a corporate non-U.S. holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second bullet above, you will be subject to tax on such gain at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses for the year, provided you have timely filed U.S. federal income tax returns with respect to such losses. You should consult your tax advisor regarding any applicable income tax or other treaties that may provide for different rules.

Backup withholding and information reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends on or of proceeds from the disposition of our common stock made to you may also be subject to backup withholding at a current rate of 24% unless you establish an exemption, for example, by properly certifying your non-U.S. status on a properly completed IRS Form W-8BEN or W-8BEN-E or another appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding may apply if either we or our paying agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act (FATCA)

The Foreign Account Tax Compliance Act, Treasury Regulations issued thereunder and official IRS guidance, collectively "FATCA," generally impose a U.S. federal withholding tax of 30% on dividends on, and, subject to the discussion of certain proposed Treasury Regulations below, the gross proceeds from a sale or other disposition of our common stock, paid to a "foreign financial institution" (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends on and, subject to the discussion of certain proposed Treasury Regulations below, the gross proceeds from a sale or other disposition of our common stock paid to a "non-financial foreign entity" (as specially defined under these rules) unless such entity provides the withholding agent with a certification identifying the substantial direct and indirect U.S. owners of the entity, certifies that it does not have any substantial U.S. owners, or otherwise establishes an exemption. The withholding tax will apply regardless of whether the payment otherwise would be exempt from U.S. nonresident and backup withholding tax, including under the other exemptions described above. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Prospective investors should consult with their own tax advisors regarding the application of FATCA withholding to their investment in, and ownership and disposition of, our common stock.

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The Treasury Secretary has issued proposed Treasury Regulations, which, if finalized in their present form, would eliminate withholding under FATCA with respect to payment of gross proceeds from a sale or other disposition of our common stock. In its preamble to such proposed Treasury Regulations, the U.S. Treasury stated that taxpayers may generally rely on the proposed Treasury Regulations until final regulations are issued.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice to investors in their particular circumstances. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Citigroup Global Markets Inc. and Jefferies LLC are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	
Citigroup Global Markets Inc.	
Jefferies LLC	
Guggenheim Securities, LLC	
Total	

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common stock directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of \$ _____ per share. After the initial offering of the shares to the public, if all of the shares of common stock are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to _____ additional shares of common stock from us. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ _____ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without exercise of option to purchase additional shares	With exercise of full option to purchase additional shares
Per share	\$	\$
Total	\$	\$

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$ _____. We have agreed to reimburse the underwriters for expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc. in an amount up to \$ _____.

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A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not, subject to certain exceptions, for a period of 180 days after the date of this prospectus (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, hedge, or otherwise dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (2) enter into any swap, hedging, or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC, Citigroup Global Markets Inc. and Jefferies LLC.

Our directors and executive officers, and substantially all of our securityholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 180 days after the date of this prospectus (restricted period), may not, without the prior written consent of J.P. Morgan Securities LLC, Citigroup Global Markets Inc. and Jefferies LLC (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, hedge, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap, hedging, or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

The restrictions described in the immediately preceding paragraph do not apply to, among other items and subject to certain additional limitations:

- (1) transfers as a bona fide gift or gifts;
- (2) transfers by will or intestacy;
- (3) transfers to any trust or other entities formed for the direct or indirect benefit of the securityholder or an immediate family member;
- (4) transfers to any immediate family member;
- (5) if the securityholder is a trust, transfers to a trustor, trustee or beneficiary of the trust or to the estate of a beneficiary of such trust;
- (6) transfers to a partnership, limited liability company or other entity of which the securityholder or the immediate family of the securityholder are the legal and beneficial owner of all of the outstanding equity securities or similar interests;

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- (7) transfers to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible under clauses (1) through (6) above;
- (8) transfers by operation of law pursuant to a qualified domestic order, divorce settlement, divorce decree or domestic separation agreement;
- (9) transfers to us under which we have the option to repurchase securities upon the termination of service of the securityholder;
- (10) if the securityholder is a corporation, partnership, limited liability company, trust or other business entity, transfers (a) to another corporation, partnership, limited liability company, trust or other business entity that is an affiliate securityholder, or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control with the securityholder, or (b) as part of a distribution, transfer or disposition without consideration by the securityholder to its stockholders, partners, members or other equity holders;
- (11) transfers in transactions consisting of shares of our securities that the securityholder may purchase in open market transactions on or after the date of this prospectus;
- (12) the receipt by the securityholder from us of shares of our common stock upon the exercise of options or the settlement of restricted stock units granted under a stock incentive plan or other equity award plan;
- (13) transfers (a) to us for the purposes of exercising on a “net exercise” or “cashless” basis options or other rights to purchase shares of our common stock and (b) in connection with the vesting or settlement of restricted stock units, any transfer to us for the payment of tax withholdings or remittance payments due as a result of the vesting or settlement of such restricted stock units, in all such cases, pursuant to equity awards granted under a stock incentive plan or other equity award plan, which plan is described in this prospectus;
- (14) transfers pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction that is approved by our board of directors and made to all holders of our capital stock involving a change of control of our company;
- (15) in connection with the conversion or reclassification of our outstanding preferred stock or other classes of common stock into shares of our common stock; and
- (16) the establishment of a trading plan by the securityholder pursuant to Rule 10b5-1 under the Exchange Act, provided such plan does not provide for the transfer of securities during the restricted period.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

We intend to apply to list our shares of common stock on the _____ under the trading symbol “ORIC.”

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option to purchase additional shares referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to

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purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the _____, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for shares of our common stock, or that the shares will trade in the public market at or above the initial public offering price.

Other relationships

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Selling restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Notice to prospective investors in the European Economic Area

In relation to each Member State of the European Economic Area (each a Member State), no shares have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the competent authority in that Member State, all in accordance with the Prospectus Regulation, except that offers of shares may be made to the public in that Member State at any time under the following exemptions under the Prospectus Regulation:

- (1) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- (2) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters; or
- (3) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and us that it is a “qualified investor” within the meaning of Article 2(e) of the Prospectus Regulation. In the case of any shares being offered to a financial intermediary as that term is used in the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Member State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an “offer to the public” in relation to shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Notice to prospective investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Regulation) (1) who have professional experience in matters relating to investments falling within

Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the Order), and/or (2) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000, as amended.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to prospective investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to prospective investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX), or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to prospective investors in the Dubai International Financial Centre

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority (DFSA). This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial advisor.

In relation to its use in the Dubai International Financial Centre (DIFC), this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

Notice to prospective investors in the United Arab Emirates

The shares have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Notice to prospective investors in Australia

This prospectus:

- does not constitute a disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the Corporations Act);
- has not been, and will not be, lodged with the Australian Securities and Investments Commission (ASIC), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document for the purposes of the Corporations Act; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, available under section 708 of the Corporations Act (Exempt Investors).

The shares may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the

exemptions in section 708 applies to that resale. By applying for the shares you undertake to us that you will not, for a period of 12 months from the date of issue of the shares, offer, transfer, assign or otherwise alienate those shares to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Notice to prospective investors in Japan

The shares have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any “resident” of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to prospective investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (1) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (the SFO), of Hong Kong and any rules made thereunder; or (2) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong (the CO), or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Notice to prospective investors in Singapore

Each representative has acknowledged that this prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each representative has represented and agreed that it has not offered or sold any shares or caused the shares to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares or cause the shares to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares, whether directly or indirectly, to any person in Singapore other than:

- (1) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the SFA)) pursuant to Section 274 of the SFA;
- (2) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or
- (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

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Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (1) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (2) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- (b) where no consideration is or will be given for the transfer;
- (c) where the transfer is by operation of law;
- (d) as specified in Section 276(7) of the SFA; or
- (e) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of the shares, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the shares are “prescribed capital markets products” (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Notice to prospective investors in Bermuda

Shares may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

Notice to prospective investors in Saudi Arabia

This document may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority (CMA) pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended. The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser.

Notice to prospective investors in the British Virgin Islands

The shares are not being, and may not be offered to the public or to any person in the British Virgin Islands for purchase or subscription by or on behalf of us. The shares may be offered to companies incorporated under the BVI Business Companies Act, 2004 (British Virgin Islands) (BVI Companies), but only where the offer will be made to, and received by, the relevant BVI Company entirely outside of the British Virgin Islands.

Notice to prospective investors in China

This prospectus will not be circulated or distributed in the PRC and the shares will not be offered or sold, and will not be offered or sold to any person for re-offering or resale directly or indirectly to any residents of the PRC except pursuant to any applicable laws and regulations of the PRC. Neither this prospectus nor any advertisement or other offering material may be distributed or published in the PRC, except under circumstances that will result in compliance with applicable laws and regulations.

Notice to prospective investors in Korea

The shares have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder (the FSCMA), and the shares have been and will be offered in Korea as a private placement under the FSCMA. None of the shares may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder (the FETL). The shares have not been listed on any of the securities exchanges in the world including, without limitation, the Korea Exchange in Korea. Furthermore, the purchaser of the shares shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the shares. By the purchase of the shares, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the shares pursuant to the applicable laws and regulations of Korea.

Notice to prospective investors in Malaysia

No prospectus or other offering material or document in connection with the offer and sale of the shares has been or will be registered with the Securities Commission of Malaysia (or Commission), for the Commission's approval pursuant to the Capital Markets and Services Act 2007. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Malaysia other than (1) a closed end fund approved by the Commission; (2) a holder of a Capital Markets Services License; (3) a person who acquires the shares, as principal, if the offer is on terms that the shares may only be acquired at a consideration of not less than RM250,000 (or its equivalent in foreign currencies) for each transaction; (4) an individual whose total net personal assets or total net joint assets with his or her spouse exceeds RM3 million (or its equivalent in foreign currencies), excluding the value of the primary residence of the individual; (5) an individual who has a gross annual income exceeding RM300,000 (or its equivalent in foreign currencies) per annum in the preceding twelve months; (6) an individual who, jointly with his or her spouse, has a gross annual income of RM400,000 (or its equivalent in foreign currencies), per annum in the preceding twelve months; (7) a corporation with total net assets exceeding RM10 million (or its equivalent in a foreign currencies) based on the last audited accounts; (8) a partnership with total net assets exceeding RM10 million (or its equivalent in foreign currencies); (9) a bank licensee or insurance licensee as defined in the Labuan Financial Services and Securities Act 2010; (10) an Islamic bank licensee or takaful licensee as defined in the Labuan Financial Services and Securities Act 2010; and (11) any

other person as may be specified by the Commission; provided that, in the each of the preceding categories (1) to (11), the distribution of the shares is made by a holder of a Capital Markets Services License who carries on the business of dealing in securities. The distribution in Malaysia of this prospectus is subject to Malaysian laws. This prospectus does not constitute and may not be used for the purpose of public offering or an issue, offer for subscription or purchase, invitation to subscribe for or purchase any securities requiring the registration of a prospectus with the Commission under the Capital Markets and Services Act 2007.

Notice to prospective investors in Taiwan

The shares have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through a public offering or in circumstances which constitutes an offer within the meaning of the Securities and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorized to offer, sell, give advice regarding or otherwise intermediate the offering and sale of the shares in Taiwan.

Notice to prospective investors in South Africa

Due to restrictions under the securities laws of South Africa, no “*offer to the public*” (as such term is defined in the South African Companies Act, No. 71 of 2008 (as amended or re-enacted) (the South African Companies Act)) is being made in connection with the issue of the shares in South Africa. Accordingly, this document does not, nor is it intended to, constitute a “*registered prospectus*” (as that term is defined in the South African Companies Act) prepared and registered under the South African Companies Act and has not been approved by, and/or filed with, the South African Companies and Intellectual Property Commission or any other regulatory authority in South Africa. The shares are not offered, and the offer shall not be transferred, sold, renounced or delivered, in South Africa or to a person with an address in South Africa, unless one or other of the following exemptions stipulated in Section 96(1) applies:

Section 96(1)(a) the offer, transfer, sale, renunciation or delivery is to:

- (1) persons whose ordinary business, or part of whose ordinary business, is to deal in securities, as principal or agent;
- (2) the South African Public Investment Corporation;
- (3) persons or entities regulated by the Reserve Bank of South Africa;
- (4) authorised financial service providers under South African law;
- (5) financial institutions recognised as such under South African law;
- (6) a wholly-owned subsidiary of any person or entity contemplated in (3), (4) or (5), acting as agent in the capacity of an authorized portfolio manager for a pension fund, or as manager for a collective investment scheme (in each case duly registered as such under South African law); or
- (7) any combination of the persons in (1) to (6); or

Section 96(1)(b) the total contemplated acquisition cost of the securities, for a single addressee acting as principal is equal to or greater than ZAR1,000,000 or such higher amount as may be promulgated by notice in the Government Gazette of South Africa pursuant to section 96(2)(a) of the South African Companies Act.

Information made available in this prospectus should not be considered as “advice” as defined in the South African Financial Advisory and Intermediary Services Act, 2002.

Legal matters

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Certain members of, and investment partnerships comprised of members of, and persons associated with, Wilson Sonsini Goodrich & Rosati, Professional Corporation, own an aggregate of 100,000 shares of our common stock. Cooley LLP, San Diego, California, is acting as counsel for the underwriters.

Experts

The financial statements of ORIC Pharmaceuticals, Inc. as of December 31, 2017 and 2018, and for each of the years in the two-year period ended December 31, 2018, have been included herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, appearing elsewhere herein, and upon the authority of said firm as experts in accounting and auditing.

Where you can find additional information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, as permitted by the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document is not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The SEC also maintains an Internet website that contains the registration statement of which this prospectus forms a part, as well as the exhibits thereto. These documents, along with future reports, proxy statements and other information about us, are available at the SEC's website, www.sec.gov.

As a result of this offering, we will become subject to the information and reporting requirements of the Exchange Act and, in accordance with this law, will file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the SEC's public reference facilities and the website of the SEC referred to above. We also maintain a website at www.oricpharma.com where these materials are available. Upon the completion of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on, or that can be accessible through, our website is not a part of this prospectus and the inclusion of our website address in this prospectus is an inactive textual reference only.

ORIC Pharmaceuticals, Inc.

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Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
ORIC Pharmaceuticals, Inc.:

Opinion on the Financial Statements

We have audited the accompanying balance sheets of ORIC Pharmaceuticals, Inc. (the Company) as of December 31, 2017 and 2018, the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' deficit, and cash flows for each of the years in the two-year period ended December 31, 2018, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2018, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

KPMG LLP

We have served as the Company's auditor since 2018.

San Diego, California

September 24, 2019, except for earnings per share and Note 2(q), as to which the date is December 13, 2019

ORIC Pharmaceuticals, Inc.

Balance sheets

(in thousands, except per share amounts)

	December 31,	
	2017	2018
Assets		
Current assets:		
Cash and cash equivalents	\$ 25,819	\$ 42,636
Prepaid expenses and other current assets	791	1,088
Total current assets	26,610	43,724
Property and equipment, net	2,902	2,514
Other assets	513	496
Total assets	\$ 30,025	\$ 46,734
Liabilities, Convertible Preferred Stock and Stockholders' Deficit		
Current liabilities:		
Accounts payable	\$ 940	\$ 446
Accrued other liabilities	1,670	2,150
Total current liabilities	2,610	2,596
Deferred rent—long term	1,689	1,251
Other liabilities—long term	—	47
Total liabilities	4,299	3,894
Commitments and contingencies (See Note 8)		
Convertible preferred stock:		
Series A convertible preferred stock, \$0.0001 par value; 15,450 authorized, issued and outstanding at December 31, 2017 and 2018; aggregate liquidation preference of \$15,450 at December 31, 2017 and 2018	15,431	15,431
Series B convertible preferred stock, \$0.0001 par value; 27,000 shares authorized, issued and outstanding at December 31, 2017 and 2018; aggregate liquidation preference of \$54,000 at December 31, 2017 and 2018	53,906	53,906
Series C convertible preferred stock, \$0.001 par value; 0 and 20,000 shares authorized at December 31, 2017 and 2018, respectively; 0 and 12,709 shares issued and outstanding at December 31, 2017 and 2018, respectively; aggregate liquidation preference of \$0 and \$38,127 at December 31, 2017 and 2018, respectively	—	37,929
Stockholders' deficit:		
Common stock, \$0.0001 par value; 55,000 and 81,000 shares authorized at December 31, 2017 and 2018, respectively; 6,688 and 7,209 shares issued and outstanding at December 31, 2017 and 2018, respectively	1	1
Additional paid-in capital	832	1,380
Accumulated deficit	(44,444)	(65,807)
Total stockholders' deficit	(43,611)	(64,426)
Total liabilities, convertible preferred stock and stockholders' deficit	\$ 30,025	\$ 46,734

See accompanying notes to financial statements

ORIC Pharmaceuticals, Inc.

Statements of operations and comprehensive loss

(in thousands, except per share amounts)

	Year ended December 31,	
	2017	2018
Operating expenses:		
Research and development	\$ 19,126	\$ 19,026
General and administrative	3,415	3,345
Total operating expenses	22,541	22,371
Loss from operations	(22,541)	(22,371)
Other income:		
Interest income, net	251	775
Other income	261	233
Total other income	512	1,008
Net loss and comprehensive loss	\$ (22,029)	\$ (21,363)
Net loss per share, basic and diluted	\$ (3.90)	\$ (3.08)
Weighted-average shares outstanding, basic and diluted	5,642	6,936
Pro forma net loss per share, basic and diluted (unaudited)		\$ (0.35)
Pro forma weighted-average shares outstanding, basic and diluted (unaudited)		60,629

See accompanying notes to financial statements

ORIC Pharmaceuticals, Inc.

Statements of convertible preferred stock and stockholders' deficit

(in thousands)

	Series A convertible preferred stock		Series B convertible preferred stock		Series C convertible preferred stock		Common stock		Additional paid-in capital	Accumulated deficit	Total stockholders' deficit
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at January 1, 2017	15,450	\$ 15,431	27,000	\$ 53,906	—	\$ —	4,588	\$ 1	\$ 355	\$ (22,415)	\$ (22,059)
Exercise of stock options	—	—	—	—	—	—	2,100	—	260	—	260
Stock-based compensation expense	—	—	—	—	—	—	—	—	217	—	217
Net loss	—	—	—	—	—	—	—	—	—	(22,029)	(22,029)
Balance at December 31, 2017	15,450	15,431	27,000	53,906	—	—	6,688	1	832	(44,444)	(43,611)
Issuance of Series C Preferred Stock, Net of issuance cost of \$198	—	—	—	—	12,709	37,929	—	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	521	—	79	—	79
Stock-based compensation expense	—	—	—	—	—	—	—	—	469	—	469
Net loss	—	—	—	—	—	—	—	—	—	(21,363)	(21,363)
Balance at December 31, 2018	15,450	\$ 15,431	27,000	\$ 53,906	12,709	\$ 37,929	7,209	\$ 1	\$ 1,380	\$ (65,807)	\$ (64,426)

See accompanying notes to financial statements

ORIC Pharmaceuticals, Inc.

Statements of cash flows

(in thousands)

	Year ended December 31,	
	2017	2018
Cash flows from operating activities:		
Net loss	\$ (22,029)	\$ (21,363)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	851	903
Stock-based compensation expense	217	469
Loss on fixed asset disposal	34	15
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	89	(297)
Accounts payable and accrued other liabilities	6	(410)
Net cash used in operating activities	(20,832)	(20,683)
Cash flows from investing activities:		
Acquisitions of property and equipment	(486)	(525)
Proceeds from notes receivable	194	17
Net cash used in operating activities	(292)	(508)
Cash flows from financing activities:		
Proceeds from stock option exercises	260	79
Proceeds from issuance of preferred stock, net of issuance costs	—	37,929
Net cash provided by financing activities	260	38,008
Net (decrease) increase in cash	(20,864)	16,817
Cash and cash equivalents at the beginning of the year	46,683	25,819
Cash and cash equivalents at the end of the year	\$ 25,819	\$ 42,636

See accompanying notes to financial statements

ORIC Pharmaceuticals, Inc.

Notes to financial statements

(1) Organization and basis of presentation

(a) Organization and nature of operations

ORIC Pharmaceuticals, Inc. ("ORIC" or the "Company") was incorporated Delaware in August 2014 and is headquartered in South San Francisco, California. The Company is a clinical-stage biopharmaceutical company dedicated to improving patients' lives by *Overcoming Resistance In Cancer*.

Since inception, the Company has devoted its primary effort to raising capital and research and development activities and has incurred losses and negative cash flows from operations. The Company had an accumulated deficit of \$65.8 million and cash and cash equivalents of \$42.6 million at December 31, 2018. Through 2018, all of the Company's financial support has been provided primarily from the sale of its convertible preferred stock.

As the Company continues its expansion, it may seek additional financing and/or strategic investments, however, there can be no assurance that any additional financing or strategic investments will be available to the Company on acceptable terms, if at all. If events or circumstances occur such that the Company does not obtain additional funding, it will most likely be required to reduce its plans and/or certain discretionary spending, which could have a material adverse effect on the Company's ability to achieve its intended business objectives. The accompanying financial statements do not include any adjustments that might be necessary if it were unable to continue as a going concern. Management believes that its capital resources including the proceeds received from the Series convertible C and D preferred stock issuances (see Note 10), will be sufficient to fund the Company's operations for at least twelve months after the date the financial statements for the period ended December 31, 2018 are issued.

(b) Basis of presentation

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP").

(2) Summary of significant accounting policies

(a) Use of estimates

The preparation of the Company's financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities, expenses, and the disclosure of contingent assets and liabilities in the Company's financial statements and accompanying notes. Accounting estimates and management judgments reflected in the financial statements include: normal recurring accruals; valuation of deferred tax assets, including valuation allowances; fair value of common stock and preferred stock; stock-based compensation; and useful lives of long-lived assets. Although these estimates are based on the Company's knowledge of current events and actions it may undertake in the future, actual results may materially differ from these estimates and assumptions.

(b) Concentration of credit risk

Financial instruments, which potentially subject the Company to concentration of credit risk, consist primarily of cash deposits. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has not experienced any losses on deposits since inception.

(c) Fair value of financial instruments

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value, and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is defined as an exit price representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability.

The carrying amounts of cash, prepaid expenses, accounts payable and accrued other liabilities are reasonable estimates of their fair value because of the short maturity of these items.

(d) Cash and cash equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. Cash equivalents primarily represent funds invested in readily available checking and money market accounts. As of December 31, 2017 and 2018, the Company had cash balances deposited at major financial institutions.

(e) Prepaid expenses

Any expenses paid prior to the related services rendered are recorded as prepaid expenses. Such prepaid expenses are reconciled and expensed in the period the expense is incurred. If the expense is for a service covering multiple periods, it is expensed from the date the services begin and over the period of the service rendered (or contract service period if services rendered dates are not defined). Prepaid expenses include subscriptions, licenses, research and development contracts and insurance.

(f) Property and equipment

Property and equipment, which consist of lab equipment, leasehold improvements, computer hardware and software, and furniture and fixtures which are stated at historical cost. Depreciation is recognized on a straight-line basis over the estimated useful lives of the related assets, which are generally three to seven years. Leasehold improvements are amortized using the straight-line method over the shorter of the lease term or the estimate useful life of the asset. The Company recorded \$0.9 million of depreciation expense for each of the years ended December 31, 2017 and 2018.

(g) Impairment of property and equipment

The Company accounts for the impairment of long-lived assets by reviewing these assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. If circumstances require a long-lived asset or asset group to be tested for possible impairment, the Company first compares undiscounted cash flows expected to be generated by that asset or asset group to its carrying value. If the carrying value of the long-lived asset or asset group is not recoverable on an undiscounted-cash-flow basis, an impairment is recognized to the extent that the carrying value exceeds its fair value. The Company did not recognize impairment losses for the years ended December 31, 2017 and 2018.

(h) Deferred rent

Deferred rent consists of the difference between cash payments and the recognition of rent expense on a straight-line basis for the office facility the Company leases. The Company's lease for its facility provides for

fixed increases in minimum annual rental payments. The total amount of rental payments due over the lease term are being charged to rent expense ratably over the life of the leases.

(i) Accrued research and development expenses

The Company is required to estimate its expenses resulting from its obligations under contracts with vendors, consultants and contract research organizations, in connection with conducting research and development activities. The financial terms of these contracts vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts.

The Company reflects research and development expenses in its financial statements by matching those expenses with the period in which services and efforts are expended. The Company accounts for these expenses according to the progress of the preclinical study or clinical trial as measured by the timing of various aspects of the study or related activities. The Company determines accrual estimates through review of the underlying contracts along with discussions with research and other key personnel as to the progress of studies or trials, or other services being conducted. During the course of a study or trial, the Company adjusts its rate of expense recognition if actual results differ from its estimates.

(j) Research and development expenses

Research and development costs are expensed in the periods in which they are incurred. External costs consist primarily payments to outside consultants, CROs, CMOs, clinical trial sites and central laboratories in connection with the Company's discovery and preclinical activities, process development, manufacturing and clinical development activities. External expenses are recognized based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its service providers or our estimate of the level of service that has been performed at each reporting date. The Company allocates external costs by the stage of program, clinical or preclinical. Internal costs consist primary of employee-related costs, laboratory supplies, facilities, depreciation and costs related to compliance with regulatory requirements. The Company does not allocate internal costs by stage of program because these costs are deployed across multiple programs and, as such, are not separately classified. Research and development expenses amounted to \$19.1 million and \$19.0 million during the years ended December 31, 2017 and 2018, respectively.

(k) Commitments and contingencies

The Company recognizes a liability with regard to loss contingencies when it believes it is probable a liability has occurred, and the amount can be reasonably estimated. If some amount within a range of loss appears at the time to be a better estimate than any other amount within the range, the Company accrues that amount. When no amount within the range is a better estimate than any other amount the Company accrues the minimum amount in the range. The Company has not recorded any such liabilities as of December 31, 2017 and 2018.

(l) Income taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

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The Company recognizes deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

As of December 31, 2017 and 2018, the Company maintained valuation allowances against its deferred tax assets as the Company concluded it had not met the “more likely than not” to be realized threshold. Changes in the valuation allowance when they are recognized in the provision for income taxes would result in a change in the estimated annual effective tax rate.

(m) Stock-based compensation

Stock-based compensation expense represents the cost of the grant date fair value of employee, officer, director and non-employee stock option grants, estimated in accordance with the applicable accounting guidance, recognized on a straight-line basis over the vesting period. The vesting period generally approximates the expected service period of the awards. The Company recognizes forfeitures as they occur.

The fair value of stock options is estimated using a Black-Scholes Merton valuation model on the date of grant. This method requires certain assumptions be used as inputs, such as the fair value of the underlying common stock, a risk-free interest rate, expected volatility of the Company's common stock, expected term of the option before exercise and expected dividend yield. Options granted have a maximum contractual term of ten years. The risk-free interest rates used are based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. treasury notes with maturities approximately equal to the expected term of the stock options. The expected volatility of stock options is based upon the historical volatility of a number of publicly traded companies in similar stages of clinical development. The Company has limited historical stock option activity and therefore estimates the expected term of stock options granted using the simplified method, which represents the average of the contractual term of the stock option and its weighted-average vesting period. The Company has historically not declared or paid any dividends and does not currently expect to do so in the foreseeable future.

(n) Common stock valuation

Due to the absence of an active market for the Company's common stock, the Company utilized methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants Audit and Accounting Practice Aid Series: *Valuation of Privately Held Company Equity Securities Issued as Compensation* to estimate the fair value of its common stock. In determining the exercise prices for options granted, the Company has considered the fair value of the common stock as of the grant date. The fair value of the common stock has been determined based upon a variety of factors, including the Company's financial position, historical and forecasted performance and operating results, the Company's stage of development, the progress of the Company's research and development programs, the prices at which the Company sold its convertible preferred stock, the superior rights, preferences and privileges of the Company's convertible preferred stock relative to its common stock, external market conditions affecting the biotechnology industry, the lack of marketability of the Company's common stock and the prospects of a liquidity event and the analysis of initial public offering and market performance of similar companies as well as recently completed mergers and acquisitions of peer companies. Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date.

(o) Deferred offering costs

The Company capitalizes costs that are directly associated with in-process equity financings until such financings are consummated at which time such costs are recorded against the gross proceeds of the offering. Should an in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the statement of operations and comprehensive loss. No deferred offering costs were capitalized as of December 31, 2017 and 2018.

(p) Comprehensive loss

Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources, including unrealized gains and losses on investments and foreign currency gains and losses. Net loss and comprehensive loss were the same for all periods presented.

(q) Net loss per share and unaudited pro forma net loss per share

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares and potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share calculation, the convertible preferred stock and common stock options are considered to be potentially dilutive securities. Basic and diluted net loss attributable to common stockholders per share is presented in conformity with the two-class method required for participating securities as the convertible preferred stock is considered a participating security. The Company's participating securities do not have a contractual obligation to share in the Company's losses. As such, the net loss was attributed entirely to common stockholders. As the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods.

The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders (in thousands, except per share amounts).

	Year ended December 31,	
	2017	2018
Numerator		
Net loss attributable to common stockholders	\$ (22,029)	\$ (21,363)
Denominator		
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted	5,642	6,936
Net loss per share attributable to common stockholders, basic and diluted	\$ (3.90)	\$ (3.08)

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The following outstanding shares of potentially dilutive securities were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented because including them would have been anti-dilutive (in thousands):

	Year ended December 31,	
	2017	2018
Options to purchase common stock	1,711	7,420
Convertible preferred stock	42,450	55,159
Total	44,161	62,579

Unaudited pro forma net loss per share

Unaudited pro forma basic and diluted net loss per share is calculated to give effect to the one-for-one conversion of all outstanding shares of the Company's convertible preferred stock into shares of common stock in using the as-converted method as though the conversion had occurred as of the beginning of the period presented or the date of issuance, if later.

The following table sets forth the computation of the basic and diluted unaudited pro forma net loss per share (in thousands, except per share amounts):

	Year ended December 31,	
	2018	
Numerator		
Pro forma net loss	\$	(21,363)
Denominator		
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted		6,936
Adjust: Conversion of convertible preferred stock		53,693
Weighted-average shares outstanding used in computing pro forma net loss per share, basic and diluted		60,629
Pro forma net loss per share, basic and diluted	\$	(0.35)

(r) Recently issued accounting standards

In March 2016, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") 2016-09, *Improvements to Employee Share-Based Payment Accounting*, which involves several aspects of the accounting for stock-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. This guidance requires all income tax effects of awards to be recognized as income tax expense or benefit in the income statement when the awards vest or are settled, as opposed to additional paid-in-capital. It also will allow an employer to repurchase more of an employee's shares than it can today for tax withholding purposes without triggering liability accounting. All tax-related cash flows resulting from stock-based payments are to be reported as operating activities on the statement of cash flows. The guidance also allows a Company to make a policy election to either estimate the number of awards that are expected to vest or account for forfeitures as they occur. The standard is effective for annual reporting periods beginning after December 15, 2017 for nonpublic entities, with early adoption permitted. The Company adopted the guidance for the year ended December 31, 2018. There was no material impact to the financial statements due to the adoption of ASU 2016-09.

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In March 2016, the FASB issued ASU 2016-02, *Leases*. The new standard establishes a right-of-use (“ROU”) model that requires a lessee to record a ROU asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the statements of operations. The standard is effective for fiscal years beginning after December 15, 2019. A modified retrospective transition approach is required for lessees for capital and operating leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements, with certain practical expedients available. The Company is currently evaluating the impact that this standard will have on its financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments*, which clarifies the treatment of several cash flow categories. In addition, ASU 2016-15 clarifies that when cash receipts and cash payments have aspects of more than one class of cash flows and cannot be separated, classification will depend on the predominant source or use. For nonpublic business entities, this update is effective for annual periods beginning after December 15, 2018, with early adoption permitted. The adoption of this standard is not expected to have a material impact on the Company’s financial statements.

(3) Property and equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2017	2018
Lab equipment	\$ 2,710	\$ 3,166
Leasehold improvements	1,710	1,710
Computer hardware and software	135	144
Furniture and fixtures	42	72
Total property and equipment, gross	4,597	5,092
Less accumulated depreciation	(1,695)	(2,578)
Total property and equipment, net	\$ 2,902	\$ 2,514

(4) Accrued other liabilities

Accrued other liabilities consisted of the following (in thousands):

	December 31,	
	2017	2018
Accrued compensation	\$ 834	\$ 917
Deferred rent—short term	388	438
Share purchase liability	175	115
Other accruals	273	680
Total accrued other liabilities	\$1,670	\$2,150

(5) Stockholders’ equity

Under its Amended and Restated Articles of Incorporation dated February 5, 2018, the Company had a total of 143,450,000 shares of capital stock authorized for issuance, consisting of 81,000,000 shares of common stock, par value of \$0.0001 per share, and 62,450,000 shares of convertible preferred stock, par value of \$0.0001 per

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share. Shares of authorized convertible preferred stock are designated as 15,450,000 shares of Series A convertible preferred stock, 27,000,000 shares of Series B convertible preferred stock and 20,000,000 shares of Series C convertible preferred stock.

(a) Series A convertible preferred stock

In 2014 and 2015, the Company issued 15,450,000 shares of Series A convertible preferred stock in a private offering in exchange for net proceeds of \$15.4 million. The purchase price for the Series A convertible preferred stock was \$1.00 per share. No Series A convertible preferred stock was issued during the years end December 31, 2017 and 2018.

(b) Series B convertible preferred stock

In 2015 and 2016, the Company issued 27,000,000 shares of Series B convertible preferred stock in a private offering in exchange for net proceeds of \$53.9 million. The purchase price for the Series B convertible preferred stock was \$2.00 per share. No Series B convertible preferred stock was issued during the years end December 31, 2017 and 2018.

(c) Series C convertible preferred stock

In 2018, the Company issued 12,709,099 shares of Series C convertible preferred stock in a private offering for net proceeds of \$37.9 million. The purchase price for the Series C convertible stock was \$3.00 per share. Under the terms of the preferred stock agreement, investors are obligated to purchase an additional 5,086,054 shares in February 2019 of Series C convertible stock at \$3.00 per share (see note 10).

(d) Common stock

As of December 31, 2017 and 2018, of the authorized 55,000,000 and 81,000,000 shares of common stock, 6,688,349 and 7,208,526 shares were issued and outstanding, respectively. The fair value of the Company's common stock was \$0.26 and \$0.40 as of December 31, 2017, and 2018, respectively, and was determined in part on third-party valuations.

The voting, dividend, and liquidation rights of the holders of the common stock are subject to, and qualified by, the rights, powers, and preferences of the holders of the convertible preferred stock. The holders of the common stock are entitled to one vote for each share of common stock held at all meetings of stockholders.

The Series A, B and C convertible preferred stock has been classified as temporary equity in the accompanying balance sheets given that a majority of the Company's Board of Directors seats are held by convertible preferred stock holders and could cause certain events to occur that are outside of the Company's control whereby the Company could be obligated to redeem the convertible preferred stock. The Company has not adjusted the carrying values of the convertible preferred stock to the respective liquidation preferences of such shares as the instruments are currently not redeemable and the Company believes it is not probable that the instruments will become redeemable at this point in time. Adjustments to increase the carrying values to the respective liquidation preferences will be made if and when it becomes probable that an event would occur obligating the Company to pay such amounts.

The Company's convertible preferred stock has the following characteristics:

(1) Dividends

Holders of the Series A, Series B and Series C convertible preferred stock, in preference to any distributions to the holders of common stock, shall be entitled to receive dividends at an annual rate of \$0.08 per share for the

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Series A convertible preferred stock holders, \$0.16 per share for the Series B convertible preferred stock holders and \$0.24 per share for the Series C convertible preferred stock holders. Such dividends shall be payable only when and if declared by the Company's Board of Directors and shall not be cumulative.

No such dividends have been declared or paid through December 31, 2018.

(2) Liquidation

The holders of the Series A, Series B and Series C convertible preferred stock are entitled to receive liquidation preferences at the Series A, Series B and Series C original issue prices of \$1.00, \$2.00 and \$3.00, respectively, plus all accrued and declared but unpaid dividends. Liquidation payments to the holders of the Series A, Series B and Series C convertible preferred stock have priority and are made in preference to any payments to the holders of common stock.

After full payment of the liquidation preference to the holders of the Series A Series B and Series C convertible preferred stock, the remaining assets, if any, will be distributed ratably to the holders of the common stock.

(3) Conversion rights

The shares of Series A, Series B and Series C convertible preferred stock are convertible into an equal number of shares of common stock, at the option of the holder, subject to certain anti-dilution adjustments. The conversion rate for the convertible preferred stock is determined by dividing the original issue price, as adjusted for stock splits, by the conversion price. The conversion price is initially the original issue prices, but is subject to adjustment for dividends, stock splits, and other distributions. The conversion rate at December 31, 2018 for the Series A, Series B and Series C convertible preferred stock is 1:1.

Each share of Series A, Series B and Series C convertible preferred stock are automatically converted into common stock at the then effective conversion rate (a) at any time upon the affirmative election of the holders of at least a majority of the outstanding shares of the Series A, Series B and Series C convertible preferred stock or (b) immediately upon the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common stock for the account of the Company in which (i) the public offering price represents a pre-money valuation of at least \$310 million and (ii) the gross cash proceeds to the Company are at least \$40 million.

(4) Redemption rights

The holders of Series A, Series B and Series C convertible preferred stock do not have any redemption rights.

(5) Voting

The holder of each share of Series A, Series B and Series C convertible preferred stock are entitled to one vote for each share of common stock into which it would convert and to vote as one class with the common stockholders on all matters.

(6) Stock-based compensation

(a) Stock option plan

In October 2014, the Company approved the 2014 Equity Incentive Plan (the "2014 Plan"). The 2014 Plan provides for the issuance of 12,263,926 shares of common stock to officers, directors, employees,

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non-employee directors, and consultants of the Company. The 2014 Plan allows for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock unit awards and other stock awards. As of December 31, 2018, there were 1,085,959 options remaining available for future issuance under the 2014 Plan.

The options that are granted from the 2014 Plan are exercisable at various dates as determined upon grant and will expire no more than ten years from their date of grant, or in the case of certain non-statutory options, ten years from the date of grant. Stock options generally vest over a four-year term. The exercise price of each option shall be determined by the Company's Board of Directors, although generally options have an exercise price equal to the fair market value of the Company's stock on the date of the option grant. In the case of incentive stock options, the exercise price shall not be less than 100% of the fair market value of the Company's common stock at the time the option is granted. For holders of more than 10% of the Company's total combined voting power of all classes of stock, incentive stock options may not be granted at less than 110% of the fair market value of the Company's common stock at the date of grant and for a term not to exceed five years.

The following table summarizes the option activity:

	Options	Weighted-average exercise price	Weighted-average remaining contractual term (in years)	Aggregate intrinsic value (in thousands)
Outstanding at January 1, 2018	1,710,966	\$ 0.15	8.2	
Granted	8,479,380	0.40	9.4	
Exercised	(520,177)	0.14	6.9	
Cancelled	(2,250,626)	0.37	9.0	
Outstanding at December 31, 2018	7,419,543	\$ 0.37	9.2	\$ 232
Exercisable at December 31, 2018	1,510,553	\$ 0.33	8.8	\$ 99

All exercisable options are vested and all outstanding options are vested or expected to vest. The aggregate intrinsic value of stock options exercised during the year December 31, 2018 was \$0.1 million.

Certain individuals were granted the ability to early exercise their stock options. The shares of common stock issued from the early exercise of unvested stock options are restricted and continue to vest in accordance with the original vesting schedule. The Company has the option to repurchase any unvested shares at the original purchase price upon any voluntary or involuntary termination. The shares purchased by the employees and non-employees pursuant to the early exercise of stock options are not deemed, for accounting purposes, to be outstanding until those shares vest. The cash received in exchange for exercised and unvested shares related to stock options granted is recorded as a liability for the early exercise of stock options on the accompanying balance sheets and will be transferred into common stock and additional paid-in capital as the shares vest. As of December 31, 2017, and 2018, there were 1,131,966 and 487,214 shares subject to repurchase by the Company, respectively. As of December 31, 2017, and 2018, the Company recorded \$0.2 million and \$0.1 million of liabilities associated with shares issued with repurchase rights, respectively.

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The fair value of stock options was estimated using the Black-Scholes Merton option pricing model with the following assumptions:

	Year ended December 31,	
	2017	2018
Stock price	\$ 0.26	\$ 0.40
Risk-free interest rate	1.9% –	2.7% –
	2.1%	3.0%
Expected volatility	97% –	93% –
	98%	98%
Expected term (in years)		6.0 –
	6.1	6.1
Expected dividend yield	0%	0%

The Company recognized stock-based compensation expense of \$0.2 million and \$0.5 million for the years ended December 31, 2017 and 2018, respectively. The total unrecognized compensation expense related to outstanding unvested stock-based awards as of December 31, 2017 and 2018 was \$0.2 million and \$2.3 million, respectively, which is expected to be recognized over a weighted-average remaining service period of 2.55 and 3.34 years, respectively.

(b) Common stock reserved for future issuance

Common stock reserved for future issuance consisted of the following:

	Year ended December 31,	
	2017	2018
Convertible preferred stock	42,450,000	55,159,099
Common stock options granted and outstanding	1,710,966	7,419,543
Common stock reserved for future option grants	2,783,189	1,085,959
Total common stock reserved for future issuance	46,944,155	63,664,601

(7) Income taxes

Significant components of the Company's provision for income taxes and income taxes computed using the U.S. federal statutory corporate tax rate were as follows (in thousands):

	Year ended December 31,	
	2017	2018
Statutory rate	\$ (7,491)	\$ (4,487)
State tax	(1,264)	(1,465)
Other permanent items	4	(15)
Research and development credit	(247)	(663)
Change in valuation allowance	4,023	6,536
Impact of Tax Cuts and Jobs Act	4,945	—
Stock-based compensation	30	94
Provisions for income taxes	\$ —	\$ —

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Significant components of the Company's deferred taxes were as follows (in thousands):

	December 31,	
	2017	2018
Deferred tax assets:		
Net operating loss carryforward	\$ 11,706	\$ 17,353
Research and development credits	1,296	2,147
Deferred rent	581	491
Accruals and other	216	255
Gross deferred tax assets	13,799	20,246
Less valuation allowance	(13,374)	(19,910)
Total deferred tax assets	425	336
Deferred tax liabilities:		
Fixed assets	(425)	(336)
Net deferred tax assets	\$ —	\$ —

A valuation allowance of \$19.9 million at December 31, 2018 has been recognized to offset the net deferred tax assets as realization of such assets is uncertain. The valuation allowance increased by \$6.5 million during the year ended December 31, 2018.

As of December 31, 2017, the Company had available federal net operating loss ("NOL") carryforwards of \$41.6 million, which begin to expire in 2034. In addition, for the period of January 1 through December 31, 2018, the Company created federal NOL carryforwards of \$20.0 million which do not expire. The Company also has available California NOL carryforwards of approximately \$63.5 million as of December 31, 2018, which begin to expire in 2034.

The Tax Cuts and Jobs Act (the "Act") was enacted on December 22, 2017. The Act reduces the U.S. federal corporate tax rate from a maximum of 35% to 21%. At December 31, 2017, the Company completed its accounting for the tax effects of enactment of the Act. The Company remeasured certain deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which is generally 21%. The amount recorded related to the remeasurement of its deferred tax balance was \$4.9 million, which was fully offset by a reduction in the valuation allowance.

Pursuant to Sections 382 and 383 of the Internal Revenue Code ("IRC"), annual use of the Company's NOL and credit carryforwards may be limited in the event a cumulative change in ownership of more than 50% occurs within a three-year period. Since the Company's formation, the Company has raised capital through the issuance of capital stock, which on its own or combined with the purchasing stockholders' subsequent disposition of those shares, may have resulted in such an ownership change, or could result in an ownership change in the future.

Upon the occurrence of an ownership change under Section 382 as outlined above, utilization of the Company's NOL and research and development credit carryforwards are subject to an annual limitation, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, which could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the NOL or R&D credit carryforwards before utilization. The Company has not completed an analysis to determine if such an ownership change has occurred.

The Company recognizes liabilities for uncertain tax positions based in a two-step process. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is

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more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount that is more than 50% likely of being realized upon settlement. While the Company believes that it has appropriate support for the positions taken on its tax returns, the Company regularly assesses the potential outcome of examinations by tax authorities in determining the adequacy of its provision for income taxes.

The following table summarizes the activity related to the Company's gross unrecognized tax benefits (in thousands):

	December 31,	
	2017	2018
Beginning balance	\$ 177	\$ 347
Increases (decreases) related to prior year tax positions	—	—
Increases related too current year tax positions	170	210
Ending balance	\$ 347	\$ 557

As of December 31, 2018, the Company had gross unrecognized tax benefits of \$0.6 million, none of which would affect the effective tax rate if recognized. The Company does not anticipate any significant changes in its unrecognized tax benefits over the next 12 months. The Company's policy is to recognize the interest expense and/or penalties related to income tax matters as a component of income tax expense. The Company had no accrual for interest or penalties on its balance sheets at December 31, 2018 and has not recognized interest and/or penalties in its statement of operations for the year ended December 31, 2018.

The Company is subject to taxation in the United States and California. The Company is not currently under examination by any taxing authorities. Due to the carryover of tax attributes, the statute of limitations is currently open for tax years since inception.

(8) Commitments and contingencies

Operating lease

The Company leases certain office and lab space in South San Francisco, California under a non-cancelable operating lease, with a five-year term through May 2022, and an option to renew for an additional five-year term. Rent expense was \$1.4 million and \$1.5 million for the years ended December 31, 2017 and 2018, respectively, excluding the offset for amortization of the leasehold incentive obligation of \$0.1 million and \$0.2 million for the years ended December 31, 2017 and 2018, respectively.

The future minimum lease payments required under non-cancelable leases as of December 31, 2018 are summarized as follows (in thousands):

Year ending December 31,	
2019	\$1,712
2020	1,763
2021	1,816
2022	686
Total minimum lease payments	\$5,977

Litigation

The Company, from time to time, is involved in legal proceedings, regulatory actions, claims and litigation arising in the ordinary course of business. Currently, the Company is not a defendant in any lawsuit.

(9) Employee benefit plan

The Company has a defined-contribution 401(k) plan for employees. Employees are eligible to participate in the plan beginning on the first day of the month following date of hire. Under the terms of the plan, employees may make voluntary contributions as a percentage of compensation and the Company has the option to make a discretionary match as determined by the Company's Board of Directors, within prescribed limits. There were no employer contributions to the plan during the years ended December 31, 2017 or 2018.

(10) Subsequent events

The Company has evaluated subsequent events from the balance sheet date through September 24, 2019, the date the financial statements were available to be issued. Except as described below, the Company has concluded that no subsequent events have occurred that require disclosure.

In February 2019, an additional 5,086,054 shares of Series C convertible preferred stock were issued as part of the second tranche closing for \$3.00 per share, resulting in net proceeds of \$15.2 million. In June and July 2019, an aggregate of 16,869,345 shares of Series D convertible preferred stock were issued for \$3.30 per share, resulting in aggregate net proceeds of \$55.5 million.

In March 2019, the Company entered into a lease agreement with Plaza Del Mar LLC for 1,555 square feet of office space in San Diego, California. The lease expires April 30, 2020. During this period, the Company is committed to paying \$5,987 per month plus operating expenses.



Common stock

Prospectus

J.P. Morgan

Citigroup

Jefferies

Guggenheim Securities

, 2020

Part II

Information not required in the prospectus

Item 13. Other expenses of issuance and distribution

The following table sets forth the expenses to be incurred in connection with the offering described in this Registration Statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimates except the Securities and Exchange Commission (SEC) registration fee, the Financial Industry Regulatory Authority, Inc. (FINRA) filing fee and the listing fee.

	Amount paid or to be paid
SEC registration fee	\$ *
FINRA filing fee	*
listing fee	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees	*
Miscellaneous expenses	*
Total	\$ *

* To be provided by amendment.

Item 14. Indemnification of directors and officers

Section 145 of the Delaware General Corporation Law empowers a corporation to indemnify its directors and officers and to purchase insurance with respect to liability arising out of their capacity or status as directors and officers, provided that the person acted in good faith and in a manner the person reasonably believed to be in our best interests, and, with respect to any criminal action, had no reasonable cause to believe the person's actions were unlawful. The Delaware General Corporation Law further provides that the indemnification permitted thereunder shall not be deemed exclusive of any other rights to which the directors and officers may be entitled under the corporation's bylaws, any agreement, a vote of stockholders or otherwise. The certificate of incorporation of the registrant to be in effect upon the completion of this offering provides for the indemnification of the registrant's directors and officers to the fullest extent permitted under the Delaware General Corporation Law. In addition, the bylaws of the registrant to be in effect upon the completion of this offering require the registrant to fully indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) by reason of the fact that such person is or was a director or officer of the registrant, or is or was a director or officer of the registrant serving at the registrant's request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, to the fullest extent permitted by applicable law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except (1) for any breach of the director's duty of loyalty to the corporation or its stockholders, (2) for acts or omissions not in good faith or

which involve intentional misconduct or a knowing violation of law, (3) for payments of unlawful dividends or unlawful stock repurchases or redemptions or (4) for any transaction from which the director derived an improper personal benefit. The registrant's certificate of incorporation to be in effect upon the completion of this offering provides that the registrant's directors shall not be personally liable to it or its stockholders for monetary damages for breach of fiduciary duty as a director and that if the Delaware General Corporation Law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of the registrant's directors shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

Section 174 of the Delaware General Corporation Law provides, among other things, that a director who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock purchase or redemption may be held liable for such actions. A director who was either absent when the unlawful actions were approved, or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

As permitted by the Delaware General Corporation Law, the registrant has entered into separate indemnification agreements with each of the registrant's directors and executive officers which would require the registrant, among other things, to indemnify them against certain liabilities which may arise by reason of their status as directors or executive officers.

The registrant expects to obtain and maintain insurance policies under which its directors and officers are insured, within the limits and subject to the limitations of those policies, against certain expenses in connection with the defense of, and certain liabilities which might be imposed as a result of, actions, suits or proceedings to which they are parties by reason of being or having been directors or officers. The coverage provided by these policies may apply whether or not the registrant would have the power to indemnify such person against such liability under the provisions of the Delaware General Corporation Law.

These indemnification provisions and the indemnification agreements entered into between the registrant and the registrant's officers and directors may be sufficiently broad to permit indemnification of the registrant's officers and directors for liabilities (including reimbursement of expenses incurred) arising under the Securities Act of 1933, as amended.

The underwriting agreement between the registrant and the underwriters filed as Exhibit 1.1 to this registration statement provides for the indemnification by the underwriters of the registrant's directors and officers and certain controlling persons against specified liabilities, including liabilities under the Securities Act with respect to information provided by the underwriters specifically for inclusion in the registration statement. The investors' rights agreement with certain holders of our capital stock also provides for cross-indemnification in connection with the registration of the registrant's common stock on behalf of such holders.

Item 15. Recent sales of unregistered securities

The following list sets forth information regarding all unregistered securities sold by us since January 1, 2017. No underwriters were involved in the sales and the certificates representing the securities sold and issued contain legends restricting transfer of the securities without registration under the Securities Act or an applicable exemption from registration.

- (1) In February 2018, May 2018, and February 2019, we issued and sold an aggregate of 17,795,153 shares of our Series C preferred stock at a purchase price of \$3.00 per share for an aggregate purchase price of approximately \$53.4 million.

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- (2) In June 2019 and July 2019, we issued and sold an aggregate of 16,869,345 shares of our Series D preferred stock at a purchase price of \$3.30 per share for an aggregate purchase price of approximately \$55.7 million.
- (3) From January 1, 2017 through December 31, 2019, we granted stock options to purchase an aggregate of 13,533,880 shares of common stock upon the exercise of options under our 2014 Plan at exercise prices per share ranging from \$0.26 to \$2.29, for an aggregate exercise price of approximately \$11.2 million.
- (4) From January 1, 2017 through December 31, 2019, we issued and sold to certain service providers of ours an aggregate of 1,153,383 shares of common stock upon the exercise of options under our 2014 Plan at exercise prices per share ranging from \$0.10 to \$0.40, for an aggregate exercise price of approximately \$0.3 million.

The offers, sales and issuances of the securities described in Items 15(1), 15(2) and 15(3) were exempt from registration under the Securities Act under Section 4(a)(2) of the Securities Act or Regulation D promulgated thereunder as transactions by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited person and had adequate access, through employment, business or other relationships, to information about the registrant.

The offers, sales and issuances of the securities described in Items 15(4) and 15(5) were exempt from registration under the Securities Act under either (1) Rule 701 in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701 or (2) Section 4(a)(2) of the Securities Act as transactions by an issuer not involving any public offering. The recipients of such securities were the registrant's employees, consultants or directors and received the securities under our 2014 Plan. The recipients of securities in each of these transactions represented their intention to acquire the securities for investment only and not with view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions.

Item 16. Exhibit and financial statement schedules

(a) Exhibits.

See the Exhibit Index immediately preceding the signature page hereto for a list of exhibits filed as part of this registration statement on Form S-1, which Exhibit Index is incorporated herein by reference.

(b) Financial statement schedules.

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. Undertakings

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreements, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against

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public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b) (1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Exhibit index

Exhibit number	Description
1.1*	Form of Underwriting Agreement.
3.1**	Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect.
3.2*	Form of Amended and Restated Certificate of Incorporation of the Registrant, to be in effect upon the completion of this offering.
3.3**	Bylaws of the Registrant, as currently in effect.
3.4*	Form of Amended and Restated Bylaws of the Registrant, to be in effect upon the completion of this offering.
4.1**	Amended and Restated Investors' Rights Agreement by and among the Registrant and certain of its stockholders, dated June 4, 2019.
4.2*	Specimen common stock certificate of the Registrant.
5.1*	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.
10.1+*	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.
10.2+**	2014 Equity Incentive Plan, as amended, and forms of agreement thereunder.
10.3+*	2020 Equity Incentive Plan and forms of agreements thereunder, to be in effect upon the completion of this offering.
10.4+*	2020 Employee Stock Purchase Plan and forms of agreements thereunder, to be in effect upon the completion of this offering.
10.5+*	Employment Letter between the Registrant and Jacob Chacko, M.D.
10.6+*	Employment Letter between the Registrant and Pratik Multani, M.D.
10.7+*	Employment Letter between the Registrant and Dominic Piscitelli.
10.8+*	Executive Incentive Compensation Plan.
10.9+*	Change in Control and Severance Policy.
10.10+*	Outside Director Compensation Policy.
10.11**	Lease between the Registrant and Britannia Pointe Grand Limited Partnership, dated June 5, 2015.
23.1*	Consent of Independent Registered Public Accounting Firm.
23.2*	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).
24.1*	Power of Attorney (see page II-6 to this Form S-1).

* To be filed by amendment.

** Previously submitted.

+ Indicated management contract or compensatory plan.

Signatures

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, California on _____, 2020.

ORIC PHARMACEUTICALS, INC.

By: _____
Jacob Chacko, M.D.
President and Chief Executive Officer

Power of attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Jacob Chacko, M.D. and Dominic Piscitelli as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and substitution, for him or her and in his or her name, place and stead, in any and all capacities to sign any or all amendments (including post-effective amendments) to this registration statement and any and all additional registration statements pursuant to Rule 462(b) of the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as they, he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agents or any of them, or their, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
_____ Jacob Chacko, M.D.	President, Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	_____, 2020
_____ Dominic Piscitelli	Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	_____, 2020
_____ Richard Heyman, Ph.D.	Chair of the Board	_____, 2020
_____ Carl Gordon, Ph.D.	Director	_____, 2020
_____ Leo Guthart, D.B.A.	Director	_____, 2020
_____ Richard Scheller, Ph.D.	Director	_____, 2020
_____ Peter Svenilson	Director	_____, 2020