

---

---

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

---

**FORM 8-K**

---

**CURRENT REPORT  
Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): January 22, 2019**

---

**UROGEN PHARMA LTD.**

(Exact name of registrant as specified in its charter)

---

**Israel**  
(State or other jurisdiction  
of incorporation)

**001-38079**  
(Commission  
File Number)

**Not applicable**  
(IRS Employer  
Identification No.)

**499 Park Avenue**  
**New York, New York**  
(Address of principal executive offices)

**10014**  
(Zip Code)

**Registrant's telephone number, including area code: (646) 768-9780**

---

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligations of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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 13(a) of the Exchange Act.

---

---

## **Item 2.02 Results of Operations and Financial Condition.**

As of December 31, 2018, UroGen Pharma Ltd. had \$101.3 million of cash and cash equivalents. This financial result is preliminary, unaudited and subject to completion and may differ from what will be reflected in our audited consolidated financial statements as of and for the year ended December 31, 2018.

## **Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.**

On January 20, 2019, the Board of Directors of the Company, upon the recommendation of its Compensation Committee, approved the payment of cash performance bonuses of \$334,000 to Ron Bentsur, the Company's former Chief Executive Officer, \$100,000 to Mark Schoenberg, the Company's Chief Medical Officer, \$223,000 to Stephen Mullennix, the Company's Chief Operating Officer, and \$97,000 to Peter Pfreundschuh, the Company's Chief Financial Officer. The foregoing cash performance bonuses were awarded based on the achievement of 2018 corporate performance goals.

## **Item 8.01 Other Information.**

On January 22, 2019, UroGen Pharma Ltd. (the "Company") issued a press release (the "Press Release") announcing the commencement of a proposed public offering of \$150 million of its ordinary shares, par value NIS 0.01. A copy of the Press Release is attached as Exhibit 99.1 to this report.

The Company is also filing the information contained in Exhibit 99.2 for the purpose of updating certain aspects of the Company's publicly disclosed descriptions of its business and risk factors.

On January 22, 2019, the Company delivered written notice to Jefferies LLC ("Jefferies") that it was suspending and terminating the prospectus supplement related to the Company's ordinary shares, par value NIS 0.01, issuable pursuant to the Open Market Sales Agreement (as defined below) (the "ATM Prospectus Supplement") pursuant to the terms of the Open Market Sale Agreement<sup>SM</sup>, dated October 12, 2018 (the "Open Market Sales Agreement"), by and between the Company and Jefferies. The Company will not make any sales of its securities pursuant to the Open Market Sales Agreement, unless and until a new prospectus supplement is filed. Other than the termination of the ATM Prospectus Supplement, the Open Market Sales Agreement remains in full force and effect.

A copy of the Open Market Sales Agreement was filed as Exhibit 1.2 to the Company's Registration Statement on Form F-3 (333-227811) filed with the Securities and Exchange Commission on October 12, 2018.

## **Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	<a href="#">Press Release, dated January 22, 2019</a>
99.2	<a href="#">Disclosure Updates</a>

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**UROGEN PHARMA LTD.**

Dated: January 22, 2019

By: /s/ Peter Pfreundschuh  
Peter Pfreundschuh  
Chief Financial Officer



## UroGen Pharma Announces Proposed Public Offering of Ordinary Shares

NEW YORK – (BUSINESS WIRE) – January 22, 2019 – UroGen Pharma Ltd. (Nasdaq:URGN), a clinical-stage biopharmaceutical company developing treatments to address unmet needs in the field of urology, with a focus on uro-oncology, today announced that it intends to offer and sell \$150 million of its ordinary shares in an underwritten public offering. The company also intends to grant the underwriters a 30-day option to purchase up to an additional 15 percent of the number of ordinary shares sold in the offering at the public offering price, less the underwriting discounts and commissions. The offering is subject to market and other conditions and there can be no assurance as to whether or when the offering may be completed, or as to the actual size or terms of the offering. All ordinary shares to be sold in this offering will be offered by the company.

Goldman Sachs & Co. LLC, J.P. Morgan and Jefferies are acting as joint book-running managers for the offering. Oppenheimer & Co. is acting as lead manager for the offering.

A shelf registration statement relating to the ordinary shares was previously filed with the Securities and Exchange Commission (the "SEC") and declared effective on October 26, 2018. A preliminary prospectus supplement and accompanying prospectus relating to the offering will be filed with the SEC and will be available on the SEC's website at <http://www.sec.gov>. Copies of the preliminary prospectus supplement (when available) and accompanying prospectus may be obtained by contacting:

- Goldman Sachs & Co. LLC, c/o Prospectus Department, 200 West Street, New York, New York 10282, or via telephone at 866-471-2526, or via email: [prospectus-ny@ny.email.gs.com](mailto:prospectus-ny@ny.email.gs.com); or
- J.P. Morgan Securities LLC, c/o: Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, New York 11717 or via telephone at 866-803-9204, or via email: [prospectus-eq\\_fi@jpmorgan.com](mailto:prospectus-eq_fi@jpmorgan.com); or
- Jefferies LLC, c/o: Equity Syndicate Prospectus Departments, 520 Madison Avenue, 2nd Floor, New York, New York 10022, or via telephone at 877-821-7388, or via email: [prospectus\\_department@jefferies.com](mailto:prospectus_department@jefferies.com).

This press release shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction. Any offer, if at all, will be made only by means of the prospectus supplement and accompanying prospectus forming a part of the effective registration statement.

### About UroGen Pharma Ltd.

UroGen Pharma Ltd. (Nasdaq:URGN) is a clinical-stage biopharmaceutical company developing advanced non-surgical treatments to address unmet needs in the field of urology, with a focus on uro-oncology. UroGen has developed RTGel™, a proprietary sustained release, hydrogel-based platform technology that has the potential to improve therapeutic profiles of existing drugs. UroGen's sustained release technology is designed to enable longer exposure of the urinary tract tissue to medications, making local therapy a potentially more effective treatment option. UroGen's lead product candidates, UGN-101 and UGN-102, are designed to potentially remove tumors by non-surgical means and to treat several forms of non-muscle invasive urothelial cancer, including low-grade upper tract urothelial carcinoma and bladder cancer, respectively. UroGen is headquartered in New York, NY with operations in Los Angeles, CA and Israel.

---

## **Forward Looking Statements**

This press release contains forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995, including with respect to the timing and size of the proposed offering and the anticipated use of proceeds, which statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to: market conditions, the timing and success of clinical trials and potential complications thereof; the ability to obtain and maintain regulatory approval; the labeling for any approved product; the scope, progress and expansion of developing and commercializing UroGen Pharma's product candidates; the size and growth of the market(s) therefor and the rate and degree of market acceptance thereof vis-à-vis alternative therapies; and UroGen Pharma's ability to attract or retain key management, members of the board of directors and personnel. In light of these risks and uncertainties, and other risks and uncertainties that are described in the Risk Factors section of UroGen Pharma's Form 20-F filed with the SEC on March 15, 2018, its Current Report on Form 8-K filed with the SEC on January 22, 2019, and in the preliminary prospectus supplement and accompanying prospectus relating to the offering to be filed with the SEC, and other filings that UroGen Pharma makes with the SEC from time to time (which are available at <http://www.sec.gov>), the events and circumstances discussed in such forward-looking statements may not occur, and UroGen Pharma's actual results could differ materially and adversely from those anticipated or implied thereby. Any forward-looking statements speak only as of the date of this press release and are based on information available to UroGen Pharma as of the date of this release.

## **UROGEN**

Kate Bechtold  
Director, Corporate Communications & Investor Relations  
[Kate.Bechtold@urogen.com](mailto:Kate.Bechtold@urogen.com)  
914-552-0456

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements in this document constitute “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. These statements relate to future events concerning our business and to our future revenues, operating results and financial condition. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “forecast,” “predict,” “propose,” “potential” or “continue,” or the negative of those terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the timing and success of preclinical studies and clinical trials conducted by or on behalf of us, including with respect to the efficacy and safety of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates, and the labeling for any approved products;
- the scope, progress, expansion and costs of developing and commercializing our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- our anticipated growth strategies;
- our expectations regarding competition;
- the anticipated trends and challenges in our business and the markets in which we operate;
- our ability to attract or retain key management and personnel;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates vis-à-vis alternative or existing therapies;
- our expectations regarding regulatory requirements;
- developments in applicable regulatory regimes; and
- the manner in which we intends to use our cash resources.

Forward-looking statements are based on our management’s current expectations, estimates, forecasts and projections about our business and the industry in which we operate and our management’s beliefs and assumptions, and are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this document may turn out to be inaccurate.

There are a number of important factors that could cause actual results to differ materially from the results anticipated by these forward-looking statements. These important factors include those that we discuss under the heading “Risk Factors” below. You should read these factors and the other cautionary statements made in this document as being applicable to all related forward-looking statements wherever they appear in this document. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

*The following summary highlights selected information about our business. Unless the context otherwise requires, the terms “UroGen,” “the Company,” “we,” “us” and “our” in this document refer to UroGen Pharma Ltd. and our wholly owned subsidiary, Urogen Pharma, Inc.*

### The Company

We are a clinical stage biopharmaceutical company focused on developing novel therapies designed to change the standard of care for urological pathologies. We have an innovative and broad pipeline of product candidates that we believe can overcome the deficiencies of current treatment options for a variety of urological conditions with a focus on uro-oncology. Our lead product candidates, UGN-101 and UGN-102, are proprietary formulations of the chemotherapy drug Mitomycin C, a generic drug, which is currently used off-label for urothelial cancer treatment only in a water-based formulation as an adjuvant, or supplemental post-surgery, therapy. We are developing our product candidates as

chemoablation agents, which means they are designed to remove tumors by non-surgical means, to treat several forms of non-muscle invasive urothelial cancer, including low-grade upper tract urothelial carcinoma, or LG UTUC, and low-grade bladder cancer, including non-muscle invasive bladder cancer, or NMIBC. We believe that UGN-101 and UGN-102, which are both local drug therapies, have the potential to significantly improve patients' quality of life by replacing costly, sub-optimal and burdensome tumor resection and kidney removal surgeries as the first-line standard of care. UGN-101 and UGN-102 may also reduce the need for bladder and upper urinary tract surgeries, including removal of the upper urinary tract, which are major surgical procedures typically performed when local endoscopic tumor resection fails to control the disease progression. Additionally, we believe that our product candidates, which are based on novel formulations of previously approved drugs, may qualify for streamlined regulatory pathways to market approval.

The following chart summarizes the current status of our product candidate pipeline:

CATEGORY	PROGRAM	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	NDA
Uro-oncology	UGN-101 <sup>1</sup> LG UTUC	[Progress bar spanning Pre-clinical, Phase 1, and Phase 2]				
	UGN-102 LG NMIBC	[Progress bar spanning Pre-clinical and Phase 1]				
Immuno-Uro-oncology	UGN-201 Carcinoma in Situ (CIS) Bladder Cancer	[Progress bar in Pre-clinical]				
Neuromodulation	BotuGel <sup>2</sup> Overactive Bladder	[Progress bar spanning Pre-clinical and Phase 1]				

<sup>1</sup> Rolling NDA submission initiated in December 2018  
<sup>2</sup> Licensed to Allergan Pharmaceuticals International Limited

We estimate that the prevalence of LG UTUC in the United States is approximately 6,000 to 8,000; the prevalence of low-grade NMIBC is approximately 80,000; and the prevalence of carcinoma in situ (CIS) bladder cancer is approximately

### Risk Factors

*Our business faces significant risks. You should carefully consider all of the information set forth in this document and in our other filings with the United States Securities and Exchange Commission, or the SEC, including the following risk factors which we face, and which are faced by our industry. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. This document also contains forward-looking statements that involve risks and uncertainties. Our results could materially differ from those anticipated in these forward-looking statements, as a result of certain factors including the risks described below and elsewhere in this document and our other filings with the SEC. See "Special Note Regarding Forward-Looking Statements" above.*

### Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

***We have a limited operating history and have incurred significant losses and negative cash flows since our inception, and we anticipate that we will continue to incur significant losses and negative cash flows for the foreseeable future, which makes it difficult to assess our future viability.***

We are a clinical stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We are not profitable and have incurred net losses in each period since we commenced operations in

2004, including net losses of \$51.9 million and \$9.9 million for the nine months ended September 30, 2018 and 2017, respectively. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Our ability to ultimately achieve recurring revenues and profitability is dependent upon our ability to successfully complete the development of our product candidates and obtain necessary regulatory approvals for and successfully manufacture, market and commercialize our products.

We believe that we will continue to expend substantial resources in the foreseeable future for the clinical development of our current product candidates or any additional product candidates and indications that we may choose to pursue in the future. These expenditures will include costs associated with research and development, conducting preclinical studies and clinical trials, and payments for third-party manufacturing and supply, as well as sales and marketing of any of our product candidates that are approved for sale by regulatory agencies. Because the outcome of any clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our clinical stage and preclinical drug candidates and any other drug candidates that we may develop in the future. Other unanticipated costs may also arise.

Our future capital requirements depend on many factors, including:

- the timing of, and the costs involved in, clinical development and obtaining regulatory approvals for our product candidates;
- changes in regulatory requirements during the development phase that can delay or force us to stop our activities related to any of our product candidates;
- the cost of commercialization activities if our products are approved for sale, including marketing, sales and distribution costs;
- the cost of third-party manufacturing of our products;
- the number and characteristics of any other product candidates we develop or acquire;
- our ability to establish and maintain strategic collaborations, licensing or other commercialization arrangements, and the terms and timing of such arrangements;
- the extent and rate of market acceptance of any approved products;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent and other intellectual property claims, including potential litigation costs, and the outcome of such litigation;
- the timing, receipt and amount of sales of, or royalties on, future approved products, if any;
- any product liability or other lawsuits related to our products;
- scientific breakthroughs in the field of urothelial cancer treatment and diagnosis that could significantly diminish the need for our product candidates or make them obsolete; and
- changes in reimbursement policies that could have a negative impact on our future revenue stream.

In addition, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Drug development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have not obtained any regulatory approvals for any of our product candidates, commercialized any of our product candidates or generated any material revenue from product sales.

***We will require substantial additional financing to achieve our goals, and a failure to obtain this capital when needed and on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, commercialization efforts or other operations.***

Since our inception, almost all our resources have been dedicated to the preclinical and clinical development of our lead product candidates, UGN-101 and UGN-102. As of December 31, 2018, we had cash and cash equivalents of \$101.3 million.



We believe we have sufficient cash and cash equivalents to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We expect that we will require additional capital to complete clinical trials, obtain regulatory approval for and commercialize our product candidates. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity, convertible debt or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. In any event, we will require additional capital to pursue preclinical and clinical activities, and pursue regulatory approval for, and to commercialize, our pipeline product candidates. Even if we believe that we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert the attention of our management from day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may negatively impact the holdings or the rights of our shareholders, and the issuance of additional securities, whether equity or debt, by us or the possibility of such issuance may cause the market price of our shares to decline. The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than would be desirable and we may be required to relinquish rights to some of our technologies, intellectual property or product candidates or otherwise agree to terms unfavorable to us, any of which may harm our business, financial condition, cash flows, operating results and prospects.

If adequate funds are not available to us on a timely basis, we may be required or choose to:

- delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for our product candidates or any of our future product candidates;
- delay, limit, reduce or terminate our other research and development activities; or
- delay, limit, reduce or terminate our establishment or expansion of manufacturing, sales and marketing or distribution capabilities or other activities that may be necessary to commercialize UGN-101, UGN-102 or any of our other product candidates.

We may also be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could harm our business, financial condition, cash flows and results of operations.

***Raising additional capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.***

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through equity, convertible debt or debt financings, as well as selectively continuing to enter into collaborations, strategic alliances and licensing arrangements. We do not currently have any committed external source of funds other than funding under the existing exclusive license agreement we entered into with Allergan Pharmaceuticals International Limited, or Allergan, a wholly owned subsidiary of Allergan plc, in October 2016, or the Allergan Agreement. Under the Allergan Agreement, we may receive additional material milestone payments upon the successful completion of certain development, regulatory and commercial milestones and royalties with respect to future sales of collaboration products by Allergan. Allergan may unilaterally terminate our existing collaboration for any reason upon advance notice.

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 of these securities may include liquidation or other preferences that adversely affect your rights as an ordinary shareholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring and distributing dividends, and may be secured by all or a portion of our assets.

If we raise funds by selectively continuing to enter into additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish additional valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity, convertible debt or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. If we are unable to raise additional funds through other collaborations, strategic alliances or licensing arrangements, we may be required to terminate product development or future commercialization efforts or to cease operations altogether.

### **Risks Related to Our Business and Strategy**

#### ***We are dependent on the success of our lead product candidates, including obtaining regulatory approval to market our product candidates in the United States.***

We have invested almost all our efforts and financial resources in the research and development of our lead product candidates, UGN-101 and UGN-102. Our future success depends on our ability to market and sell these product candidates. However, these drugs are in various stages of clinical development and each of these drugs has yet to receive marketing approval from the U.S. Food and Drug Administration, or the FDA, or any other regulatory agency. Our product candidates' marketability is subject to significant risks associated with successfully completing current and future clinical trials, including:

- the FDA's timely acceptance of our investigational new drug, or IND, filings for our product candidates. Without such IND acceptances, we will be unable to commence clinical trials in the United States;
- the FDA's acceptance of our parameters for regulatory approval relating to UGN-101, UGN-102 and our other product candidates, including our proposed indications, primary and secondary endpoint assessments and measurements, safety evaluations and regulatory pathways;
- the FDA's acceptance of the number, design, size, conduct and implementation of our clinical trials, our trial protocols and the interpretation of data from preclinical studies or clinical trials;
- our ability to successfully complete the clinical trials of our product candidates, including timely patient enrollment and acceptable safety and efficacy data and our ability to demonstrate the safety and efficacy of the product candidates undergoing such clinical trials;
- the FDA's timely acceptance for filing of our New Drug Application, or NDA, for UGN-101, upon completion of our rolling submission expected in the second half of 2019, and our eligibility for priority review of our NDA by the FDA;
- our ability to complete in a timely fashion the single pivotal Phase 3 clinical trial for UGN-101 for the treatment of low-grade upper tract urothelial carcinoma, or LG UTUC, and that the single pivotal Phase 3 clinical trial, even if successfully completed, will be sufficient to support NDA submission and subsequently, FDA approval;
- our ability to successfully complete the FDA requirements related to chemistry, manufacturing and control, or CMC, for UGN-101, UGN-102 and our other product candidates, and if completed, will they be sufficient to support an NDA;
- the FDA's need to schedule an advisory committee meeting, and to conduct such meeting, in a timely manner to evaluate and decide on the approval of our potential future NDAs for UGN-101 and UGN-102;
- the recommendation of the FDA's advisory committee to approve our applications to market UGN-101, UGN-102 and our other product candidates in the United States, without limiting the approved labeling, specifications, distribution or use of the products, or imposing other restrictions;
- the FDA's satisfaction with the safety and efficacy of our product candidates;
- the prevalence and severity of adverse events associated with our product candidates as there are no drugs and related drug administration procedures approved for LG UTUC or low-grade non-muscle invasive bladder cancer, or LG NMIBC, that are based on RTGel technology;
- the timely and satisfactory performance by third-party contractors of their obligations in relation to our clinical trials;

- our success in educating physicians and patients about the benefits, administration and use of our product candidates, if approved, particularly in light of the fact that there are currently no drugs approved by the FDA for the treatment of upper tract urothelial carcinoma, or UTUC, and the FDA has not approved a drug for the treatment of non-muscle invasive bladder cancer, or NMIBC, in more than 15 years;
- the availability, perceived advantages, relative cost, safety and efficacy of alternative and competing treatments for the indications addressed by our product candidates;
- the effectiveness of our marketing, sales and distribution strategy, and operations, as well as that of any current and future licensees;
- our ability to develop, validate and maintain a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMP;
- our ability to secure supply of the raw materials from TAPI (Teva Active Pharmaceutical Ingredients) or other suppliers for our product candidates to support the clinical trial and commercial use;
- our ability to obtain, protect and enforce our intellectual property rights with respect to our product candidates; and
- our ability to properly train physicians or nurses for the skillful administration of our products, including UGN-101 and UGN-102, and our ability to develop a broad experiential knowledge base of aggregated clinician feedback from which we can refine appropriate procedures for product administration, without which there could be a risk of adverse events.

Many of these clinical, regulatory and commercial risks are beyond our control. Accordingly, we cannot assure you that we will be able to advance any of our product candidates through clinical development, or to obtain regulatory approval of or commercialize any of our product candidates. If we fail to achieve these objectives or overcome the challenges presented above, we could experience significant delays or an inability to successfully commercialize our product candidates. Accordingly, we may not be able to generate sufficient revenues through the sale of our product candidates to enable us to continue our business.

***We may be unable to obtain regulatory approval for our product candidates.***

The research, development, testing, manufacturing, labeling, packaging, approval, promotion, advertising, storage, recordkeeping, marketing, distribution, post-approval monitoring and reporting, and export and import of drug products are subject to extensive regulation by the FDA and by foreign regulatory authorities. These regulations differ from country to country. To gain approval to market our product candidates, we must provide clinical data that adequately demonstrate the safety and efficacy of the product for the intended indication. We have not yet obtained regulatory approval to market any of our product candidates in the United States or any other country. Our business depends upon obtaining these regulatory approvals. There are currently no drugs approved by the FDA for the treatment of UTUC and only three drugs have been approved by the FDA for NMIBC, with the last approval having occurred over 15 years ago. The FDA can delay, limit or deny approval of our product candidates for many reasons, including:

- our inability to satisfactorily demonstrate that the product candidates are safe and effective for the target indication;
- the FDA's disagreement with our trial protocol, the interpretation of data from preclinical studies or clinical trials or conduct and control of clinical trials;
- the patient population studied in the clinical trial may not be sufficiently large, broad or representative to assess efficacy and safety in the patient population for which we seek approval;
- our inability to demonstrate that clinical or other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's determination that the 505(b)(2) regulatory pathway is not available for our product candidates;
- the FDA's determination that additional preclinical studies or clinical trials are required;
- the FDA's determination that the Fast Track Designation, or FTD, for UGN-101 is no longer warranted or our trial results do not meet the criteria for FTD;

- the FDA’s determination that the Orphan Drug Designation, or ODD, for UGN-101, for the treatment of UTUC is not valid;
- the FDA’s determination that UGN-101 for the treatment of LG UTUC no longer meets the conditions for breakthrough therapy designation;
- the FDA’s determination that the quality of our drug substance or drug product, formulation, labeling or the specifications of our product candidates is insufficient for approval;
- the FDA’s failure to accept the manufacturing processes or facilities of third-party manufacturers with which we contract;
- the potential for approval policies or regulations of the FDA to significantly change in a manner rendering our clinical data insufficient for approval; or
- resistance to approval from the FDA’s advisory committee for any reason including safety or efficacy concerns.

Although we have initiated a rolling NDA submission for UGN-101 for LG UTUC, our NDA may receive a refuse to file communication from FDA during the filing review period or a complete response letter at the conclusion of a substantive FDA review period. Even if we eventually complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA may grant approval contingent on the performance of costly and potentially time-consuming additional post-approval clinical trials or subject to restrictive risk evaluation and mitigation strategies. The FDA may also approve our product candidates for a more limited indication or a narrower patient population than we originally requested, and the FDA may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our product candidates. To the extent we seek regulatory approval in foreign countries, we may face challenges similar to those described above with regulatory authorities in applicable jurisdictions. Any delay in obtaining, or inability to obtain, applicable regulatory approval for any of our product candidates would delay or prevent commercialization of our product candidates and would thus negatively impact our business, results of operations and prospects.

***To date we have only generated limited clinical data for our product candidates.***

Positive results in preclinical testing and early clinical trials do not ensure that later clinical trials will be successful. A number of pharmaceutical companies have suffered significant setbacks in clinical trials, including in Phase 3 clinical trials, after promising results in preclinical testing and early clinical trials. These setbacks have included negative safety and efficacy observations in later clinical trials, including previously unreported adverse effects. To date, our clinical trials and other programs have involved small patient populations and because of the small sample size, the results of these clinical trials may be subject to substantial variability and may not be indicative of future results. For instance, we enrolled only 22 patients in the UGN-101 Compassionate Use program and enrolled only 71 patients in our ongoing pivotal Phase 3 OLYMPUS clinical trial for UGN-101. To date, in our preclinical testing, completed Compassionate Use program for UGN-101 and clinical trials, we have observed several adverse events and serious adverse events, including ureteral edema, transient inhibition of urine flow, rash, flank pain, kidney swelling, kidney infection, urgency in urination and pain during urination. In addition, we have observed transient perturbation of laboratory measures of renal and hematopoietic function as well as renal stricture and stenosis. These adverse events are known Mitomycin C, or MMC, or procedure-related adverse events and many are indicated as potential side effects of MMC usage on the MMC label. However, we cannot assure you that adverse events related to UGN-101 and UGN-102 that are not directly attributable to MMC specifically will not occur. In addition, our clinical trials may not be successful. If our clinical trials do not ultimately indicate that our product candidates are safe and efficacious for their intended application, the FDA may not approve any NDA that we may file to market such product candidates, and our business would not be able to generate revenue from the sale of any such 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. 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 as patient data become available and following a more comprehensive review of the data related to the particular study or trial. 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. In particular, interim data may reflect small sample sizes, be subject to substantial variability and may not be indicative of either future interim results or final results. For instance, at the time when we announced topline results from our ongoing pivotal Phase 3 OLYMPUS clinical trial for UGN-101 in January 2019, only 61 of the 71 patients enrolled in the trial had reached the primary disease evaluation, or PDE, at that time, and the remaining 10 patients were awaiting PDE evaluation. Moreover, while we announced that all evaluated patients who had achieved a complete response, or CR, at PDE remained disease free at six months, we only had six-month durability data on approximately half of the patients who had achieved a CR at PDE. Durability is a key secondary endpoint for our ongoing pivotal Phase 3 OLYMPUS clinical trial. In addition, it is possible that when we obtain and report six-, nine- and twelve-month durability data for the patients who achieved a CR at PDE, durability data for certain patients may not be available due to patients being lost to follow-up, which may result in a smaller sample of durability data than we anticipated. Moreover, while we announced that the safety profile for UGN-101 was observed to be acceptable, with most treatment-emergent adverse events characterized as mild or moderate and transient and in line with ureteral procedures, we continue to accrue safety and adverse event data in our ongoing pivotal Phase 3 OLYMPUS clinical trial and additional adverse events may occur. 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 ordinary shares. See the description of risks under the heading “Risks Related to Ownership of our Ordinary Shares” for additional disclosures related to the risk of volatility in the price of our ordinary shares.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. 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. For instance, both our ongoing pivotal Phase 3 OLYMPUS clinical trial for UGN-101 and our ongoing Phase 2b clinical trial for UGN-102 are conducted on an open-label basis. Because these clinical trials are not blinded, we regularly receive interim updates on the data accumulated in such trials but may only provide periodic public updates on such trials. Furthermore, we may report interim analyses of only certain endpoints rather than all endpoints. 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, 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, UGN-101, UGN-102 or any other product candidate may be harmed, which could harm our business, financial condition, results of operations and prospects.

***We have limited experience in conducting clinical trials and have never obtained approval for any product candidates and may be unable to do so successfully.***

As a company, we have limited experience in conducting clinical trials and have never progressed a product candidate through to regulatory approval. In part because of this lack of experience, our clinical trials may require more time and incur greater costs than we anticipate. We cannot be certain that the planned clinical trials will begin or conclude on time, if at all. Large-scale trials will require significant additional financial and management resources. In addition, due to the significant lack of drug development for non-muscle invasive urothelial cancers over the past 15 years, neither we nor any third-party clinical investigators, clinical research organizations, or CROs, and/or consultants are likely to have extensive experience conducting clinical trials for the indications we are targeting. Third-party clinical investigators do not operate under our control. Any performance failure on the part of such third parties could delay the clinical development of our product candidates or delay or prevent us from obtaining regulatory approval or commercializing our current or future product candidates, depriving us of potential product revenue and resulting in additional losses.

***We have not applied for regulatory approvals to market any of our product candidates, and we may be delayed in obtaining or failing to obtain such regulatory approvals and to commercialize our product candidates.***

The process of developing, obtaining regulatory approval for and commercializing our product candidates is long, complex, costly and uncertain, and delays or failure can occur at any stage. The research, testing, manufacturing, labeling, marketing, sale and distribution of drugs are subject to extensive and rigorous regulation by the FDA and foreign regulatory agencies, as

applicable. These regulations are agency-specific and differ by jurisdiction. We are not permitted to market any product candidate in the United States until we receive approval of an NDA from the FDA, or in any foreign countries until we receive the requisite approval from the respective regulatory agencies in such countries. To gain approval of an NDA or other equivalent regulatory approval, we must provide the FDA or relevant foreign regulatory authority with preclinical and clinical data that demonstrates the safety and efficacy of the product for the intended indication.

Before we can submit an NDA to the FDA or comparable similar applications to foreign regulatory authorities, we must conduct Phase 3 clinical trials, or a pivotal/registration trial equivalent, for each product candidate. Our pivotal clinical trial for UGN-101 is intended to evaluate 71 patients, and we initiated a rolling submission to the FDA of an NDA for UGN-101 in December 2018. We cannot assure you that we will be able to complete the submission of the NDA for UGN-101 in a timely fashion. We cannot assure you that the FDA will not decide to require us to perform additional clinical trials, including potentially requiring us to perform an additional pivotal study with a control arm, during the trial or before approving our rolling NDA submission for UGN-101.

Phase 3 clinical trials often produce unsatisfactory results even though prior clinical trials were successful. Moreover, the results of clinical trials may be unsatisfactory to the FDA or foreign regulatory authorities even if we believe those clinical trials to be successful. The FDA or applicable foreign regulatory agencies may suspend one or all of our clinical trials or require that we conduct additional clinical, preclinical, manufacturing, validation or drug product quality studies and submit that data before considering or reconsidering any NDA or comparable foreign regulatory application that we may submit. Depending on the extent of these additional studies, approval of any applications that we submit may be significantly delayed or may cause the termination of such programs or may require us to expend more resources than we have available.

If any of these outcomes occur, we may not receive regulatory approval for the corresponding product candidates, and our business would not be able to generate revenue from the sale of any such product candidates.

***Changes in 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 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 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 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, over the last several years, including beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government 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, 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.

***We may not be able to advance our preclinical product candidates into clinical development and through regulatory approval and commercialization.***

Certain of our product candidates are currently in preclinical development and are therefore currently subject to the risks associated with preclinical development, including the risks associated with:

- generating adequate and sufficient preclinical safety and efficacy data in a timely fashion to support the initiation of clinical trials;
- obtaining regulatory approval to commence clinical trials in any jurisdiction, including the submission and acceptance of INDs;
- contracting with the necessary parties to conduct a clinical trial;

- enrolling sufficient numbers of patients in clinical trials in timely fashion, if at all; and
- timely manufacture of sufficient quantities of the product candidate for use in clinical trials.

If we are unsuccessful in advancing our preclinical product candidates into clinical trials in a timely fashion, our business may be harmed. Even if we are successful in advancing our preclinical product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in “Risk Factors.” Accordingly, we cannot assure you that we will be able to develop, obtain regulatory approval for, commercialize or generate significant revenue from our product candidates.

***Clinical drug development involves a lengthy and expensive process with an uncertain outcome, results of earlier studies and trials may not be predictive of future trial results, and our clinical trials may fail to adequately demonstrate the safety and efficacy of our product candidates.***

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. A failure of one or more of our clinical trials can occur at any time during the clinical trial process. We do not know whether our ongoing and future clinical trials, if any, will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical trials can be delayed, suspended or terminated for a variety of reasons, including failure to:

- generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- obtain regulatory approval or feedback on trial design, in order to commence a trial;
- identify, recruit and train suitable clinical investigators;
- reach agreement on acceptable terms with prospective CROs and clinical trial sites, and have such CROs and sites effect the proper and timely conduct of our clinical trials;
- obtain and maintain institutional review board, or IRB, approval at each clinical trial site;
- identify, recruit and enroll suitable patients to participate in a trial;
- have a sufficient number of patients enrolled, complete a trial or return for post-treatment follow-up;
- ensure clinical investigators and clinical trial sites observe trial protocol or continue to participate in a trial;
- address any patient safety concerns that arise during the course of a trial;
- address any conflicts with new or existing laws or regulations;
- add a sufficient number of clinical trial sites;
- manufacture sufficient quantities at the required quality of product candidate for use in clinical trials; or
- raise sufficient capital to fund a trial.

Patient enrollment is a significant factor in the timing and success of clinical trials and is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians’ and patients’ or caregivers’ perceptions as to the potential advantages of the drug candidate being studied in relation to other available therapies, including any new drugs or treatments that may be developed or approved for the indications we are investigating.

We may also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the trial’s data safety monitoring board, by the FDA or by the applicable foreign regulatory authorities. Such authorities may suspend or terminate one or more of our clinical trials due to a number of factors, including our failure to conduct the clinical trial in accordance with relevant regulatory requirements or clinical protocols, inspection of the clinical trial operations or trial site by the FDA or foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

If we experience delays in carrying out or completing any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from any of these product candidates will be delayed.

In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business and financial condition. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

***The market opportunities for our product candidates may be limited to those patients who are ineligible for established therapies or for whom prior therapies have failed and may be small.***

Cancer therapies are sometimes characterized as first-line, second-line or third-line. When cancer is detected early enough, first-line therapy, often chemotherapy, hormone therapy, surgery, radiotherapy or a combination of these, is sometimes adequate to cure the cancer or prolong life. Second- and third-line therapies are administered to patients when prior therapy is not or is no longer effective. For urothelial cancers, the current first-line standard of care is surgery designed to remove one or more tumors. Chemotherapy is currently used in treating urothelial cancer only as an adjuvant, or supplemental therapy, after tumor resection. We are designing our lead product candidates with the goal of replacing surgery as the first-line standard of care for certain urothelial cancers. We intend to seek approval of UGN-101 for the first-line treatment of low-grade UTUC and of UGN-102 for the first-line treatment of low-grade NMIBC in both cases as a chemoablation agent to replace tumor resection surgeries. However, there is no guarantee that our product candidates, if approved, would be approved for first-line or even later lines of therapy, and, that prior to any such approvals, we will not have to conduct additional clinical trials.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers who have previously failed prior treatments, and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or third-party market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers and the number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. For instance, our ongoing pivotal Phase 3 OLYMPUS clinical trial for UGN-101 is designed to evaluate the use of UGN-101 for the treatment of tumors in the renal pelvis (the funnel-like dilated part of the ureter in the kidney) and is not designed to evaluate the use of UGN-101 for the treatment of tumors in the ureter (the tube that connects the kidneys to the bladder). Even if UGN-101 is approved for the treatment of LG UTUC, physicians may choose to only use it to treat tumors in the renal pelvis and not tumors in the ureter, which would limit the degree of physician adoption and market acceptance of UGN-101. Even if we receive regulatory approval for our product candidates and obtain significant market share, because the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications, including the use of the products as first- or second-line therapy. For example, LG UTUC is a rare malignant tumor of the cells lining the urinary tract and there is limited scientific literature or other research on the incidence and prevalence of LG UTUC. If our estimates of the incidence and prevalence of LG UTUC are incorrect, UGN-101's commercial viability may prove to be limited, which may negatively affect our financial results.

***UGN-101, UGN-102 or any of our other product candidates may produce undesirable side effects that we may not have detected in our previous preclinical studies and clinical trials or that are not expected with MMC treatment or inconsistent with catheter administration procedures. This could prevent us from gaining marketing approval or market acceptance for these product candidates, or from maintaining such approval and acceptance, and could substantially increase commercialization costs and even force us to cease operations.***

As with most pharmaceutical products, use of UGN-101, UGN-102 or our other product candidates may be associated with side effects or adverse events that can vary in severity and frequency. Our proprietary reverse thermal gelation hydrogel, or RTGel, which is used in the formulation of UGN-101 and UGN-102, has not undergone extensive testing in humans. Side effects or adverse events associated with the use of UGN-101 and UGN-102 may be observed at any time, including in clinical trials or once a product is commercialized, and any such side effects or adverse events may negatively affect our ability to obtain regulatory approval or market our product candidates. To date, in our preclinical testing, completed Compassionate Use program for UGN-101 and clinical trials, we have observed several adverse events and serious adverse events, including ureteral edema, transient inhibition of urine flow, rash, flank pain, kidney swelling, kidney infection, urgency in urination and pain during urination. In addition, we have observed transient perturbation of laboratory measures of



renal and hematopoietic function as well as renal stricture and stenosis. These adverse events are known MMC, or procedure-related adverse events and many are indicated as potential side effects of MMC usage on the MMC label. However, we cannot assure you that we will not observe additional drug or procedure-related serious adverse events in the future or that the FDA will not determine them as such. Side effects such as toxicity or other safety issues associated with the use of our product candidates could require us to perform additional studies or halt development or sale of these product candidates or expose us to product liability lawsuits, which will harm our business.

Furthermore, our single pivotal Phase 3 clinical trial for UGN-101 and our Phase 2b clinical trial for UGN-102 involve larger patient bases than in our prior studies of these candidates, and the commercial marketing of UGN-101 and UGN-102, if approved, will further expand the clinical exposure of the drugs to a wider and more diverse group of patients than those participating in the clinical trials, which may identify undesirable side effects caused by these products that were not previously observed or reported.

The FDA and foreign regulatory agency regulations require that we report certain information about adverse medical events if our products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date upon which we become aware of the adverse event as well as the nature and severity of the event. We may fail to report adverse events of which we become aware within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA or a foreign regulatory agency could take action including enforcing a hold on or cessation of clinical trials, withdrawal of approved drugs from the market, criminal prosecution, the imposition of civil monetary penalties or seizure of our products.

Additionally, in the event we discover the existence of adverse medical events or side effects caused by one of our product candidates, a number of other potentially significant negative consequences could result, including:

- our inability to submit an NDA or similar application for our product candidates because of insufficient risk-reward, or the denial of such application by the FDA or foreign regulatory authorities;
- the FDA or foreign regulatory authorities suspending or terminating our clinical trials or suspending or withdrawing their approval of the product;
- the FDA or foreign regulatory authorities requiring the addition of labeling statements, such as Box or other warnings or contraindications or distribution and use restrictions;
- the FDA or foreign regulatory authorities requiring us to issue specific communications to healthcare professionals, such as letters alerting them to new safety information about our product, changes in dosage or other important information;
- the FDA or foreign regulatory authorities issuing negative publicity regarding the affected product, including safety communications;
- our being limited with respect to the safety-related claims that we can make in our marketing or promotional materials;
- our being required to change the way the product is administered, conduct additional preclinical studies or clinical trials or restrict or cease the distribution or use of the product; and
- our being sued and held liable for harm caused to patients.

Any of these events could prevent us from achieving approval or market acceptance of the affected product candidate and could substantially increase commercialization costs or even force us to cease operations. We cannot assure you that we will resolve any issues related to any product-related adverse events to the satisfaction of the FDA or any regulatory agency in a timely manner or ever, which could harm our business, prospects and financial condition.

***Even if our product candidates receive marketing approval, we may continue to face future developmental and regulatory difficulties. In addition, we are subject to government regulations and we may experience delays in obtaining required regulatory approvals to market our proposed product candidates.***

Even if we complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA or

applicable foreign regulatory agency may grant approval contingent on the performance of additional costly post-approval clinical trials, risk mitigation requirements and surveillance requirements to monitor the safety or efficacy of the product, which could negatively impact us by reducing revenues or increasing expenses, and cause the approved product candidate not to be commercially viable. Absence of long-term safety data may further limit the approved uses of our products, if any.

The FDA or applicable foreign regulatory agency also may approve our product candidates for a more limited indication or a narrower patient population than we originally requested or may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our product candidates. Furthermore, any such approved product will remain subject to extensive regulatory requirements, including requirements relating to manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, distribution and recordkeeping.

If we fail to comply with the regulatory requirements of the FDA or other applicable foreign regulatory authorities, or previously unknown problems with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks, including the following:

- suspension or imposition of restrictions on operations, including costly new manufacturing requirements;
- regulatory agency refusal to approve pending applications or supplements to applications;
- suspension of any ongoing clinical trials;
- suspension or withdrawal of marketing approval;
- an injunction or imposition of civil or criminal penalties or monetary fines;
- seizure or detention of products;
- bans or restrictions on imports and exports;
- issuance of warning letters or untitled letters;
- suspension or imposition of restrictions on operations, including costly new manufacturing requirements; or
- refusal of regulatory authorities to approve pending applications or supplements to applications.

In addition, various aspects of our operations are subject to federal, state or local laws, rules and regulations, any of which may change from time to time. Costs arising out of any regulatory developments could be time-consuming and expensive and could divert management resources and attention and, consequently, could adversely affect our business, financial condition, cash flows and results of operations.

***Even if our product candidates receive regulatory approval, they may fail to achieve the broad degree of physician adoption and use and market acceptance necessary for commercial success.***

Even if we obtain FDA or foreign regulatory approvals for our product candidates, the commercial success of such products will depend significantly on their broad adoption and use by physicians, for approved indications, including, in the case of UGN-101, for the first-line treatment of low-grade UTUC, and in the case of UGN-102, for the first-line treatment of low-grade NMIBC, and for other therapeutic indications that we may seek to pursue with any of our product candidates. Physicians treating low-grade UTUC and low-grade NMIBC have never had to consider first-line treatments other than surgery. The degree and rate of physician and patient adoption of our product candidates, if approved, will depend on a number of factors, including:

- the clinical indications for which the product is approved;
- the prevalence and severity of adverse side effects and the level of risk/reward observed in our clinical trials;
- sufficient patient satisfaction with the results and administration of our product and overall treatment experience, including relative convenience, ease of use and avoidance of, or reduction in, adverse side effects;
- the extent to which physicians recommend our products to patients;
- physicians' and patients' willingness to adopt new therapies in lieu of other products or treatments, including willingness to adopt our lead product candidates as locally-administered drug replacements to current surgical standards of care;

- the cost of treatment, safety and efficacy of our product candidates in relation to alternative treatments, including the recurrence rate of our treatments;
- the extent to which the costs of our product candidates are covered and reimbursed by third-party payors, including the availability of a physician reimbursement code for our treatments, and patients' willingness to pay for our products;
- whether treatment with our product candidates, including the treatment of low-grade UTUC with UGN-101 and the treatment of low-grade NMIBC with UGN-102, will be deemed to be an elective procedure by third-party payors; if so, the cost of treatment would be borne by the patient and would be less likely to be broadly adopted;
- proper training of physicians or nurses for the skillful administration of our products, including UGN-101 and UGN-102, and development of a broad experiential knowledge base of aggregated clinician feedback from which we can refine appropriate procedures for product administration, without which there could be a risk of adverse events;
- the revenues and profitability that our products will offer physicians as compared to alternative therapies; and
- the effectiveness of our sales and marketing efforts, especially the success of any targeted marketing efforts directed toward physicians and clinics and any direct-to-consumer marketing efforts we may initiate.

If UGN-101, UGN-102 or any of our other product candidates is approved for use but fails to achieve the broad degree of physician adoption and market acceptance necessary for commercial success, our operating results and financial condition would be adversely affected.

***If we are not successful in developing, receiving regulatory approval for and commercializing our preclinical and clinical product candidates other than UGN-101 or UGN-102, our ability to expand our business and achieve our strategic objectives could be impaired.***

Although we will devote a substantial portion of our resources to the continued clinical testing and potential approval of UGN-101 for the treatment of low-grade UTUC and UGN-102 for the treatment of low-grade NMIBC, another key element of our strategy is to discover, develop and commercialize a portfolio of products based on our proprietary RTGel platforms to serve additional therapeutic markets. We are seeking to do so through our internal research programs, but our resources are limited, and those that we have are geared towards clinical testing and seeking regulatory approval of UGN-101, UGN-102 and our other existing product candidates. We may also explore strategic collaborations for the development or acquisition of new products, but we may not be successful in entering into such relationships. While we have commenced a single pivotal Phase 3 clinical trial for UGN-101 and a Phase 2b clinical trial for UGN-102, all of our other potential product candidates remain in the preclinical and/or early clinical stages of development. Research programs to identify product candidates require substantial technical, financial and human resources, regardless of whether any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- a product candidate may in a subsequent trial be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable; and
- intellectual property or other proprietary rights of third parties for product candidates we develop may potentially block our entry into certain markets or make such entry economically impracticable.

If we fail to develop and successfully commercialize other product candidates, our business and future prospects may be harmed, and our business will be more vulnerable to any problems that we encounter in developing and commercializing our product candidates.

***Our product candidates, if approved, will face significant competition with competing technologies and our failure to compete effectively may prevent us from achieving significant market penetration.***

The biopharmaceutical industry is intensely competitive and subject to rapid and significant technological change. Our potential competitors include large and experienced companies that enjoy significant competitive advantages over us, such as greater financial, research and development, manufacturing, personnel and marketing resources, greater brand recognition and more experience and expertise in obtaining marketing approvals from the FDA and foreign regulatory authorities. These companies may develop new drugs to treat the indications that we target or seek to have existing drugs approved for use for the treatment of the indications that we target.

The FDA has approved four immunotherapy drugs known as checkpoint inhibitors; Tecentriq (atezolizumab), Bavenico (Avelumab), Imfinzi (durbalunab) and Keytruda (pembrolizumab) for the treatment of locally advanced or metastatic bladder cancer, a form of muscle invasive bladder cancer.

We are aware of several pharmaceutical companies that are developing drugs in the fields of urology and uro-oncology, such as Roche, Vyriad, GSK, Celgene, Lipac Oncology, Samyang biopharma, Merck Sharp & Dohme Corp., Eleven biotherapeutics, Vivalytics Limited, AADi, LLC, Biocancell Ltd., Altor BioScience Corporation, FKD Therapies Oy and Spectrum Pharmaceuticals, Inc. We do not know whether these potential competitors are already developing, or plan to develop, low-grade UTUC or high-grade UTUC treatments or other indications that we are pursuing.

We are also aware that other companies, such as Taris and Lipac are conducting, or have recently conducted clinical trials for product candidates for the treatment of low-grade NMIBC, including carcinoma in situ, or CIS. Outside of these indications where we are developing products, we are aware of other companies doing work in both Bladder and Upper Tract cancers, but these are with agents or on targets in high-grade, metastatic, or muscle invasive cancers. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in this industry. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective, easier to administer or less costly than our product candidates.

In addition, we face competition from existing standards of treatment, including transurethral resection of bladder tumor, or TURBT, surgery for bladder cancer. If we are not able to demonstrate that our product candidates are at least as safe and effective as such courses of treatment, medical professionals may not adopt our product candidates in replacement of the existing standard of care, which is first-line tumor surgical procedures.

***We have no experience in marketing or distributing products and no internal capability to do so and are therefore subject to certain risks in relation to the commercialization of our product candidates once approved.***

We have not yet established a commercial organization for the marketing, sale and distribution of our product candidates. Therefore, even if we receive approval to market our product candidates in the United States or other markets, in order to successfully commercialize our product candidates, we will need to either build marketing, sales, distribution, managerial and other non-technical capabilities or contract with third parties to obtain these capabilities. This involves many challenges, such as recruiting and retaining talented personnel, training employees, setting the appropriate system of incentives, managing additional headcount and integrating new business units into an existing corporate infrastructure. The development of our own sales infrastructure or contracting with third parties will involve substantial expense, much of which we will incur well in advance of any marketing or sales. Moreover, we do not have experience as a company in establishing a significant sales infrastructure, and we cannot be certain that we will successfully develop this capability or contract successfully with third parties for the necessary services. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain personnel for medical affairs, marketing and sales. If we fail to establish an effective sales and marketing infrastructure or contract with third parties to do so, we will be unable to successfully commercialize our product candidates, which in turn would have an adverse effect on our business, financial condition and results of operations.

***We have entered into a licensing agreement and in the future may enter into collaborations with other third parties for the development or commercialization of our product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.***

In October 2016, we entered into the Allergan Agreement. Under the Allergan Agreement, we granted Allergan an exclusive worldwide license to research, develop, manufacture and commercialize pharmaceutical products that contain RTGel and clostridial toxins (including BOTOX), alone or in combination with certain other active ingredients, which we refer to

collectively as the Licensed Products. Either party may terminate the Allergan Agreement for uncured material breach by the other party and for the insolvency of the other party. We may terminate the Allergan Agreement if Allergan or its affiliates challenges any of our patents licensed to Allergan and such patent challenge is not required under a court order or subpoena and is not a defense against a claim, action or proceeding asserted by us, our affiliates or licensees against Allergan, its affiliates or sublicensees. In addition, Allergan may unilaterally terminate the Allergan Agreement for any reason upon advance notice. If Allergan has the right to terminate the Allergan Agreement due to our uncured material breach, Allergan may elect to continue the agreement and reduce all future milestone and royalty payment obligations to us by a specified percentage. In the event of any termination of the Allergan Agreement, Allergan will assign or grant a right of reference to any regulatory documentation related to RTGel to us, all rights and licenses to Allergan will terminate, and the license Allergan granted to us under their improvements to RTGel will continue. If any of these events occurs, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for the Licensed Products and will not be able to, or may be delayed in our efforts to, successfully commercialize the Licensed Products, and our business will be harmed.

We may utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to develop our product candidates and commercialize our approved product candidates, if any. We are not currently party to any such arrangement. 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.

Our existing collaboration with Allergan and any future collaborations that we enter into, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- product candidates developed by collaborators may not perform sufficiently in clinical trials to be determined to be safe and effective, thereby delaying or terminating the drug approval process and reducing or eliminating milestone payments to which we would otherwise be entitled if the product candidates had successfully met their endpoints and/or received FDA approval;
- clinical trials conducted by collaborators could give rise to new safety concerns;
- clinical trials, such as the ongoing Phase 2 trial being conducted by Allergan for overactive bladder with BotuGel, could fail to meet its efficacy objectives;
- collaborators may not pursue development and commercialization of our product candidates that receive marketing approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create 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 products or 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;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise 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. If the Allergan Agreement, and any future collaborations that we enter into, do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed, and we may need additional resources to develop our product candidates. All the risks relating to product development, regulatory approval and commercialization described in this document also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours were to be involved in a business combination, it might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be harmed.

***If in the future we acquire or in-license technologies or product candidates, we may incur various costs, may have integration difficulties and may experience other risks that could harm our business and results of operations.***

In the future, we may acquire or in-license additional product candidates and technologies. Any product candidate or technologies we in-license or acquire will likely require additional development efforts prior to commercial sale, including extensive preclinical or clinical testing, or both, and approval by the FDA and applicable foreign regulatory authorities, if any. All product candidates are prone to risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate, or product developed based on in-licensed technology, will not be shown to be sufficiently safe and effective for approval by regulatory authorities. If intellectual property related to product candidates or technologies we in-license is not adequate, we may not be able to commercialize the affected products even after expending resources on their development. In addition, we may not be able to manufacture economically or successfully commercialize any product candidate that we develop based on acquired or in-licensed technology that is granted regulatory approval, and such products may not gain wide acceptance or be competitive in the marketplace. Moreover, integrating any newly acquired or in-licensed product candidates could be expensive and time-consuming. If we cannot effectively manage these aspects of our business strategy, our business may be materially harmed.

***We currently contract with third-party subcontractors and single-source suppliers for certain raw materials, compounds and components necessary to produce UGN-101, UGN-102 and UGN-201 for preclinical studies and clinical trials, and expect to continue to do so to support commercial scale production of UGN-101, UGN-102 and UGN-201, if approved. There are significant risks associated with the manufacture of pharmaceutical products and contracting with contract manufacturers and with single-source suppliers. Furthermore, our existing third-party subcontractors and single-source suppliers may not be able to meet the increased need for certain raw materials, compounds and components that may result from our potential commercialization efforts. This increases the risk that we will not have sufficient quantities of UGN-101, UGN-102 or UGN-201 or be able to obtain such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.***

We currently rely on third party subcontractors and suppliers for certain compounds and components necessary to produce UGN-101, UGN-102 and UGN-201 for our preclinical studies, clinical trials and commercial use, should our drug candidates receive regulatory approval. We currently depend on Teva Pharmaceuticals Industries Ltd., or Teva, as our single-source supplier of MMC active pharmaceutical ingredient, or API, for UGN-101 and UGN-102. Teva is in the midst of a corporate restructuring. Although we are not aware of any impact of the restructuring as currently in effect on Teva's ability or willingness to supply us with MMC API in the quantities and on the timeline required, it is possible that the restructuring could adversely affect our ability to obtain MMC in any given period and could require us to expend funds and effort to identify and engage one or more alternate suppliers of MMC. We also currently depend on single sources for the gel

contained in UGN-101 and UGN-102, and Imiquimod for UGN-201. Because there are a limited number of suppliers for the raw materials that we use to manufacture our product candidates, we may need to engage alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical trials, and if approved, ultimately for commercial sale. We do not have any control over the availability of raw materials. If we or our manufacturers are unable to purchase these raw materials on acceptable terms, at sufficient quality levels, or in adequate quantities, if at all, the development and commercialization of our product candidates or any future product candidates, would be delayed or there would be a shortage in supply, which would impair our ability to meet our development objectives for our product candidates or generate revenues from the sale of any approved products.

We expect to continue to rely on these or other subcontractors and suppliers to support our commercial requirements if UGN-101, UGN-102 or any of our other product candidates is approved for marketing by the FDA or foreign regulatory authorities. We also rely on a single third-party manufacturer to produce the MMC drug product, or final MMC formulation, necessary for our clinical trial and commercial requirements. We have yet to complete the MMC drug product validation process, and scale-up work at this manufacturer that would be required for approval and commercial purposes, and there is a risk that we will not be able to do so in a timely or satisfactory manner. Even if we establish ourselves as an approved commercial supplier of MMC through this drug product manufacturer, we plan to continue to rely on third parties for such production of MMC API, as well as for the raw materials, compounds and components necessary to produce our product candidates and for preclinical studies and clinical trials. We would expect that if we become a commercial supplier of MMC, through a third-party manufacturer of MMC, it would provide us with enhanced control of material supply for both clinical trials and the commercial market, enable the more rapid implementation of process changes, and allow for better long-term margins. However, we have no experience as a company in the commercial supply of drugs and may never be successful as a commercial supplier of MMC.

Even if we are successful in being approved as a commercial supplier of MMC, cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures, production failures or product recalls, and numerous other factors could prevent us from realizing the intended benefits of our sales strategy and have a material adverse effect on our business. Further, establishing ourselves as a commercial supplier of MMC, if we choose to pursue this, will require additional investment, will be time-consuming and may be subject to delays, including because of shortage of labor, compliance with regulatory requirements or receipt of necessary regulatory approvals. In addition, building out our MMC commercial supply capabilities may cost more than we currently anticipate, and delays or problems may adversely impact our ability to provide supply for the development and commercialization of our product candidates as well as our financial condition.

Moreover, before we can begin to commercially manufacture our product candidates, whether in a third-party facility or in our own facility, once established, we must obtain regulatory approval from the FDA for our manufacturing process and facility in order to sell such products in the United States. A manufacturing authorization would also have to be obtained from the appropriate European Union regulatory authorities in order to sell such products in the European Union. In order to obtain approval, we will need to ensure that all of the processes, methods and equipment of such manufacturing facilities are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any vendors, contract laboratories or suppliers is found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any product candidate that we may develop.

Our continuing reliance on third party subcontractors and suppliers entails a number of risks, including reliance on the third party for regulatory compliance and quality assurance, the possible breach of the manufacturing or supply agreement by the third party, and the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. In addition, third party subcontractors and suppliers may not be able to comply with cGMP or quality system regulation, also called QSR, or similar regulatory requirements outside the United States. If any of these risks transpire, we may be unable to timely retain alternate subcontractors or suppliers on acceptable terms and with sufficient quality standards and production capacity, which may disrupt and delay our clinical trials or the manufacture and commercial sale of our product candidates, if approved.

Our failure or the failure of our third-party subcontractors and suppliers 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 products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of UGN-101, UGN-102 or any of our other product candidates that we may

develop. Any failure or refusal to supply or any interruption in supply of the components for UGN-101, UGN-102 or any other product candidates that we may develop could delay, prevent or impair our clinical development or commercialization efforts.

***Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.***

In order to market and sell our products in the European Union and other jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. Regulatory approval processes outside the United States generally include all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to submit for marketing approvals and may not receive the necessary approvals to commercialize our product candidates in any particular market.

***We intend to rely on third parties and consultants to assist us in conducting our single pivotal Phase 3 clinical trial for UGN-101, our Phase 2b clinical trial for UGN-102 and certain clinical trials for our other product candidates. If these third parties or consultants do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize UGN-101, UGN-102 or any of our other product candidates.***

We do not have the ability to independently conduct many of our preclinical studies or our clinical trials. We rely on medical institutions, clinical investigators, contract laboratories, and other third parties, such as CROs to conduct clinical trials on our product candidates. Third parties play 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, we have limited ability to control the amount or timing of resources that any such third party will devote to our clinical trials. Due to the limited drug development for non-muscle invasive urothelial cancers over the past 15 years, neither we nor any third-party clinical investigators, CROs and/or consultants are likely to have extensive experience conducting clinical trials for the indications we are targeting. If our CROs or any other third parties upon which we rely for administration and conduct of our clinical trials do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements, or for other reasons, or if they otherwise perform in a substandard manner, our clinical trials may be extended, delayed, suspended or terminated, and we may not be able to complete development of, obtain regulatory approval for, or successfully commercialize our product candidates.

We and the third parties upon whom we rely are required to comply with Good Clinical Practice, or GCP, regulations, which are regulations and guidelines enforced by regulatory authorities around the world for products in clinical development. Regulatory authorities enforce these GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or our third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed, or the regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, a regulatory authority will determine that any of our clinical trials comply or complied with applicable GCP regulations. In addition, our clinical trials must be conducted with material produced under current cGMP regulations, which are enforced by regulatory authorities. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be impacted if our CROs, clinical investigators or other third parties violate federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

In order for our clinical trials to be carried out effectively and efficiently, it is imperative that our CROs and other third parties communicate and coordinate with one another. Moreover, our CROs and other third parties may also have relationships with other commercial entities, some of which may compete with us. Our CROs and other third parties may terminate their agreements with us upon as few as 30 days' notice under certain circumstances. If our CROs or other third parties conducting our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical trial protocols or GCPs, or for any other reason, we may need to conduct additional clinical trials or enter into new arrangements with alternative CROs, clinical



investigators or other third parties. We may be unable to enter into arrangements with alternative CROs on commercially reasonable terms, or at all. Switching or adding CROs, clinical investigators or other third parties can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays may occur, which can impact our ability to meet our desired clinical development timelines. Although we carefully manage our relationship with our CROs, clinical investigators and other third parties, there can be no assurance that we will not encounter such challenges or delays in the future or that these delays or challenges will not have a negative impact on our business, prospects, financial condition or results of operations.

***Our ability to market our product candidates, if approved, will be limited to certain indications. If we want to expand the indications for which we may market our products, we will need to obtain additional regulatory approvals, which may not be granted.***

We are currently developing UGN-101 for the treatment of low-grade UTUC, and UGN-102 and UGN-201 for the treatment of various forms of bladder cancer. The FDA and other applicable regulatory agencies will restrict our ability to market or advertise our products to the scope of the approved label for the applicable product and for no other indications, which could limit physician and patient adoption. We may attempt to develop and, if approved, promote and commercialize new treatment indications for our products in the future, but we cannot predict when or if we will receive the regulatory approvals required to do so. Failure to receive such approvals will prevent us from promoting or commercializing new treatment indications. In addition, we would be required to conduct additional clinical trials or studies to support approvals for additional indications, which would be time consuming and expensive, and may produce results that do not support regulatory approvals. If we do not obtain additional regulatory approvals, our ability to expand our business will be limited.

***If our product candidates are approved for marketing, and we are found to have improperly promoted off-label uses, or if physicians misuse our products, we may become subject to prohibitions on the sale or marketing of our products, significant sanctions, and product liability claims, and our image and reputation within the industry and marketplace could be harmed.***

The FDA and other regulatory agencies strictly regulate the marketing and promotional claims that are made about drug products. In particular, a product may not be promoted for uses or indications 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 UGN-101 for the treatment of low-grade UTUC, the first indication we are pursuing, we cannot promote the use of our product in a manner that is inconsistent with the approved label. However, physicians are able, in their independent medical judgment, to use UGN-101 on their patients in an off-label manner, such as for the treatment of other urology indications. If we are found to have promoted such off-label uses, we may receive warning letters and become subject to significant liability, which would harm our business. The federal government has levied large administrative, civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. If we become the target of such an investigation or prosecution based on our marketing and promotional practices, we could face similar sanctions, which would harm our business. In addition, management's attention could be diverted from our business operations, significant legal expenses could be incurred, and our reputation could be damaged. 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 are deemed by the FDA to have engaged in the promotion of our products for off-label use, we could be subject to prohibitions on the sale or marketing of our products or significant fines and penalties, and the imposition of these sanctions could also affect our reputation with physicians, patients and caregivers, and our position within the industry.

Physicians may also misuse our products or use improper techniques, potentially leading to adverse results, side effects or injury, which may lead to product liability claims. If our products are misused or used with improper technique, we may become subject to costly litigation. Product liability claims could divert management's attention from our core business, be expensive to defend, and result in sizable damage awards against us that may not be covered by insurance. We currently carry product liability insurance covering our clinical trials with policy limits that we believe are customary for similarly situated companies and adequate to provide us with coverage for foreseeable risks. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Furthermore, the use of our products for conditions other than those approved by the FDA may not effectively treat such conditions, which could harm our reputation in the marketplace among physicians and patients.

***If we fail to manage our growth effectively, our business could be disrupted.***

As of December 31, 2018, we had 70 full-time employees, of whom 38 are based in Israel and 32 are based in the United States. We will need to continue to expand our development, quality, sales, managerial, operational, finance, marketing and

other resources to manage our operations and clinical trials, continue our development activities and commercialize our product candidates, if approved. Our management, personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our expansion strategy requires that we:

- manage our clinical trials effectively;
- identify, recruit, retain, incentivize and integrate additional employees;
- manage our internal development efforts effectively while carrying out our contractual obligations to third parties; and
- continue to improve our operational, financial and management controls, reporting systems and procedures.

Due to our limited financial resources and our limited experience in managing a larger company, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage expansion could delay the execution of our development and strategic objectives or disrupt our operations; and if we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our revenues will suffer and we would incur significant additional losses.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of any of our other products we develop.***

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products we develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants or cancellation of clinical trials;
- costs to defend the related litigation, which may be only partially recoverable even in the event of successful defenses;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenues;
- exhaustion of any available insurance and our capital resources; and
- the inability to commercialize any product we develop.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of products we may develop. We currently carry general clinical trial product liability insurance in an amount that we believe is adequate to cover the scope of our ongoing clinical programs. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain

insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing UGN-101, UGN-102 or any other product candidate, we intend to expand our insurance coverage to include the commercialization of UGN-101, UGN-102 or any other approved product that we may have; however, we may be unable to obtain this liability insurance on commercially reasonable terms.

***If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize any of the products we develop.***

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We believe that our future success is highly dependent upon the contributions of members of our senior management, as well as our senior scientists and other members of our management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates.

Although we have not historically experienced unique difficulties in attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the pharmaceutical field is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output.

***Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a disruption of our drug development programs.***

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from cyber-security threats, including computer viruses, harmful code and unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. If a disruption event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

***Under applicable employment laws, we may not be able to enforce covenants not to compete.***

We generally enter into non-competition agreements as part of our employment agreements with our employees. These agreements generally prohibit our employees, if they cease working for us, from competing directly with us or working for our competitors or clients for a limited period. We may be unable to enforce these agreements under the laws of the jurisdictions in which our employees work, and it may be difficult for us to restrict our competitors from benefitting from the expertise our former employees or consultants developed while working for us.

For example, Israeli labor courts have required employers seeking to enforce non-compete undertakings of a former employee to demonstrate that the competitive activities of the former employee will harm one of a limited number of material interests of the employer which have been recognized by the courts as justification for the enforcement of non-compete undertakings, such as the protection of a company's trade secrets or other intellectual property.

***Our employees, independent contractors, clinical investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.***

We are exposed to the risk that our employees, independent contractors, clinical investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct, breach of contract or other unauthorized activities that violate: FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA; manufacturing standards; federal, state and foreign healthcare fraud and abuse laws; or laws that require the reporting of financial information or data accurately.

Specifically, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to

extensive laws intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive and other business arrangements. Activities subject to these laws also include 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 Corporate Code of Ethics and Conduct, but it is not always possible to identify and deter misconduct by employees and other third 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 be in compliance with such laws. If any such actions are instituted against us, even if we are successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business. Violations of such laws subject us to numerous penalties, including, but not limited to, the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

***Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.***

Our research and development activities and our third-party subcontractors' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including MMC, key components of our product candidates, and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Despite our efforts, we cannot eliminate the risk of contamination. This could cause an interruption of our commercialization efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by us and our subcontractors and suppliers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and interrupt our business operations.

Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance.

***Exchange rate fluctuations between the U.S. Dollar and the New Israeli Shekel may negatively affect our earnings.***

The U.S. dollar is our functional and reporting currency. However, a significant portion of our operating expenses are incurred in New Israeli Shekels, or NIS, which is the lawful currency of the State of Israel. As a result, we are exposed to the risks that the NIS may appreciate relative to the dollar, or, if the NIS instead devalues relative to the dollar, that the inflation rate in Israel may exceed such rate of devaluation of the NIS, or that the timing of such devaluation may lag behind inflation in Israel. In any such event, the dollar cost of our operations in Israel would increase and our dollar-denominated results of operations would be adversely affected. We cannot predict any future trends in the rate of inflation in Israel or the rate of devaluation (if any) of the NIS against the dollar. For example, the level of devaluation of the NIS against the dollar in 2018 was 8.1%, and if the dollar cost of our operations in Israel continues to increase, our dollar-measured results of operations will be adversely affected.

### **Risks Related to Our Intellectual Property**

***If our efforts to obtain, protect or enforce our patents and other intellectual property rights related to our product candidates and technologies are not adequate, we may not be able to compete effectively, and we otherwise may be harmed.***

Our commercial success depends in part upon our ability to obtain and maintain patent protection and utilize trade secret protection for our intellectual property and proprietary technologies, our products and their uses, as well as our ability to operate without infringing upon the proprietary rights of others. We rely upon a combination of patents, trade secret protection and confidentiality agreements, assignment of invention agreements and other contractual arrangements to protect the intellectual property related to hydrogel-based pharmaceutical compositions for optimal delivery of a drug in internal cavities such as the bladder, the method for treating urothelial cancer using hydrogel-based compositions, the method for

treating overactive bladder topically without the need for injections, an in-dwelling ureter catheter system for optimal delivery of a drug into the renal cavity, and pharmaceutical compositions comprising an imidazoquinolin (amine) and lactic acid for use in a method for the treatment of bladder diseases.

We seek patent protection for our product candidates, and we have established several patent families comprised of issued patents and pending patent applications covering our proprietary RTGel formulation technology and the formulations, methods of use and manufacturing aspects of our product candidates. In the United States, we currently have 15 granted patents that are directed to protect our lead product candidates, UGN-101, UGN-102, BotuGel, UGN-201 and RTGel as well as to our future product candidates that are under company research. These patents claim methods, systems, and novel compositions for treating cancer in internal cavities, in particular urinary tract cancer. These issued patents are expected to expire between 2024 and 2035. Moreover, our IP portfolio includes more than 45 patent applications filed worldwide that are directed to various methods, systems and compositions for treating cancer locally, by intravesical means. We have four pending patent applications relating to the product candidate BotuGel in the European Union, China and Israel as well as one granted patent in Russia. In addition, we have two granted patents related to UGN-201 in the United States as well as two granted patents in the European Union, two granted patents in Japan and one granted patent in each of Australia, Mexico, China, Russia, and Hong Kong, each of which is expected to remain in effect until approximately 2035. In addition to the issued patents mentioned above, our portfolio includes pending patent applications relating to UGN-201 in the European Union, Hong Kong, Canada, Brazil and Israel. Moreover, we hold five granted patents in the United States as well as patent applications filed worldwide that relate to novel formulations of phospholipid drug analogs (saturated lipid conjugate compositions) for the treatment of urinary tract cancer.

Limitations on the scope of our intellectual property rights may limit our ability to prevent third parties from designing around such rights and competing against us. For example, our patents do not claim a new compound. Rather, the active pharmaceutical ingredients of our products are existing compounds and our granted patents and pending patent applications are directed to, among other things, novel formulations of these existing compounds with our RTGel. Accordingly, other parties may compete with us, for example, by independently developing or obtaining competing topical formulations that design around our patent claims, but which may contain the same active ingredients, or by seeking to invalidate our patents. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, eroding our competitive position in the market.

However, the patent applications that we own or license may fail to result in granted patents in the United States or foreign jurisdictions, or if granted may fail to prevent a potential infringer from marketing its product or be deemed invalid and unenforceable by a court. Competitors in the field of reverse thermal gel therapies have created a substantial amount of scientific publications, patents and patent applications and other materials relating to their technologies. Our ability to obtain and maintain valid and enforceable patents depends on various factors, including interpretation of our technology and the prior art and whether the differences between them allow our technology to be patentable. Patent applications and patents granted from them are complex, lengthy and highly technical documents that are often prepared under very limited time constraints and may not be free from errors that make their interpretation uncertain. The existence of errors in a patent may have an adverse effect on the patent, its scope and its enforceability. Our pending patent applications may not issue, and the scope of the claims of patent applications that do issue may be too narrow to adequately protect our competitive advantage. Also, our granted patents may be subject to challenges or narrowly construed and may not provide adequate protection.

***We may be subject to claims that we infringe, misappropriate or otherwise violate the intellectual property rights of third parties.***

Even if our patents do successfully issue, third parties may challenge the validity, enforceability or scope of such granted patents or any other granted patents we own or license, which may result in such patents being narrowed, invalidated or held unenforceable. For example, patents granted by the European Patent Office may be opposed by any person within nine months from the publication of their grant. Also, patents granted by the United States Patent and Trademark Office, or USPTO, may be subject to reexamination and other challenges.

Furthermore, even if they are not challenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. To meet such challenges, which are part of the risks and uncertainties of developing and marketing product candidates, we may need to evaluate third party intellectual property rights and, if appropriate, to seek licenses for such third party intellectual property or to challenge such third party intellectual property, which may be costly and may or may not be successful, which could also have an adverse effect on the commercial potential for UGN-101, UGN-102 and any of our product candidates.

***We may receive only limited protection, or no protection, from our issued patents and patent applications.***

If we encounter delays in our clinical trials or regulatory approval of our product candidates, the period of time during which we could market any of our product candidates under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to either (i) file any patent application related to hydrogel-based pharmaceutical compositions for optimal delivery of a drug in internal cavities such as the bladder, the method for treating urothelial cancer using hydrogel-based compositions, the method for treating overactive bladder topically without the need for injections, an in-dwelling ureter catheter system for optimal delivery of a drug into the renal cavity, and pharmaceutical compositions comprising an imidazoquinolin (amine) and lactic acid for use in a method for the treatment of bladder diseases or any of our product candidates or (ii) conceive and invent any of the inventions claimed in our patents or patent applications.

The patent application process, also known as patent prosecution, is expensive and time consuming, and we or any future licensors and licensees may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or any future licensors or licensees will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, etc., although we are unaware of any such defects that we believe are of material import. If we or any future licensors or licensees fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If any future licensors or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The strength of patents in the pharmaceutical field involves complex legal and scientific questions and can be uncertain. This uncertainty includes changes to the patent laws through either legislative action to change statutory patent law or court action that may reinterpret existing law in ways affecting the scope or validity of issued patents. The patent applications that we own or in-license may fail to result in issued patents in the United States or foreign countries with claims that cover our product candidates. Even if patents do successfully issue from the patent applications that we own or in-license, third parties may challenge the validity, enforceability or scope of such patents, which may result in such patents being narrowed, invalidated or held unenforceable. For example, patents granted by the European Patent Office may be challenged, also known as opposed, by any person within nine months from the publication of their grant. Any successful challenge to our patents could deprive us of exclusive rights necessary for the successful commercialization of our product candidates. Furthermore, even if they are unchallenged, our patents may not adequately protect our product candidates, provide exclusivity for our product candidates, or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents we hold or pursue with respect to our product candidates is challenged, it could dissuade companies from collaborating with us to develop or threaten our ability to commercialize our product candidates.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our product candidates, we may be open to competition from generic versions of our product candidates. Further, if we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

A considerable number of our patents and patent applications are entitled to effective filing dates prior to March 16, 2013. For U.S. patent applications in which patent claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party, for example a competitor, or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by those patent claims. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our participation in an interference proceeding may fail and, even if successful, may result in substantial costs and distract our management.

***Our trade secrets may not have sufficient intellectual property protection.***

In addition to the protection afforded by patents, we also rely on trade secret protection to protect proprietary know-how that may not be patentable or that we elect not to patent, processes for which patents may be difficult to obtain or enforce, and any other elements of our product candidates, and our product development processes (such as manufacturing and formulation technologies) that involve proprietary know-how, information or technology that is not covered by patents. However, trade

secrets can be difficult to protect. If the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating any trade secrets. Misappropriation or unauthorized disclosure of our trade secrets could significantly affect our competitive position and may have an adverse effect on our business. Furthermore, trade secret protection does not prevent competitors from independently developing substantially equivalent information and techniques and we cannot guarantee that our competitors will not independently develop substantially equivalent information and techniques. The FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

In an effort to protect our trade secrets and other confidential information, we require our employees, consultants, advisors, and any other third parties that have access to our proprietary know-how, information or technology, for example, third parties involved in the formulation and manufacture of our product candidates, and third parties involved in our clinical trials to execute confidentiality agreements upon the commencement of their relationships with us. These agreements require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us is kept confidential and not disclosed to third parties. However, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed despite having such confidentiality agreements. Adequate remedies may not exist in the event of unauthorized use or disclosure of our trade secrets. In addition, in some situations, these confidentiality agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants, or advisors have previous employment or consulting relationships. To the extent that our employees, consultants or contractors use any intellectual property owned by third parties in their work for us, disputes may arise as to the rights in any related or resulting know-how and inventions. If we are unable to prevent unauthorized material disclosure of our trade secrets to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could harm our business, operating results and financial condition.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly on obtaining and enforcing patents. Obtaining and enforcing patents in the pharmaceutical industry involves both technological and legal complexity, and therefore, is costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Further, recent U.S. Supreme Court rulings have either narrowed the scope of patent protection available in certain circumstances or weakened 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.

For our U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, or the America Invents Act, or AIA, was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO is currently developing regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA. It is not clear what other, if any, impact the AIA will have on the operation of our business. Moreover, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business and financial condition.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date 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 the 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, we cannot be certain that we were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our patents or patent applications.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and provide opportunities for third parties to challenge any issued patent in the USPTO. This applies to all

of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in a United States federal court 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.

Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, 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 patents and patents that we might obtain in the future.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent prosecution process.

Periodic maintenance fees and various other governmental fees on any issued patent and/or pending patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of a patent or patent application. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees. While an inadvertent lapse may sometimes be cured by payment of a late fee or by other means in accordance with the applicable rules, there are many 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 we fail to maintain the patents and patent applications directed to our product candidates, our competitors might be able to enter the market earlier than should otherwise have been the case, which could harm our business.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as 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. 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 on infringing activities is inadequate. These products may compete with our products, and our patents 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 certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally.

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 at risk of being invalidated or interpreted narrowly and our patent applications 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. In addition, certain countries in Europe and certain developing countries, including India and China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if our patents are infringed or if we are compelled to grant a license to our patents to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. 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 own or license. Finally, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.



***If we are unable to protect our trademarks from infringement, our business prospects may be harmed.***

We own trademarks that identify UGN-101, UGN-102 and UGN-201 and have registered these trademarks in the United States and Israel. Although we take steps to monitor the possible infringement or misuse of our trademarks, it is possible that third parties may infringe, dilute or otherwise violate our trademark rights. Any unauthorized use of our trademarks could harm our reputation or commercial interests. In addition, our enforcement against third-party infringers or violators may be unduly expensive and time-consuming, and the outcome may be an inadequate remedy.

***We may become involved in lawsuits to protect or enforce our patents or other intellectual property or the patents of our licensors, which could be expensive and time consuming.***

Third parties may infringe or misappropriate our intellectual property, including our existing patents, patents that may issue to us in the future, or the patents of our licensors to which we have a license. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. Further, we may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Generic drug manufacturers may develop, seek approval for, and launch generic versions of our products. If we file an infringement action against such a generic drug manufacturer, that company may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us and/or our licensors to engage in complex, lengthy and costly litigation or other proceedings.

For example, if we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering our product candidates, the defendant could counterclaim that the patent covering our product candidates is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent.

In addition, within and outside of the United States, there has been a substantial amount of litigation and administrative proceedings, including interference and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in various foreign jurisdictions, regarding patent and other intellectual property rights in the pharmaceutical industry. Recently, the AIA introduced new procedures including inter partes review and post grant review. The implementation of these procedures brings uncertainty to the possibility of challenges to our patents in the future, including challenges by competitors who perceive our patents as blocking entry into the market for their products, and the outcome of such challenges.

Such litigation and administrative proceedings could result in revocation of our patents or amendment of our patents such that they do not cover our product candidates. They may also put our pending patent applications at risk of not issuing or issuing with limited and potentially inadequate scope to cover our product candidates. 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. Additionally, it is also possible that prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, may, nonetheless, ultimately be found by a court of law or an administrative panel 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 would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a negative impact on our business.

Enforcing our or our licensors' intellectual property rights through litigation is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time.

Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could harm our business, financial condition or results of operations.

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, during the course of litigation or administrative proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our ordinary shares could be significantly harmed.

***We may become subject to claims for remuneration or royalties for assigned service invention rights by our employees, which could result in litigation and adversely affect our business.***

A significant portion of our intellectual property has been developed by our employees during their employment. Under the Israeli Patent Law, 5727-1967, or the Patent Law, inventions conceived by an employee during the scope of his or her employment with a company are regarded as “service inventions.” The Israeli Compensation and Royalties Committee, or the Committee, a body constituted under the Patent Law, has previously held, in certain cases, that employees may be entitled to remuneration for service inventions that they develop during their service for a company despite their explicit waiver of such right. Therefore, although we enter into agreements with our employees pursuant to which they waive their right to special remuneration for service inventions created in the scope of their employment or engagement and agree that any such inventions are owned exclusively by us, we may face claims by employees demanding remuneration beyond their regular salary and benefits.

***Third-party claims alleging intellectual property infringement may adversely affect our business.***

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties, for example, the intellectual property rights of competitors. Our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents owned or controlled by third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our activities related to our product candidates may give rise to claims of infringement of the patent rights of others. We cannot assure you that our product candidates will not infringe existing or future patents. We may not be aware of patents that have already issued that a third party might assert are infringed by our product candidates. It is also possible that patents of which we are aware, but which we do not believe are relevant to our product candidates, could nevertheless be found to be infringed by our product candidates. Nevertheless, we are not aware of any issued patents that we believe would prevent us from marketing our product candidates, if approved. There may also be patent applications that have been filed but not published that, when issued as patents, could be asserted against us.

Third parties making claims against us for infringement or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Further, if a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. Defense of these claims, regardless of their merit, would cause us to incur substantial expenses, and would be a substantial diversion of management time and employee resources from our business. In the event of a successful claim of infringement against us by a third party, we may have to (i) pay substantial damages, including treble damages and attorneys’ fees if we are found to have willfully infringed the third party’s patents; (ii) obtain one or more licenses from the third party; (iii) pay royalties to the third party; and/or (iv) redesign any infringing products. Redesigning any infringing products may be impossible or require substantial time and monetary expenditures. Further, we cannot predict whether any required license would be available at all or whether it would be available on commercially reasonable terms. In the event that we could not obtain a license, we may be unable to further develop and commercialize our product candidates, which could harm our business significantly. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms.

Defending ourselves or our licensors in litigation is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could harm our business, financial condition or results of operations.

***We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.***

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise improperly used or disclosed confidential information of these third parties or our employees’ former employers. Further, we

may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. We may also be subject to claims that former employees, consultants, independent contractors, collaborators 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 our right to and use of confidential and proprietary information. If we fail in defending any such claims, in addition to paying monetary damages, we may lose our rights therein. Such an outcome could have a negative impact on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

### **Risks Related to Government Regulation**

***If the FDA does not conclude that UGN-101, UGN-102, or our other product candidates satisfy the requirements under Section 505(b)(2) of the Federal Food Drug and Cosmetic Act, or Section 505(b)(2), or if the requirements for such product candidates are not as we expect, the approval pathway for these product candidates will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.***

We are conducting a single pivotal Phase 3 clinical trial for UGN-101 and a Phase 2b clinical trial of UGN-102 under the FDA's Section 505(b)(2) regulatory pathway. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, added Section 505(b)(2) to the Federal Food, Drug and Cosmetic Act. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies that were not conducted by or for the applicant, and for which the applicant has not received a right of reference, which could expedite the development program for UGN-101, UGN-102 and our other product candidates by potentially decreasing the amount of preclinical and clinical data that we would need to generate in order to obtain FDA approval. However, while we believe that our product candidates are reformulations of existing drugs or biologics and, therefore, will not be treated as new chemical entities, or NCEs, the submission of an NDA under the Section 505(b)(2) or similar regulatory pathway does not preclude the FDA from determining that the product candidate that is the subject of such submission is an NCE and therefore not eligible for review under such regulatory pathway.

If the FDA does not allow us to pursue the Section 505(b)(2) or similar regulatory pathway as anticipated, we may need to conduct additional preclinical experiments and clinical trials, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for these product candidates, and complications and risks associated with these product candidates, would likely increase significantly. Moreover, inability to pursue the Section 505(b)(2) or similar regulatory pathway could result in new competitive products reaching the market more quickly than our product candidates, which would likely harm our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) or similar regulatory pathway, our product candidates may not receive the requisite approvals for commercialization.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2) over the last few years, certain competitors and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, the FDA may be required to change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2). In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our potential future NDAs for up to 30 months depending on the outcome of any litigation. It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay, or even prevent, the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway for our product candidates, there is no guarantee this would ultimately lead to faster product development or earlier approval.

Moreover, even if these product candidates are approved under the Section 505(b)(2) pathway, as the case may be, the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

***Fast track designation for one or more of our product candidates may not actually lead to a faster development or regulatory review or approval process.***

In August 2017, we received fast track designation for UGN-101 for the treatment of UTUC. If a product is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a product sponsor may apply for FDA fast track designation. Even though we have received fast track designation for UGN-101 for the treatment of UTUC, fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

***A breakthrough therapy designation by the FDA for UGN-101 for LG UTUC may not lead to a faster development or regulatory review or approval process, and it will not increase the likelihood that the product candidate will receive marketing approval.***

We received breakthrough therapy designation for UGN-101 for LG UTUC. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the NDA.

Designation as a breakthrough therapy is within the discretion of the FDA. The receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, the FDA may later decide that the product candidate no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened.

***We expect current and future legislation affecting the healthcare industry, including healthcare reform, to impact our business generally and to increase limitations on reimbursement, rebates and other payments, which could adversely affect third-party coverage of our products, our operations, and/or how much or under what circumstances healthcare providers will prescribe or administer our products, if approved.***

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, laws intended, among other things, to broaden access to health insurance, improve quality of care, and reduce or constrain the growth of healthcare spending.

Provisions of the ACA relevant to the pharmaceutical industry include the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, not including orphan drug sales;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (70% commencing on January 1, 2019) point-of-sale discounts on negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report annually certain financial arrangements with physicians and teaching hospitals; as defined in the ACA and its implementing regulations, including reporting any payment or "transfer of value" provided to physicians and teaching hospitals and any ownership and investment interests held by physicians and their immediate family members during the preceding calendar year;
- expansion of healthcare fraud and abuse laws, including the federal civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

There have been judicial and Congressional challenges to certain aspects of the ACA. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the ACA. For example, since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements 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 been signed into law. The Tax Cuts and the Jobs Act includes a provision that repealed, 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, or the BBA, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, published a 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 U.S. District Court judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. While the Texas District Court Judge, as well as the Trump Administration and CMS, have stated that the ruling will have no immediate effect, it is unclear how this decision, 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 since the ACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction, or a Joint Selection Committee, to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of an amount greater than \$1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, which started in 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will stay in effect through 2027 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 categories of healthcare providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additionally, there have been several recent U.S. Congressional inquiries and proposed and enacted legislation at the federal and state levels designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump Administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 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. The U.S. Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and is concurrently implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump Administration have both stated that they 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. If healthcare policies or reforms intended to curb healthcare costs are adopted, or if we experience negative publicity with respect to the pricing of our products or the pricing of pharmaceutical drugs generally, the prices that we charge for any approved products may be limited, our commercial opportunity may be limited and/or our revenues from sales of our products may be negatively impacted.

If we obtain regulatory approval and commercialization of UGN-101, UGN-102 or any of our other product candidates, these laws may result in additional reductions in healthcare funding, which could have an adverse effect on our customers and accordingly, our financial operations. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of UGN-101, UGN-102 or our other product candidates may be.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the 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 drug products that have completed a Phase I 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 pharmaceutical manufacturer to make its drug products available to eligible patients under the Right to Try Act.

Although we cannot predict the full effect on our business of the implementation of existing legislation or the enactment of additional legislation pursuant to healthcare and other legislative reform, we believe that legislation or regulations that would reduce reimbursement for, or restrict coverage of, our products could adversely affect how much or under what circumstances healthcare providers will prescribe or administer our products. This could adversely affect our business by reducing our ability to generate revenues, raise capital, obtain additional licensees and market our products. In addition, we believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of pharmaceutical products, which may adversely impact product sales.

***We may be unable to obtain Orphan Drug Designation or exclusivity for future product candidates we may develop. If our competitors are able to obtain orphan drug exclusivity for their products that are for the same indication as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.***

Under the Orphan Drug Act of 1983, or the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat an orphan disease or condition, defined as a patient population of fewer than 200,000 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.

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 receives the first FDA approval for the indication for which it has Orphan Drug Designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity.

Although the FDA has granted Orphan Drug Designation to UGN-101 for the treatment of UTUC and to UGN-201 for treatment of CIS, we may not receive Orphan Drug Designation for any of our other product candidates. If our competitors are able to obtain orphan drug exclusivity for their products that are the same or similar to our product candidates before our drug candidates are approved, we may not be able to have competing product candidates approved by the FDA for a significant period of time. Any delay in our ability to bring our product candidates to market would negatively impact our business, revenue, cash flows and operations.

***Orphan Drug Designation may not ensure that we will enjoy market exclusivity in a particular market, and if we fail to obtain or maintain orphan drug exclusivity for our product candidates, we may be subject to earlier competition and our potential revenue will be reduced.***

Orphan Drug Designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax advantages, user-fee waivers and market exclusivity for certain periods of time.

UGN-101 and UGN-201 have been granted Orphan Drug Designation for the treatment of UTUC and CIS, respectively, in the United States. Even if we obtain Orphan Drug Designation for our other product candidates, we may not be the first to obtain regulatory approval for any particular orphan indication due to the uncertainties associated with developing biopharmaceutical products. Further, even if we obtain Orphan Drug Designation for a product candidate, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for the same indication, approval of our product candidate would be blocked during the period of marketing exclusivity unless we could demonstrate that our product candidate is clinically superior to the approved product. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate, we are pursuing for a different orphan indication, this may negatively impact the market opportunity for our product candidate. There have been legal challenges to aspects of the FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, and future challenges could lead to changes that affect the protections afforded our product candidates in ways that are difficult to predict.

***Even if we receive regulatory approval for our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expenses, limit or withdraw regulatory approval and subject us to penalties if we fail to comply with applicable regulatory requirements.***

If and when regulatory approval has been granted, our product candidates or any approved product will be subject to continual regulatory review by the FDA and/or foreign regulatory authorities. Additionally, any product candidates, if approved, will be subject to extensive and ongoing regulatory requirements, including labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indications for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. In addition, if the applicable regulatory agency approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product 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 continued compliance with cGMP and GCP for any clinical trials that we conduct post-approval.

Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or problems with our third-party manufacturers' processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;

- refusal by the FDA to approve pending applications or supplements to approved applications submitted by us, or suspension or revocation of product license approvals; and
- product seizure or detention, or refusal to permit the import or export of products; and injunctions or the imposition of civil or criminal penalties.

Our ongoing regulatory requirements may also change from time to time, potentially harming or making costlier our commercialization efforts. 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 other countries. 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, which would adversely affect our business.

***Our relationships with healthcare professionals, independent contractors, clinical investigators, CROs, consultants and vendors 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. If we are unable to comply, or have not fully complied, with such laws, we could face penalties.***

We may currently be or may become subject to various U.S. federal and state health care laws, including those intended to prevent health care fraud and abuse.

The federal Anti-Kickback Statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, by a federal healthcare program such as Medicare and Medicaid. Remuneration has been broadly defined to include anything of value, including, but not limited to, cash, improper discounts, and free or reduced-price items and services.

Federal false claims laws, including the federal civil False Claims Act, or the FCA, and civil monetary penalties law impose penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or making a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government. The FCA has been used to, among other things, prosecute persons and entities submitting claims for payment that are inaccurate or fraudulent, that are for services not provided as claimed, or for services that are not medically necessary. The FCA includes a whistleblower provision that allows individuals to bring actions on behalf of the federal government and share a portion of the recovery of successful claims.

Many states have similar fraud and abuse statutes and regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. State and federal authorities have aggressively targeted medical technology companies for, among other things, alleged violations of these anti-fraud statutes, based on unlawful financial inducements paid to prescribers and beneficiaries, as well as impermissible promotional practices, including certain marketing arrangements that rely on volume-based pricing and off-label promotion of FDA-approved products.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including public and private payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

Additionally, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, impose, among other things, specified requirements on covered entities, including certain healthcare providers, health plans, and healthcare clearinghouses, and their business associates relating to the privacy and, security and transmission of individually identifiable health information, including mandatory contractual terms and required implementation of certain safeguards of such information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, 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 HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways, may not have the same effect and may not be preempted by HIPAA, thus complicating compliance efforts.

Our operations will also be subject to the federal Open Payments program pursuant to the Physician Payments Sunshine Act, created under Section 6002 of the ACA and its implementing regulations, which requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to annually report, information related to payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians and their immediate family members to CMS. We may also be subject to state 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/or state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidelines promulgated by the federal government.

Many states have also adopted laws similar to each of the above federal laws, which may be broader in scope and apply to items or services reimbursed by any payor, including commercial insurers. If any of our business activities, including but not limited to our relationships with healthcare providers, are found to violate any of the aforementioned laws, we may be subject to administrative, civil and/or criminal penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, diminished profits and future earnings and curtailment or restructuring of our operations.

Also, the U.S. Foreign Corrupt Practices Act and similar worldwide anti-bribery laws generally prohibit companies and their intermediaries from making improper payments to non-U.S. officials for the purpose of obtaining or retaining business. We cannot assure you that our internal control policies and procedures will protect us from reckless or negligent acts committed by our employees, future distributors, partners, collaborators or agents. Violations of these laws, or allegations of such violations, could result in fines, penalties or prosecution and have a negative impact on our business, results of operations and reputation.

***Legislative or regulatory healthcare reforms in the United States or abroad may make it more difficult and costly for us to obtain regulatory clearance or approval of our product candidates or any future product candidates and to produce, market, and distribute our products after clearance or approval is obtained.***

From time to time, legislation is drafted and introduced in Congress in the United States or by governments in foreign jurisdictions that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the reimbursement thereof. In addition, FDA or foreign regulatory agency regulations and guidance are often revised or reinterpreted by the FDA or the applicable foreign regulatory agency in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of our product candidates or any future product candidates. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- changes to manufacturing methods;
- recall, replacement, or discontinuance of one or more of our products; and
- additional recordkeeping.

Each of these would likely entail substantial time and cost and could harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products would harm our business, financial condition, and 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 negatively impact 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.

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 or other work-related injuries with policy limits that we believe are customary for similarly situated companies and adequate to provide us with coverage for foreseeable risks. Although we maintain such insurance, this insurance may not provide adequate coverage against potential liabilities. 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 production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

***It may be difficult for us to profitably sell our product candidates if coverage and reimbursement for these products is limited by government authorities and/or third-party payor policies.***

In addition to any healthcare reform measures which may affect reimbursement, market acceptance and sales of UGN-101, UGN-102 and our other product candidates, if approved, will depend on the coverage and reimbursement policies of third-party payors, like government authorities, private health insurers, and managed care organizations. Third-party payors decide which medications they will cover and separately establish reimbursement levels.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government and other third-party payors are increasingly challenging the prices charged for health care products, examining the cost effectiveness of drugs in addition to their safety and efficacy, and limiting or attempting to limit both coverage and the level of reimbursement for prescription drugs. We cannot be sure that coverage will be available for UGN-101, UGN-102 or our other product candidates, if approved, or, if coverage is available, the level of reimbursement will be adequate to make our products affordable for patients or profitable for us.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, decisions about reimbursement for new medicines under Medicare are made by CMS, as the administrator for the Medicare program. Private third-party payors often use CMS as a model for their coverage and reimbursement decisions, but also have their own methods and approval process apart from CMS's determinations. It is difficult to predict what CMS as well as other third-party payors will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products.

Reimbursement may impact the demand for, and/or the price of, any product for which we obtain marketing approval. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided, and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or applicable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution.

Reimbursement by a third-party payor may depend upon a number of factors including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and

- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. Further, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process may 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 applied consistently or obtained in the first instance. We may not be able to provide data sufficient to gain acceptance with respect to coverage and/or sufficient reimbursement levels. We cannot be sure that coverage or adequate reimbursement will be available for UGN-101, UGN-102 or any of our other product candidates, if approved. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our future products. If reimbursement is not available, or is available only to limited levels, we may not be able to commercialize UGN-101, UGN-102 or our other product candidates, or achieve profitably at all, even if approved.

***Legislative or regulatory healthcare reforms in the United States may make it more difficult and costly for us to obtain regulatory clearance or approval of UGN-101, UGN-102 or any of our other product candidates and to produce, market, and distribute our products after clearance or approval is obtained.***

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of UGN-101, UGN-102 or any of our other product candidates. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- changes to manufacturing methods;
- change in protocol design;
- additional treatment arm (control);
- recall, replacement, or discontinuance of one or more of our products; and
- additional recordkeeping.

Each of these would likely entail substantial time and cost and could harm our business and our financial results.

#### **Risks Related to Ownership of Our Ordinary Shares**

***The market price of our ordinary shares has been and may continue to be subject to fluctuation and you could lose all or part of your investment.***

The stock market in general has been, and the market price of our ordinary shares in particular has been and may continue to be, subject to fluctuation, whether due to, or irrespective of, our operating results and financial condition. The market price of our ordinary shares on the Nasdaq Global Market may fluctuate as a result of a number of factors, some of which are beyond our control, including, but not limited to:

- actual or anticipated variations in our and our competitors' results of operations and financial condition;
- physician and market acceptance of our products;
- the mix of products that we sell;
- our success or failure to obtain approval for and commercialize our product candidates;
- changes in earnings estimates or recommendations by securities analysts, if our ordinary shares are covered by analysts;
- development of technological innovations or new competitive products by others;

- announcements of technological innovations or new products by us;
- publication of the results of preclinical or clinical trials for UGN-101, UGN-102 or our other product candidates;
- failure by us to achieve a publicly announced milestone;
- delays between our expenditures to develop and market new or enhanced product candidates and the generation of sales from those products;
- developments concerning intellectual property rights, including our involvement in litigation brought by or against us;
- regulatory developments and the decisions of regulatory authorities as to the approval or rejection of new or modified products;
- changes in the amounts that we spend to develop, acquire or license new products, technologies or businesses;
- changes in our expenditures to promote our products;
- our sale or proposed sale, or the sale by our significant shareholders, of our ordinary shares or other securities in the future;
- changes in key personnel;
- success or failure of our research and development projects or those of our competitors;
- the trading volume of our ordinary shares; and
- general economic and market conditions and other factors, including factors unrelated to our operating performance.

These factors and any corresponding price fluctuations may negatively impact the market price of our ordinary shares and result in substantial losses being incurred by our investors. In the past, following periods of market volatility, public company shareholders have often instituted securities class action litigation. If we were to become involved in securities litigation, it could impose a substantial cost upon us and divert the resources and attention of our management from our business.

***If equity research analysts do not publish research or reports about our business or if they issue unfavorable commentary or downgrade our ordinary shares, the price of our ordinary shares could decline.***

The trading market for our ordinary shares relies in part on the research and reports that equity research analysts publish about us and our business, if at all. We do not have control over these analysts and we do not have commitments from them to write research reports about us. The price of our ordinary shares could decline if no research reports are published about us or our business, or if one or more equity research analysts downgrade our ordinary shares or if those analysts issue other unfavorable commentary or cease publishing reports about us or our business.

***Future sales of our ordinary shares could reduce the market price of our ordinary shares.***

If our existing shareholders, particularly our directors, their affiliates, or our executive officers, sell a substantial number of our ordinary shares in the public market, the market price of our ordinary shares could decrease significantly. The perception in the public market that our shareholders might sell our ordinary shares could also depress the market price of our ordinary shares and could impair our future ability to obtain capital, especially through an offering of equity securities.

As of the date of the report to which this document is attached, the holders of approximately 4,515,674 ordinary shares are entitled to registration rights. In addition, our sale of additional ordinary shares or similar securities in order to raise capital might have a similar negative impact on the share price of our ordinary shares. A decline in the price of our ordinary shares might impede our ability to raise capital through the issuance of additional ordinary shares or other equity securities and may cause you to lose part or all of your investment in our ordinary shares.

***Future equity offerings could result in future dilution and could cause the price of our ordinary shares to decline.***

In order to raise additional capital, we may in the future offer additional ordinary shares or other securities convertible into or exchangeable for our ordinary shares at prices that we determine from time to time, and investors purchasing shares or other securities in the future could have rights superior to existing shareholders. We may choose to raise additional capital due to

market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. In October 2018, we entered into an Open Market Sale Agreement<sup>SM</sup> with Jefferies LLC, which allows us to sell our ordinary shares through Jefferies LLC as our sales agent. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

***The significant share ownership position of our officers, directors and entities affiliated with certain of our directors may limit your ability to influence corporate matters.***

Our officers, directors and entities affiliated with certain of our directors beneficially own or control, directly or indirectly, approximately 14.3% of our outstanding ordinary shares, as of December 31, 2018. Accordingly, these persons are able to significantly influence, though not independently determine, the outcome of matters required to be submitted to our shareholders for approval, including decisions relating to the election of our board of directors, and the outcome of any proposed merger or consolidation of our company. These interests may not be consistent with those of our other shareholders. In addition, these persons' significant interest in us may discourage third parties from seeking to acquire control of us, which may adversely affect the market price of our ordinary shares.

***We have never paid cash dividends on our share capital, and we do not anticipate paying any cash dividends in the foreseeable future.***

We have never declared or paid cash dividends on our share capital, nor do we anticipate paying any cash dividends on our share capital in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of our ordinary shares will be investors' sole source of gain for the foreseeable future. In addition, Israeli law limits our ability to declare and pay dividends and may subject our dividends to Israeli withholding taxes.

***We expect to be classified as a passive foreign investment company for the taxable years ended December 31, 2018, and December 31, 2019, and, as such, our U.S. shareholders may suffer adverse tax consequences.***

Generally, for any taxable year, if at least 75% of our gross income is passive income, or at least 50% of the value of our assets is attributable to assets that produce passive income or are held for the production of passive income, including cash, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. For purposes of these tests, passive income includes dividends, interest gains from commodities and securities transactions, the excess of gains over losses from the disposition of assets which produce passive income (including amounts derived by reason of the temporary investment of funds raised in offerings of our shares) and rents and royalties other than rents and royalties which are received from unrelated parties in connection with the active conduct of a trade or business. We believe that we were classified as a PFIC for the taxable year ended December 31, 2018 and, based upon the expected nature and composition of our income and assets, we anticipate that we will be classified as a PFIC for the taxable year ending December 31, 2019. If we are characterized as a PFIC, our U.S. Holders (as defined in Item 10.E of our Annual Report on Form 20-F for the year ended December 31, 2017, filed with the SEC on March 15, 2018, under the heading "Material U.S. Federal Income Tax Consequences to U.S. Holders") may suffer adverse tax consequences, including having gains realized on the sale of our ordinary shares treated as ordinary income, rather than capital gain, the loss of the preferential rate applicable to dividends received on our ordinary shares by individuals who are U.S. Holders, having interest charges apply to distributions by us and gains from the sales of our shares, and additional reporting requirements under U.S. federal income tax laws and regulations. A U.S. Holder that (i) owns our ordinary shares at any point during a year in which we are characterized as a PFIC and (ii) does not timely make a QEF Election (as described below) will treat such ordinary shares as stock in a PFIC for all subsequent tax years, even if we no longer qualify as a PFIC under the relevant tests in such subsequent tax years. A U.S. Holder may be able to elect out of such treatment if we are no longer characterized as a PFIC by making a "purging election."

Our status as a PFIC depends on the nature and composition of our income and the nature, composition and value of our assets (which may be determined based on the fair market value of each asset, with the value of goodwill and going concern value determined in large part by reference to the market value of our ordinary shares, which may be volatile) from time to time. We cannot provide any assurances regarding our PFIC status for the current or future taxable years, and our U.S. tax counsel has not provided any opinion regarding our PFIC status.

Because we believe that we are a PFIC, we plan on providing to investors, by annually posting a "PFIC Annual Information Statement" on our website, with the information required to allow investors to make a qualified electing fund election, or a QEF Election, for United States federal income tax purposes.

***Future changes to tax laws could have a material adverse effect on us and reduce net returns to our shareholders.***

Our tax treatment is subject to changes in tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, as well as tax policy initiatives and reforms related to the Organisation for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS Project, the European Commission's state aid investigations and other initiatives.

Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or, in the specific context of withholding tax dividends paid. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our financial position and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders, and increase the complexity, burden and cost of tax compliance.

In addition, on December 22, 2017, the Tax Cuts and Jobs Act was signed into law and significantly revised the U.S. Internal Revenue Code of 1986, as amended, or the Code. The Tax Cuts and Jobs Act, among other things, contains significant changes to U.S. corporate income taxation, including the reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for business interest expense to 30% of adjusted earnings (except with respect to certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repealing of many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act. The impact of this tax reform on holders of our ordinary shares is also uncertain and could be adverse. We urge you to consult with your legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our ordinary shares.

***Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.***

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, the U.S. Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable nexus, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

***If a United States person is treated as owning at least 10% of our ordinary shares, such holder may be subject to adverse U.S. federal income tax consequences.***

If a U.S. Holder is treated as owning (directly, indirectly or constructively) at least 10% of the value or voting power of our ordinary shares, such U.S. Holder may be treated as a "United States shareholder" with respect to each "controlled foreign corporation" in our group (if any). Because our group includes at least one U.S. subsidiary (Urogen Pharma, Inc.), if we were to form or acquire any non-U.S. subsidiaries in the future, they may be treated as controlled foreign corporations of any U.S. Holder owning (directly, indirectly or constructively) at least 10% of the value or voting power of our ordinary shares. A United States shareholder of a controlled foreign corporation may be required to annually report and include in its U.S. taxable income its pro rata share of "Subpart F income," "global intangible low-taxed income" and investments in U.S. property by controlled foreign corporations, regardless of whether we make any distributions. An individual that is a United States shareholder with respect to a controlled foreign corporation generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a United States shareholder that is a U.S. corporation. We cannot provide any assurances that we will assist investors in determining whether any non-U.S. subsidiaries that we may form or acquire in the future would be treated as a controlled foreign corporation or whether such investor would be treated as a United States shareholder with respect to any of such controlled foreign corporations. Further, we cannot provide any assurances that we

will furnish to any U.S. shareholder information that may be necessary to comply with the reporting and tax paying obligations discussed above. Failure to comply with these reporting obligations may subject you to significant monetary penalties and may prevent the statute of limitations with respect to your U.S. federal income tax return for the year for which reporting was due from starting. U.S. Holders should consult their tax advisors regarding the potential application of these rules to their investment in our ordinary shares.

***Our ability to use our net operating loss carryforwards to offset future taxable income may be subject to certain limitations.***

In general, under Section 382 of the Code, a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-change net operating loss carryforwards, or NOLs, to offset future taxable income. We have not performed a detailed analysis to determine whether an ownership change under Section 382 of the Code has occurred after each of our previous issuances of ordinary shares. In addition, if we undergo an ownership change, our ability to utilize NOLs could be limited by Section 382 of the Code. As of December 31, 2018, our NOLs were immaterial to the overall company. Future changes in our share ownership, some of which are outside of our control, could result in an ownership change under Section 382 of the Code. Furthermore, our ability to utilize our NOLs may be subject to limitations. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes, which could negatively impact our future cash flows.

***Unlike in prior years, as of January 1, 2019, we are required to comply with the domestic reporting regime under the Exchange Act and will incur significant legal, accounting and other expenses, and our management will be required to devote substantial additional time to new compliance initiatives and corporate governance matters.***

We determined that, as of December 31, 2018, we no longer qualified as a “foreign private issuer” under the rules and regulations of the SEC. While we were a foreign private issuer, we were exempt from compliance with certain laws and regulations of the SEC, including the proxy rules, the short-swing profits recapture rules and certain governance requirements, such as independent director oversight of the nomination of directors and executive compensation. In addition, we were not required to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as U.S. companies registered under the Exchange Act. As a result of this determination, beginning January 1, 2019, we were no longer entitled to “foreign private issuer” exemptions and must report as a domestic U.S. filer, including filing quarterly reports on Form 10-Q, current reports on Form 8-K and proxy statements under Section 14 of the Exchange Act. In addition, our “insiders” are now subject to the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act and we are no longer exempt from the requirements of Regulation FD promulgated by the SEC under the Exchange Act. Moreover, as a domestic filer, we are required to comply with the corporate governance obligations imposed by the Nasdaq Stock Market and no longer have the option to follow our home country rules in lieu of such obligations.

The regulatory and compliance costs associated with the reporting and governance requirements applicable to U.S. domestic issuers may be significantly higher than the costs we previously incurred as a foreign private issuer. As a result, we expect that the loss of foreign private issuer status will increase our legal and financial compliance costs and will make some activities highly time-consuming and costly. In addition, we need to develop our reporting and compliance infrastructure and may face challenges in complying with the new requirements applicable to us.

Furthermore, we also determined that, as of December 31, 2018, we no longer qualified as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012. Because we no longer qualify as an emerging growth company, and as certain extended transition periods available to emerging growth companies expire, we will become subject to additional reporting requirements and standards and accelerated filing deadlines for our periodic reports. For example, we have incurred significant expenses and devoted substantial management effort toward ensuring compliance with the requirements of Section 404 of the Sarbanes-Oxley Act. If we are unable to implement these changes effectively or efficiently, it could harm our operations, financial reporting or financial results and could result in an adverse opinion on internal control from our independent registered public accounting firm. If we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. We will also be subject to enhanced disclosures obligations regarding executive compensation in our periodic reports and proxy statements and requirements to hold a nonbinding advisory vote on executive compensation. While we are taking steps to implement the systems and processes required to comply with these additional requirements, we cannot assure you that the measures we have taken to date, and are continuing to implement, will enable us to comply fully and in a timely manner.

## Risks Related to our Operations in Israel

***Our research and development and other significant operations are located in Israel and, therefore, our results may be adversely affected by political, economic and military instability in Israel.***

Our research and development facilities are located in Ra'anana, Israel. In addition, the majority of our key employees are residents of Israel. If these or any future facilities in Israel were to be damaged, destroyed or otherwise unable to operate, whether due to war, acts of hostility, earthquakes, fire, floods, hurricanes, storms, tornadoes, other natural disasters, employee malfeasance, terrorist acts, power outages or otherwise, or if performance of our research and development is disrupted for any other reason, such an event could delay our clinical trials or, if our product candidates are approved and we choose to manufacture all or any part of them internally, jeopardize our ability to manufacture our products as promptly as our prospective customers will likely expect, or possibly at all. If we experience delays in achieving our development objectives, or if we are unable to manufacture an approved product within a timeframe that meets our prospective customers' expectations, our business, prospects, financial results and reputation could be harmed.

Political, economic and military conditions in Israel may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its neighboring countries, Hamas (an Islamist militia and political group that controls the Gaza Strip) and Hezbollah (an Islamist militia and political group based in Lebanon). In addition, several countries, principally in the Middle East, restrict doing business with Israel, and additional countries may impose restrictions on doing business with Israel and Israeli companies whether as a result of hostilities in the region or otherwise. Any hostilities involving Israel, terrorist activities, political instability or violence in the region or the interruption or curtailment of trade or transport between Israel and its trading partners could adversely affect our operations and results of operations and adversely affect the market price of our ordinary shares.

Our commercial insurance does not cover losses that may occur as a result of an event associated with the security situation in the Middle East. Although the Israeli government is currently committed to covering the reinstatement value of direct damages that are caused by terrorist attacks or acts of war, there can be no assurance that this government coverage will be maintained, or if maintained, will be sufficient to compensate us fully for damages incurred. Any losses or damages incurred by us could have a material adverse effect on our business, financial condition and results of operations.

Further, our operations could be disrupted by the obligations of our employees to perform military service. As of December 31, 2018, we had 38 employees based in Israel. Of these employees, some may be military reservists, and may be called upon to perform military reserve duty of up to 36 days per year (and in some cases more) until they reach the age of 40 (and in some cases, up to the age of 45 or older). Additionally, they may be called to active duty at any time under emergency circumstances. In response to increased tension and hostilities in the region, there have been, at times, call-ups of military reservists, and it is possible that there will be additional call-ups in the future. Our operations could be disrupted by the absence of these employees due to military service. Such disruption could harm our business and operating results.

***The Israeli government grants we have received for research and development activities restrict our ability to manufacture products and transfer technologies outside of Israel and require us, in addition to the payment of royalties, to satisfy specified conditions. If we fail to satisfy these conditions, we may be required to refund grants previously received and incur financial penalties.***

We have received grants under the Israeli Law for the Encouragement of Industrial Research, Development and Technological Innovation, 5754-1984, or the R&D Law, from the Israel Innovation Authority in Israel, or the IIA, formerly known as the Office of the Chief Scientist of the Ministry of Economy and Industry, an independent and impartial public entity, for some of our development programs. Through December 31, 2018, we had received grants in the aggregate amount of \$2.1 million. As of September 30, 2018, we have accrued \$0.8 million in royalties due to the IIA, which has been recorded in cost of revenues in our results of operations for the nine and three months ended September 30, 2018. We may in the future apply to receive additional grants from the IIA. However, we cannot predict whether we will be entitled to any future grants, or the amounts of any such grants.

A recipient of a grant from the IIA is obligated to pay royalties generally at a rate of 3% to 5% on revenues from sales of products developed with IIA-funded technology, up to the amount of the grant related to any such products plus accrued interest. Under the R&D Law, a company that received grants from the IIA may not transfer IIA-funded technology or manufacture products developed with IIA-funded technology outside of the State of Israel without first obtaining the approval of the IIA. For example, under the Allergan Agreement, Allergan has the option to manufacture products developed with IIA-funded technology outside of Israel and, although Allergan has not yet exercised this option, we have requested approval from the IIA for a possible transfer and are currently awaiting their response. We may not receive any such approval upon any request, which could prevent us, for example, from out-licensing our product candidates or complying with our existing agreements. Even if we do receive such approvals, we may be required to pay increased royalties of up to 300% of the amount of the original grant and other amounts. If we do not receive such approvals, we may be required to pay significant penalties.



In June 2017, new rules published by the IIA for granting a right to use know-how developed from research and development that was conducted pursuant to a plan approved by the IIA outside of Israel, or Licensing Rules, came into effect. The Licensing Rules allow a recipient of a grant from the IIA to grant third parties outside of Israel the right to use know-how, or License, provided that the IIA authorized the grant of the License. In such case, the recipient of the grant has to pay the IIA for the License. The amount of payment is based on various factors, including the consideration received by the licensor and, in accordance with the formulas set forth in the Licensing Rules, may equal up to six times the IIA-funding amount plus interest. When the consideration for the grant includes nonmonetary compensation or monetary compensation that is not fixed, or when a “special relationship” exists between the licensor and licensee (e.g., when a party controls the other party or is the other party’s exclusive distributor) or when the agreed consideration does not reflect, in the IIA’s opinion, the market value, the IIA may base the value of the transaction on an economic assessment that it obtains for such purpose.

The IIA may also impose certain conditions on any arrangement under which it permits us to transfer IIA-funded technology outside of the State of Israel. Furthermore, the consideration available to our shareholders in a transaction involving the transfer outside of the State of Israel of IIA-funded technology (such as a merger or similar transaction) may be reduced by any amounts that we are required to pay to IIA. The restrictions under the R&D Law will continue to apply even after we have repaid the full amount of royalties due to the IIA. If we fail to satisfy the conditions of the R&D Law, we may be required to refund the amounts of the grants previously received, together with interest and penalties, and may become subject to criminal charges.

***Provisions of Israeli law and our articles of association may delay, prevent or otherwise impede a merger with, or an acquisition of, us, even when the terms of such a transaction are favorable to us and our shareholders.***

Israeli corporate law regulates mergers, requires tender offers for acquisitions of shares above specified thresholds, requires special approvals for transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to such types of transactions. For example, a tender offer for all of a company’s issued and outstanding shares can only be completed if shareholders not accepting the tender offer hold less than 5% of the issued share capital. Completion of the tender offer also requires approval of a majority of the offerees that do not have a personal interest in the tender offer, unless shareholders not accepting the tender offer hold less than 2% of the company’s outstanding shares. Furthermore, the shareholders, including those who indicated their acceptance of the tender offer, may, at any time within six months following the completion of the tender offer, petition an Israeli court to alter the consideration for the acquisition, unless the acquirer stipulated in its tender offer that a shareholder that accepts the offer may not seek such appraisal rights.

Furthermore, Israeli tax considerations may make potential transactions unappealing to us or to our shareholders whose country of residence does not have a tax treaty with Israel exempting such shareholders from Israeli tax. For example, Israeli tax law does not recognize tax-free share exchanges to the same extent as U.S. tax law. With respect to mergers, Israeli tax law allows for tax deferral in certain circumstances but makes the deferral contingent on the fulfillment of a number of conditions, including, in some cases, a holding period of two years from the date of the transaction during which sales and dispositions of shares of the participating companies are subject to certain restrictions. Moreover, with respect to certain share swap transactions, the tax deferral is limited in time, and when such time expires, the tax becomes payable even if no disposition of the shares has occurred. These provisions could delay, prevent or impede an acquisition of us or our merger with another company, even if such an acquisition or merger would be beneficial to us or to our shareholders.

***It may be difficult to enforce a judgment of a U.S. court against us, our officers and directors or the Israeli experts named in our reports filed with the SEC in Israel or the United States, to assert U.S. securities laws claims in Israel or to serve process on our officers and directors and these experts.***

We are incorporated in Israel. Several of our directors reside outside of the United States, and most of our assets and most of the assets of these persons are located outside of the United States. Therefore, a judgment obtained against us, or any of these persons, including a judgment based on the civil liability provisions of the U.S. federal securities laws, may not be collectible in the United States and may not be enforced by an Israeli court. It may also be difficult for you to effect service of process on these persons in the United States or to assert U.S. securities law claims in original actions instituted in Israel. Israeli courts may refuse to hear a claim based on an alleged violation of U.S. securities laws reasoning that Israel is not the most appropriate forum in which to bring such a claim. In addition, even if an Israeli court agrees to hear a claim, it may determine that Israeli law and not U.S. law is applicable to the claim. If U.S. law is found to be applicable, the content of applicable U.S. law must be proven as a fact by expert witnesses, which can be a time consuming and costly process. Certain matters of procedure will also be governed by Israeli law.

There is little binding case law in Israel that addresses the matters described above. As a result of the difficulty associated with enforcing a judgment against us in Israel, you may not be able to collect any damages awarded by either a U.S. or foreign court.

***Your rights and responsibilities as a shareholder will be governed by Israeli law, which differs in some material respects from the rights and responsibilities of shareholders of U.S. companies.***

The rights and responsibilities of the holders of our ordinary shares are governed by our articles of association and by Israeli law. These rights and responsibilities differ in some material respects from the rights and responsibilities of shareholders in U.S. companies. In particular, a shareholder of an Israeli company has a duty to act in good faith and in a customary manner in exercising its rights and performing its obligations towards the company and other shareholders, and to refrain from abusing its power in the company, including, among other things, in voting at a general meeting of shareholders on matters such as amendments to a company's articles of association, increases in a company's authorized share capital, mergers and acquisitions and related party transactions requiring shareholder approval, as well as a general duty to refrain from discriminating against other shareholders. In addition, a shareholder who is aware that it possesses the power to determine the outcome of a vote at a meeting of the shareholders or to appoint or prevent the appointment of a director or executive officer in the company has a duty of fairness toward the company.

There is limited case law available to assist us in understanding the nature of these duties or the implications of these provisions. These provisions may be interpreted to impose additional obligations and liabilities on holders of our ordinary shares that are not typically imposed on shareholders of U.S. companies.

### **Risks Related to Our Management and Employees**

***We depend on our executive officers and key clinical and technical personnel to operate our business effectively, and we must attract and retain highly skilled employees in order to succeed.***

Our success depends upon the continued service and performance of our executive officers who are essential to our growth and development. The loss of one or more of our executive officers could delay or prevent the continued successful implementation of our growth strategy, could affect our ability to manage our company effectively and to carry out our business plan, or could otherwise be detrimental to us. As of December 31, 2018, we had 70 full-time employees. Therefore, knowledge of our product candidates and clinical trials is concentrated among a small number of individuals. Members of our executive team as well as key clinical, scientific and technical personnel may resign at any time and there can be no assurance that we will be able to continue to retain such personnel. If we cannot recruit suitable replacements in a timely manner, our business will be adversely impacted.

Our growth and continued success will also depend on our ability to attract and retain additional highly qualified and skilled research and development, operational, managerial and finance personnel. However, we face significant competition for experienced personnel in the pharmaceutical field. Many of the other pharmaceutical 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 more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to quality candidates than what we have to offer. If we cannot retain our existing skilled scientific and operational personnel and attract and retain sufficiently skilled additional scientific and operational personnel, as required, for our research and development and manufacturing operations on acceptable terms, we may not be able to continue to develop and commercialize our existing product candidates or new products. Further, any failure to effectively integrate new personnel could prevent us from successfully growing our company.