UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2018

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from_____to_____

Commission file number: 001-38079

UROGEN PHARMA LTD.

(Exact name of registrant as specified in its charter)

Israel	**Not applicable**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**
499 Park Avenue, New York, New York	**10014**
(Address of principal executive offices)	**(Zip Code)**

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

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Ordinary Shares, par value NIS0.01 per share	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☑ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☑

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☑ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

Large accelerated filer	☑	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☑

The aggregate market value of the ordinary shares held by non-affiliates of the registrant as of June 30, 2018 totaled approximately $719.5 million based on the closing price for the registrant's ordinary shares on that day as reported by the Nasdaq Global Market. Such value excludes ordinary shares held by executive officers, and directors as of June 29, 2018.

As of February 22, 2019, there were 20,476,443 of the registrant's ordinary shares outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Document Description	**10-K Part**
Portions of the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days after registrant's fiscal year end of December 31, 2018 are incorporated by reference into Part III of this report	III

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PART I

INTRODUCTION

Unless otherwise indicated, "UroGen Pharma," "the Company," "our Company," "we," "us" and "our" refer to UroGen Pharma Ltd. and its subsidiary, Urogen Pharma, Inc.

UroGen and RTGel are trademarks of ours that we use in this Annual Report. This Annual Report also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, our trademarks and tradenames referred to in this Annual Report appear without the ® or ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to our trademark and tradenames. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

We maintain our books and records in U.S. dollars, and prepare our financial statements in accordance with accounting principles generally accepted in the United States, or U.S. GAAP, as issued by the Financial Accounting Standards Board, or FASB.

The terms "shekel," "Israeli shekel" and "NIS" refer to New Israeli Shekels, the lawful currency of the State of Israel, and the terms "dollar," "U.S. dollar" or "$" refer to United States dollars, the lawful currency of the United States. All references to "shares" in this Annual Report refer to ordinary shares of UroGen Pharma Ltd., par value NIS 0.01 per share.

We have made rounding adjustments to some of the figures included in this Annual Report. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by those sections. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below under Part I, Item 1A, "Risk Factors" in this Annual Report.

We may, in some cases, use words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes to identify these forward-looking statements. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements and are based upon our current expectations, beliefs, estimates and projections, and various assumptions, many of which, by their nature, are inherently uncertain and beyond our control. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- the timing and conduct of our clinical trials of UGN-101, UGN-102 and our other product candidates, including statements regarding the timing, progress and results of current and future preclinical studies and clinical trials, and our research and development programs;
- the clinical utility, potential advantages and timing or likelihood of regulatory filings and approvals of UGN-101, UGN-102 and our other product candidates;
- our plans regarding utilization of regulatory pathways that would allow for accelerated marketing approval in the United States;
- our expectations regarding timing for application for and receipt of regulatory approval for any of our product candidates;
- our ongoing and planned discovery and development of product candidates;
- our expectations regarding future growth, including our ability to develop, and obtain regulatory approval for, new product candidates;
- our ability to obtain and maintain adequate intellectual property rights and adequately protect and enforce such rights;
- our ability to maintain our collaboration with Allergan Pharmaceuticals International Limited, or Allergan, a wholly owned subsidiary of Allergan plc, enter into and successfully complete other collaborations, licensing arrangements or in-license or acquire rights to other products, product candidates or technologies;
- our plans to develop and commercialize our product candidates;
- our estimates regarding the market opportunity for our product candidates;

- our estimates regarding expenses, future revenues, capital requirements and the need for additional financing; our planned level of capital expenditures and our belief that our existing cash, cash equivalents and short-term investments will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next 12 months;
- the impact of our research and development expenses as we continue developing product candidates;
- our expected use of the remaining net proceeds from our initial public offering; and
- the impact of government laws and regulations.

We caution you that the risks, uncertainties and other factors referenced above may not contain all of the risks, uncertainties and other factors that are important to you. In addition, we cannot guarantee future results, level of activity, performance or achievements. You should refer to the section of this Annual Report under Part I, Item 1A, "Risk Factors" for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

If our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. Any forward-looking statement made by us in this Annual Report speaks only as of the date of this Annual Report or as of the date on which it is made. 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.

You should read this Annual Report and the documents that we reference in this Annual Report and have filed as exhibits to this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

This Annual Report may contain market data and industry forecasts that were obtained from industry publications. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We have not independently verified any third-party information. While we believe the market position, market opportunity and market size information included in this Annual Report is generally reliable, such information is inherently imprecise.

Item 1. Business

Overview

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 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 primary intervention without surgical removal or resection ("chemoablation" or "chemoablate") agents, which means they are designed to ablate tumors by minimally invasive means, to treat several forms of non-muscle invasive urothelial cancer, including low-grade upper tract urothelial carcinoma, or LG UTUC, and low-grade non-muscle invasive bladder cancer or LG 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. 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.

Our lead product candidates, UGN-101 and UGN-102, are formulated using our proprietary reverse thermal hydrogel, or RTGel, technology. We believe that RTGel-based drug formulations, which provide for the sustained release of an active drug, may improve the efficacy of treatment of various types of urothelial cancer without compromising the safety of the patient or interfering with the natural flow of urine from the upper urinary tract to the bladder. Our formulations are designed to achieve this by increasing the dwell time as well as the tissue coverage of the active drug. Consequently, we believe that RTGel-based drug formulations may enable us to overcome the anatomical and physiological challenges that have historically contributed to the lack of drug development for the treatment of urothelial cancer. No drugs have been approved by the U.S. Food and Drug Administration, or the FDA, for the treatment of LG NMIBC, in more than 15 years and for the treatment of LG UTUC, there are no drugs approved.

We are currently evaluating the safety and efficacy of UGN-101, our novel sustained-release formulation of mitomycin, in patients with LG UTUC in a Phase 3 pivotal, single-arm, open label clinical trial, which follows a recently completed "Compassionate Use" program for UGN-101 for the treatment of the same indication. The Compassionate Use Program was conducted in the U.S., Europe and Israel. "Compassionate Use" is the use outside of a clinical trial of an investigational, or not approved, medical product when patient enrollment in a clinical trial is not possible, typically due to patient ineligibility or a lack of ongoing clinical trials. In the Compassionate Use Program, 22 patients were enrolled, 18 of whom had confirmed LG UTUC. Of the 18 patients, 13 patients had completed the six-weekly treatment regimen and were evaluated for tumor response. These 13 patients were evaluated for tumor response at the primary evaluation time either endoscopically or through the use of a nonsurgical viewing instrument. Complete response was also confirmed by a cytology (urine) confirmation. Eight, or approximately 44%, achieved a complete response, with a median durability of response without recurrence of 12 months to date, based on investigator reports.

Five out of the 13 evaluated patients achieved a partial response at the primary evaluation time. One patient who achieved a partial response received three additional monthly courses of UGN-101, and thereafter achieved a complete response. In this Compassionate Use program, UGN-101 had been observed to be well-tolerated. We have obtained Orphan Drug, Fast Track and Breakthrough Therapy Designations for UGN-101 for the treatment of patients with LG UTUC. We have initiated a rolling review of the UGN-101 New Drug Application, or NDA, using the 505(b)(2) pathway through submission of nonclinical data to the FDA in December 2018, and expect to complete the NDA submission process in 2019.

In addition, we evaluated the safety and dosing schedule of UGN-102, our novel sustained-release high dose formulation of mitomycin, for the treatment of LG NMIBC in a Phase 2a study that was conducted in Europe and Israel. The 80mg mitomycin dose was associated with acceptable treatment emergent adverse events and was observed to produce tumor ablation in the majority of subjects treated with this dose. Treatment with UGN-102 was also observed to produce durable complete response at 12 months. We submitted an IND for UGN-102 in June 2018 and have commenced a U.S.-based Phase 2b clinical trial for UGN-102 evaluating the safety and efficacy of UGN-102 in the U.S. We also intend to pursue a 505(b)(2) regulatory pathway for UGN-102. We believe that UGN-102 has the potential to be a new therapeutic option for the treatment of intermediate risk LG NMIBC patients.

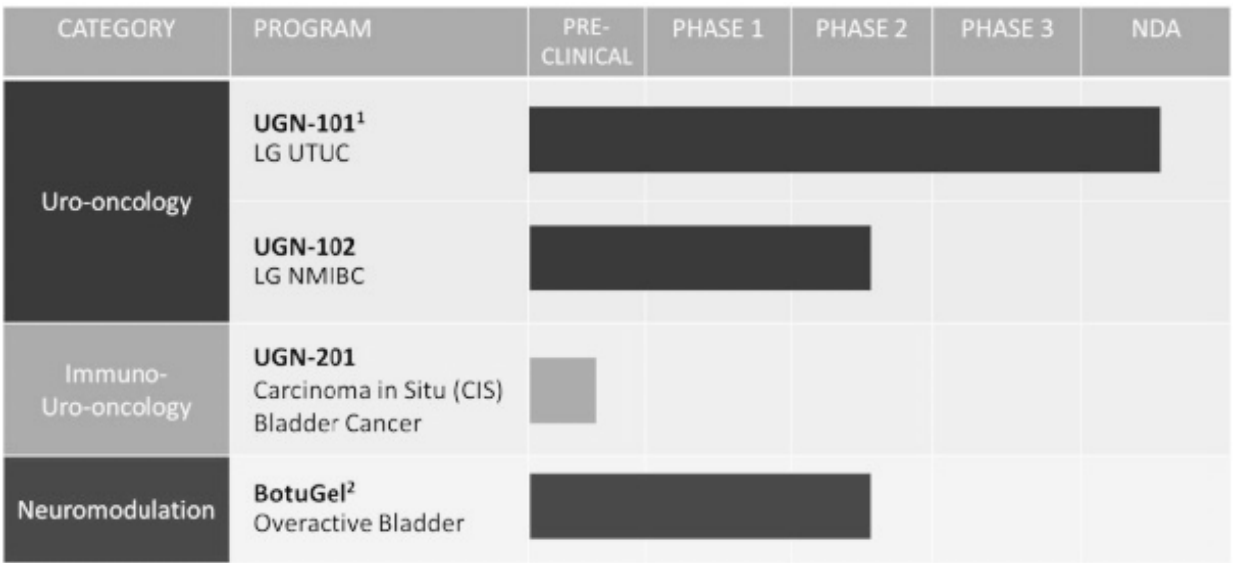
We believe that urothelial cancer, which is comprised of bladder cancer and UTUC, affects a large and underserved patient population. Annual expenditures for Medicare alone in the United States for the treatment of urothelial cancer were estimated to have been at least $4.0 billion in 2010 and are projected to be at least $5.0 billion in 2020. The majority of the expenditures is spent on tumor resection surgeries such as transurethral resection of bladder tumor, or TURBT, and upper urinary tract removals. In 2015, the estimated prevalence of urothelial cancer in the United States was 700,000 with an annual incidence of approximately 80,000. The prevalence of each of LG NMIBC and LG UTUC in the United States was approximately 343,000 and 14,500, respectively.

Our clinical stage pipeline also includes UGN-201, our proprietary immunotherapy product candidate for the treatment of high-grade NMIBC, which may include Carcinoma in Situ, or CIS. UGN-201 is a novel, liquid formulation of imiquimod, a generic toll-like receptor 7, or TLR7, agonist. Toll-like receptor agonists play a key role in initiating the innate immune response system. We believe that the combination of UGN-201 with additional immunotherapy drugs, such as immune checkpoint inhibitors or sustained release chemotherapy drugs like UGN-102, could represent a valid alternative to the current standard of care for the post-TURBT adjuvant treatment of high-grade NMIBC.

BotuGel is a proprietary novel RTGel-based formulation of BOTOX®, a branded drug, that we believe can potentially serve as an effective treatment option for patients suffering from overactive bladder. In October 2016, we announced the licensing of the worldwide rights to RTGel in combination with neurotoxins, including BOTOX®, to Allergan Pharmaceuticals International Limited, or Allergan, a wholly owned subsidiary of Allergan plc (the "Allergan Agreement"). In August 2017, we announced that Allergan had submitted an IND to the FDA in order to be able to commence clinical trials in the United States using the RTGel in combination with BOTOX®. In October 2017, Allergan commenced a Phase 2 clinical trial of BotuGel for the treatment of overactive bladder.

Our Product Candidate Pipeline

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



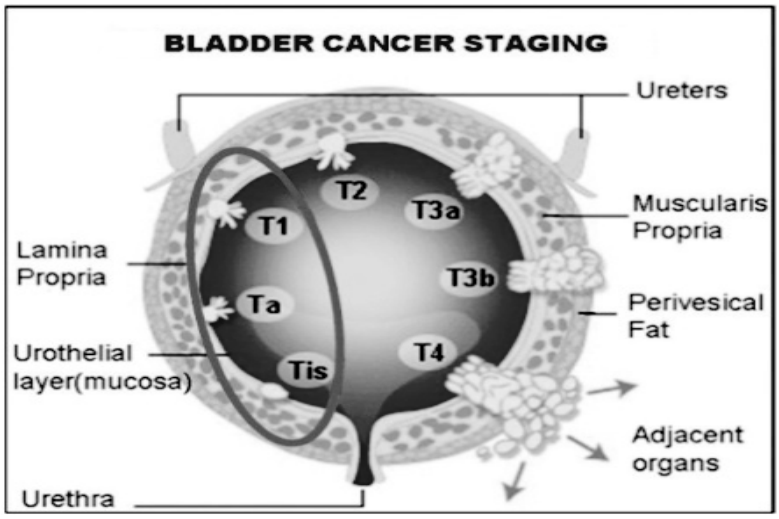
1 Rolling NDA submission initiated in December 2018
2 Licensed to Allergan

Uro-Oncological Indications Targeted by Our Product Candidates

Our product candidates are administered locally using the standard practice of intravesical instillation directly into the bladder or upper urinary tract via a catheter. The instillation into the bladder is expected to take place in a physician's office as a same-day treatment, in comparison with TURBT or similar tumor surgical procedures, which are operations conducted under general anesthesia in a hospital setting and may require at least an overnight stay. Surgical tumor removal often has limited success due to the inability to properly identify, reach and resect all tumors. We believe that an effective chemoablation agent can potentially provide better eradication of tumors irrespective of the detectability and location of the tumors. In addition, by removing the need for surgery, patients may avoid potential complications associated with surgery and hospital-acquired infections.

Bladder Cancer

The bladder is a hollow organ in the pelvis with flexible muscular walls. Its main function is to store urine before it leaves the body. Urine is produced by the kidneys and is then carried to the bladder through the upper urinary tract tubes, called ureters. The bladder wall has four main layers. The innermost lining is comprised of cells called urothelial or transitional cells, and this inner layer is called the urothelium or transitional epithelium. Beneath the urothelium, there is a layer called the lamina propria. Next is a thick layer of muscle called the muscularis propria followed by a layer of perivesical fat.

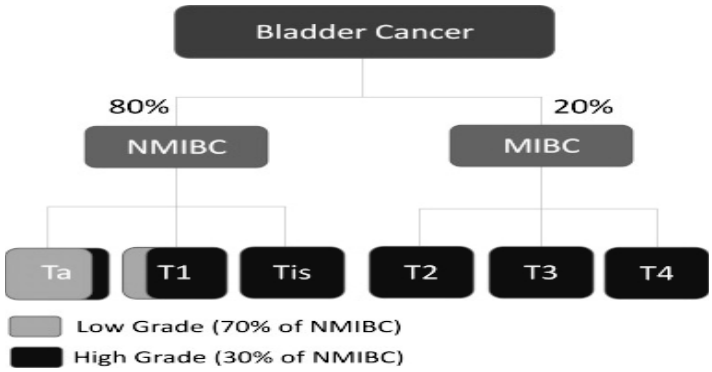


NMIBC tumor types are circled

Bladder cancer accounts for approximately 90% to 95% of all new cases of urothelial cancer in the United States. Bladder cancer is nearly three to four times more common in men than women, and, with an average age at diagnosis of 72, mostly affects the elderly. Bladder cancers are described as non-muscle invasive or muscle-invasive based on how far into the wall of the bladder they have invaded. The magnitude and rate of the spreading of the cancer is called "staging," which ranges from Ta to T1 for NMIBC, and T2 to T4 for muscle-invasive bladder cancers, as defined by the American Joint Committee on Cancer TNM System. In addition, Carcinoma in Situ, or CIS, a form of NMIBC, has a staging designation of Tis. Muscle-invasive bladder cancer, or MIBC, has an average five-year survival rate of 15% to 63%, depending on severity. MIBC represents a worse prognosis than NMIBC, which has a five-year survival rate of approximately 90%. NMIBC accounts for approximately 80% of all new cases of bladder cancer diagnosed in the United States each year, which corresponds to an estimated annual incidence and prevalence of approximately 60,000 and 500,000 cases, respectively.

Non-muscle invasive bladder cancers are divided into two grades, low and high, with high-grade tumors more likely to recur and progress into muscle-invasive tumors. CIS tumors are all high-grade. Overall, approximately 70% of patients with NMIBC present with low-grade disease at diagnosis.

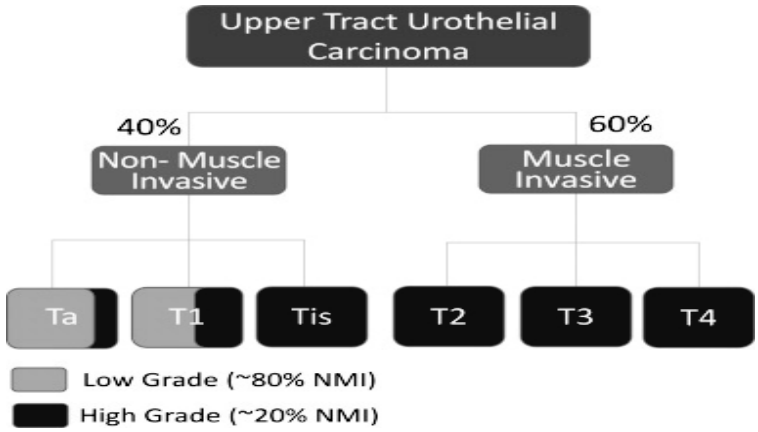
The chart below indicates the prevalence of stage and grade of bladder cancer in the United States.



Upper Tract Urothelial Carcinoma

UTUC refers to malignant changes of the transitional urothelial cells lining the upper urinary tract of the renal pelvis and ureter. UTUC typically exhibits high local recurrence and in cases of high-grade disease, development of metastases. Similar to NMIBC, the prognosis of patients with UTUC correlates with the stage and grade of disease at the time of initial diagnosis. The key prognostic factor at the time of diagnosis of UTUC is whether the tumor is in the muscle-invasive or non-muscle invasive stage. The number, size and location of tumors presented also represent important prognostic factors for UTUC. Approximately 40% of the patients diagnosed annually with UTUC in the United States present with non-muscle invasive UTUC. Non-muscle invasive UTUC is also divided into two grades, low and high.

The chart below indicates the prevalence of stage and grade of UTUC in the United States.



UTUC accounts for approximately 5% to 10% of all new cases of urothelial cancer, which corresponds to an estimated annual incidence in the United States of up to 7,500 cases. In 2015, the estimated prevalence of LG UTUC in the United States was approximately 14,500. UTUC is nearly three times more common in men than women and affects mostly the elderly.

There are currently no drugs approved by the FDA for the treatment of LG UTUC, representing a significant unmet medical need. Moreover, the anatomical complexity of the upper urinary tract, particularly the renal pelvis, presents significant challenges to the proper identification and ability to reach and resect all tumors in tumor resection surgical procedures (i.e. endoscopic laser ablation). Consequently, patients with high-grade disease or patients with low-grade disease that present with a large number of tumors typically undergo radical nephroureterectomy, which is kidney and upper urinary tract removal. In addition, the stage and grade of UTUC are often misdiagnosed. Due to these factors, the current standard of care for the treatment of UTUC is radical nephroureterectomy.

Endoscopic tumor resection, which aims to be a kidney sparing surgical procedure, is conducted only in patients with low-grade disease that present with a limited number of tumors. However, the upper urinary tract's anatomical constraints limit the effectiveness of surgical procedures and adjuvant chemotherapy treatments, leading to high rates of recurrence and risk for progression in this patient population. In a study published in 2009 in the Journal of Endourology evaluating 57 patients with LG UTUC who underwent tumor resections, 89.5% of patients recurred with a mean of 5.5 recurrences per patient over a four-year period. Moreover, approximately 20% of the patients in this study progressed and ultimately underwent kidney and upper urinary tract removal.

Non-Muscle Invasive Bladder Cancer

Patients treated with the current standard of care have up to an approximately 60% rate of recurrence of NMIBC within one year, and the rate of progression of NMIBC to MIBC is between 20% and 30%. As a consequence, NMIBC patients often undergo multiple repeat TURBT procedures.

The standard of care for treating LG NMIBC patients is TURBT. TURBT is a surgical operation for tumor removal conducted under general anesthesia in a hospital setting and may require an overnight stay. Moreover, TURBT's success is tied to the physician's ability to overcome challenges in properly identifying, reaching and resecting all tumors. No drugs have been approved by the FDA as first-line treatment for NMIBC and only three drugs have been approved by the FDA for NMIBC, all used as adjuvant treatment, following TURBT. Efficacy of drug treatments has historically been limited due to challenges presented by bladder physiology, specifically the fact that urine is produced and voided frequently, thus diluting the concentration of the drug almost immediately and causing the excretion of the drug from the bladder at first urine voiding.

Recent Developments

Appointment of New Chief Executive Officer

On January 3, 2019, we appointed Elizabeth Barrett as our President and Chief Executive Officer, replacing Ron Bentsur in those capacities. Concurrently, Ms. Barrett was appointed as a member of our board of directors and Mr. Bentsur resigned from our board of directors.

Phase 3 OLYMPUS Clinical Trial of UGN-101: Interim Data

On January 8, 2019, we announced interim results from our ongoing pivotal Phase 3 OLYMPUS clinical trial of UGN-101 (mitomycin gel) for instillation, an investigational mitomycin formulation for the non-surgical treatment of LG UTUC. This analysis showed that on an intent-to-treat basis, 57% of patients achieved a complete response, or CR, rate at their primary disease evaluation (PDE, or the primary endpoint) which was conducted four to six weeks after completion of UGN-101 treatment. All evaluated patients in CR for whom six-month follow-up data was available remained disease free at six months. Durability is a secondary endpoint for the trial.

The Phase 3 OLYMPUS clinical trial is an international, multi-center trial, which completed enrollment with 71 patients in December 2018. At the time of the interim data analysis, of the 71 patients enrolled in the trial, 61 patients had been evaluated for the primary endpoint which was a CR as defined as a negative ureteroscopic evaluation and a negative wash cytology. The remaining 10 patients were awaiting PDE evaluation.

Approximately 45% of tumors treated were categorized as unresectable by surgery at baseline. Of the patients who achieved CR, we now have six-month durability on half of these patients.

With regard to the safety profile of UGN-101, most treatment-emergent adverse events were characterized as mild or moderate and were transient and in line with ureteral procedures. These included ureteral stricture/stenosis, urinary tract infection/urosepsis, nausea and vomiting, flank pain and renal failure.

We intend to seek regulatory approval of UGN-101 in LG UTUC based on primary endpoint data from substantially all 71 patients. We initiated a rolling submission of an NDA to the FDA in December 2018. The FDA previously granted Orphan Drug, Fast Track, and Breakthrough Therapy Designations to UGN-101 for the treatment of UTUC. If approved, UGN-101 would be the first drug approved by the FDA for the treatment of LG UTUC.

January 2019 Underwritten Public Offering

On January 28, 2019, we completed an underwritten public offering of 4,207,317 of our ordinary shares, including 548,780 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $41.00 per share. The net proceeds to us from the offering were approximately $161.8 million, after deducting the underwriting discounts and commissions and payment of other offering expenses.

Our Competitive Strengths

We believe our lead product candidates for uro-oncology, which are being developed by leveraging our expertise in drug development and our proprietary formulation technology, have the ability to replace the costly, sub-optimal and burdensome tumor resection procedures that represent the current first-line standard of care. Furthermore, we believe our proprietary formulation technology has broad applications and may allow us to develop additional product candidates for indications within and beyond the urinary tract.

Potential ability to develop minimally invasive, first-line drug therapies for uro-oncology. Leveraging our innovative formulation technology, we are developing two lead product candidates, UGN-101 and UGN-102, as potential replacements to first-line treatment for LG UTUC and NMIBC, respectively. Both UGN-101 and UGN-102 are chemoablation agents designed to overcome the challenges posed by the anatomy of the urinary tract by increasing the dwell time and enhancing the tissue coverage of mitomycin. Clinical data generated to date supports our belief that our lead product candidates may provide new therapeutic options to the current first-line tumor surgical procedures, providing a chemoablation treatment that has the potential to better eradicate tumors irrespective of their detectability and location within the urinary tract. Of the 13 LG UTUC patients treated with UGN-101 in a recently-completed Compassionate Use program and evaluated endoscopically or through the use of a nonsurgical viewing instrument for efficacy, eight achieved a complete response and the remaining five achieved a partial response at the primary evaluation time. In the case of UGN-102, 19 of 22, or approximately 86%, of the patients treated with the high dose of UGN-102 in a recently-completed Phase 2a trial conducted in Europe and Israel, evaluating the efficacy and safety of UGN-102's chemoablation properties, achieved a complete response at the primary evaluation time.

Expertise in developing proprietary formulations of drugs for clinical benefit. We focus on developing proprietary RTGel formulations of previously approved drugs whose efficacy for a particular indication is limited by current formulations or routes of administration. While we have not yet brought a drug to market, our expertise has enabled us to develop proprietary RTGel-based formulations for several previously approved drugs to date, including clinical stage proprietary formulations of mitomycin and botulinum toxin. Our formulations are designed to significantly increase the dwell time and exposure of the drugs to the target sites and limit the need for urine retention, potentially providing enhanced clinical activity, reduced patient burden and increased patient compliance over existing formulations and modes of administration. We have a strong research and development team to advance our product candidates.

Lower development risks and costs for our pipeline product candidates. We expect the approval process for each of our current uro-oncology product candidates to be conducted according to the FDA's 505(b)(2) regulatory pathway, a streamlined, lower-cost pathway to drug approval when compared to traditional drug development. Furthermore, two of our product candidates, UGN-101 and UGN-201, have received Orphan Drug Designation from the FDA for the treatment of LG UTUC and CIS, respectively, which we expect will provide seven years of regulatory exclusivity following FDA approval, if received. UGN-101 was also granted Fast Track and Breakthrough Therapy designations by the FDA. We submitted an IND for UGN-101 in November 2016, which was accepted by the FDA in December 2016. We commenced a single pivotal, open-label, single-arm Phase 3 clinical trial for the treatment of LG UTUC in the first quarter of 2017. The clinical trial was conducted in the United States and Israel with enrollment of 71 patients. We submitted an IND for UGN-102 in June 2018 which was accepted by the FDA. We have commenced an open-label, single-arm Phase 2b clinical trial for the treatment of LG NMIBC. Additionally, we expect that our lead candidates are more likely to show an acceptable safety profile because they are novel formulations of previously approved drugs.

Leverageable proprietary formulation technology. We believe that RTGel has multiple potential applications beyond urology. Our formulation know-how may enable us to develop different drug formulations to facilitate the delivery, retention and sustained release of active drugs to a variety of targeted body cavities. We believe that our proprietary formulation technology can improve the efficacy of locally administered drugs in body cavities such as the stomach, uterus and rectum that present anatomical and physiological challenges related to frequent wash out, rapid excretion and bodily secretions. In October 2016, we announced that we licensed worldwide rights to a proprietary RTGel formulation with BOTOX® to Allergan for the treatment of overactive bladder and related indications pursuant to the Allergan Agreement.

Strong intellectual property position. We have a robust intellectual property portfolio that includes 32 issued patents worldwide and more than 45 pending patent applications filed worldwide. In the United States, we have 15 granted patents that are directed to protect our lead product candidates UGN-101, UGN-102, UGN-201 and Botugel as well as our RTGel technology and our other potential product candidates that are under preclinical review. These patents claim methods, systems, and novel compositions and combinations for treating cancer in internal cavities, in particular treating a urinary tract cancer. These issued patents are expected to expire between 2024 and 2035. Additionally, the FDA has granted Orphan Drug Designation to UGN-101 for the treatment of LG UTUC and UGN-201 for the treatment of CIS bladder cancer, which potentially entitles us to regulatory exclusivity for UGN-101 and UGN-201 for seven years following approval, if granted, by the FDA.

Experienced and accomplished leadership team with proven track record. We have an experienced management team, with each member possessing deep experience in the biopharmaceutical and related industries. Our Chief Executive Officer, Liz Barrett was CEO of Novartis Oncology and a member of the Executive Committee of Novartis. She previously served as Global President of Oncology at Pfizer Inc. At Pfizer, she held numerous leadership positions, including President of Global Innovative Pharma for Europe, President of the Specialty Care Business Unit for North America, and President of United States Oncology. Prior to Pfizer, she was Vice President and General Manager of the Oncology Business Unit at Cephalon Inc. Ms. Barrett also worked at Johnson & Johnson. In addition, our Chairman, Arie Belldegrun, M.D., is a seasoned biotech executive and was the founder, Chairman, Chief Executive Officer and President of Kite Pharma, Inc., which was recently sold to Gilead Sciences, Inc. Dr. Belldegrun is also a urologist by training. We believe that our leadership team is well-positioned to lead us through clinical development, regulatory approval and commercialization for our product candidates.

Our Growth Strategy

We intend to become the leading biopharmaceutical company focused on the development of novel therapies for local treatment of urological pathologies. The key elements of our strategy are as follows:

Establish each of our lead product candidates, UGN-101 and UGN-102, as the first-line treatment in its target indication. We believe that data from treatments in our Compassionate Use program conducted in the United States, Europe and Israel provide preliminary evidence of the potential safety and efficacy of UGN-101 for the treatment of LG UTUC. We submitted an IND for UGN-101 with the FDA in November 2016, which was accepted by the FDA in December 2016, and we commenced a single pivotal Phase 3 clinical trial in the first quarter of 2017 pursuant to the FDA's 505(b)(2) regulatory pathway. We completed enrollment in that trial in December 2018, and commenced a rolling NDA submission to the FDA.

We completed a Phase 2a randomized, open-label, single-arm, active-controlled clinical trial of UGN-102 for the treatment of LG NMIBC, conducted in Europe and Israel. We submitted an IND for UGN-102 in June 2018, and, have commenced a Phase 2b clinical trial in NMIBC. We also expect to pursue a 505(b)(2) regulatory pathway for UGN-102. We believe that these local drug treatments have the potential to offer an alternative to costly, sub-optimal and burdensome tumor resection and kidney removal surgeries to become the first-line standard of care.

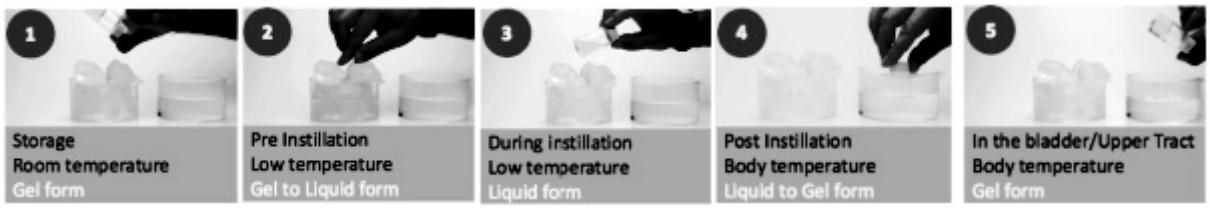
Expand our uro-oncology product pipeline. A Phase 2 clinical trial of UGN-201 was completed under an IND in 12 patients with CIS, an aggressive form of high-grade urinary bladder cancer. In the trial, 10 patients were evaluated for response, of which 20% achieved a complete response rate with UGN-201 as a single-agent treatment. We believe that combining UGN-201 with immune checkpoint inhibitors or chemotherapy has the potential to serve as a treatment option for high-grade urothelial tumors. We are also pursuing preclinical oncology programs that take advantage of our RTGel technology. We are conducting preclinical programs for high-grade bladder cancer. We may also evaluate in-licensing or acquiring additional product candidates for the treatment of urological cancers.

Utilize our proprietary technology to expand our pipeline to other body cavities and indications. We believe that RTGel may be suitable for multiple additional applications. Our know-how may enable us to develop different drug formulations to facilitate the delivery, retention, increased dwell time and sustained release of active drugs to a variety of targeted body cavities. Beyond the urinary tract, we may target the gastrointestinal tract and the female reproductive system. In the future, we may also choose to develop our RTGel technology in combination with other drugs to treat cancer and other indications endemic to such body cavities.

Evaluate and selectively pursue potential collaborations to develop improved formulations and product life-cycle management strategies. We entered into the Allergan Agreement as part of our strategy to research, develop, manufacture and commercialize pharmaceutical products that contain RTGel alone or in combination with certain other active ingredients. This collaboration provides us with funding for our research and development efforts and may accelerate the development and commercialization of our approved products, if any. In addition, we may in-license or acquire additional product candidates for urological indications. Such collaborations would allow us to obtain financial support and to capitalize on the expertise and resources of our potential partners, which could allow for new and improved versions of approved or clinical stage drugs and could accelerate the development and commercialization of additional product candidates.

RTGel: Our Reverse Thermal Hydrogel Platform Technology

We have developed RTGel, a novel proprietary polymeric biocompatible, reverse thermal gelation hydrogel, which, unlike the general characteristics of most forms of matter, is liquid at lower temperatures and converts into gel form when heated. We believe that these characteristics promote ease of delivery into and retention of drugs in body cavities, including the bladder and the upper urinary tract, by conforming to the anatomy of the target organ while preventing rapid excretion of the drug. The following images show the progression of five stages of RTGel at different temperatures.



RTGel's components are polymer-based and are inactive ingredients that have been approved by the FDA for use in other products such as Oraqix, a periodontal gel, Namenda, an oral solution for Alzheimer's disease, and Xeloda, an oral chemotherapy. We formulate RTGel with an active drug: mitomycin in the case of UGN-101 and UGN-102, and botulinum toxin in the case of BotuGel. The resulting formulations are instilled intravesically in liquid form directly into the bladder or upper urinary tract using standard instillation methodologies via catheters and thereafter convert into gel form at body temperature. Subsequently, upon contact with urine, RTGel gradually dissolves and releases the active drug over a period of several hours and is less affected by urine creation and voiding cycles as compared to water formulations.

We believe that RTGel, when formulated with an active drug, may allow for the improved efficacy of treatment of various types of urothelial cancer without compromising the safety of the patient or interfering with the natural flow of fluids from the urinary tract to the bladder. RTGel achieves this by:

- increasing the exposure of active drugs in the bladder and upper urinary tract by significantly extending the dwell time of the active drug while conforming to the anatomy of the bladder and the upper urinary tract, which allows for enhanced drug tissue coverage. For example, the average dwell time of the standard mitomycin water formulation, currently used as adjuvant treatment, in the upper urinary tract is approximately five minutes, compared to approximately six hours when mitomycin is formulated with RTGel;

- administering higher doses of an active drug than would otherwise be possible using standard water-based formulations. For instance, it is only possible to dissolve 0.5 mg of mitomycin in 1 ml of water while it is possible to formulate up to 8 mg of mitomycin with 1 ml of RTGel; and
- maintaining the active drug's molecular structure and mode of action.

These characteristics of RTGel enable sustained release of mitomycin in the urinary tract for both UGN-101 and UGN-102, and of botulinum toxin in the case of BotuGel. Further, RTGel may be particularly effective in the bladder and upper urinary tract where tumor visibility and access are challenging, and where there exists a significant amount of urine flow and voiding. We believe that these characteristics of RTGel may prove useful for the local delivery of active drugs to other bodily cavities in addition to the bladder and upper urinary tract.

Mitomycin—Our Target Active Drug for the Treatment of UTUC and NMIBC

Mitomycin is a generic drug currently utilized off-label as the standard adjuvant chemotherapy for the treatment of LG UTUC and NMIBC after tumor resection, such as TURBT. Mitomycin, a chemotherapy agent, is typically administered using a water-based formulation, which has a relatively short dwell time in the bladder limited to first voiding. Mitomycin often causes temporary irritation of the bladder, including the need to urinate frequently and urgently. This often results in first voiding occurring shortly after instillation. In the upper urinary tract, the dwell time is limited to approximately five minutes as urine flows continuously and no active retention by the patient is feasible. Numerous in vitro models, in vivo studies and computer simulations have shown that increased dwell time of mitomycin in the bladder results in more efficacious treatment of bladder cancer. In one such study, it was shown that mitomycin activity increased with exposure time. Specifically, the MIC90, or mean inhibitory concentration that causes 90% inhibition in cell growth, was 11-fold lower when exposure time was increased from 30 minutes to eight hours.

Mitomycin's main effect is on the cancer cell's DNA and has been demonstrated to be most effective when the cancer cell is in its S-phase, or synthesis phase, during which the DNA is replicated. Each cancer cell goes through various phases during the cell cycle. However, the cell cycle is not synchronized in all cancer cells, which means that at any given point in time only a portion of the cancer cells are at their S-phase, or susceptible to the instilled mitomycin in the bladder. Thus, because our RTGel-based mitomycin sustained-release formulations, UGN-101 and UGN-102, provide for a significantly longer dwell time of mitomycin in the upper urinary tract and in the bladder as compared to standard mitomycin water formulations, there is a greater chance that tumor cells will go through their S-phase while the instilled mitomycin is still present using UGN-101 or UGN-102, potentially resulting in a higher percentage of tumor cells being affected by the instilled mitomycin.

Limitations of Current Therapies for Upper Tract Urothelial Carcinoma

There are currently no drugs approved by the FDA for the treatment of UTUC, representing a significant unmet medical need. The current standard-of-care for the treatment of UTUC is radical nephroureterectomy, which is complete kidney and upper urinary tract removal. Recent advances in resection instrument technology have allowed physicians in some cases to treat patients with LG UTUC using endoscopic tumor resection, a kidney-sparing treatment, rather than nephroureterectomy followed by adjuvant chemotherapy, typically mitomycin, treatment. However, the specific anatomy and physiology of the upper urinary tract make the performance of organ-sparing endoscopic tumor resection and instillation of adjuvant chemotherapy challenging, leading to high recurrence rates. Patients often undergo multiple endoscopic resection procedures, which increases the probability of potential complications of resection, including perforation and ureteral stricture, or a narrowing of the ureter. A recent study published in 2009 in the Journal of Endourology, evaluating 57 patients with LG UTUC who underwent tumor resections showed that recurrence occurred in 89.5% of patients, with a mean of 5.5 recurrences per patient, over a four-year period. Moreover, approximately 20% of the patients in this study progressed and ultimately underwent kidney and upper tract removal.

Mitomycin is currently administered using a water-based formulation, which limits the dwell time in the bladder until first voiding. In the upper urinary tract, the dwell time of mitomycin is approximately five minutes as urine flows continuously and no active retention by the patient is feasible.

Our Solution: UGN-101

UGN-101 is our novel sustained-release RTGel-based formulation of mitomycin that we are developing for the treatment of LG UTUC. RTGel is liquid at lower temperatures and converts into gel form at body temperature. This temperature-dependent viscosity characteristic allows for simple and convenient instillation of the cooled UGN-101 in its liquid form to the upper urinary tract via standard catheters. Once instilled, UGN-101 converts into gel form at body temperature. Subsequently, upon contact with urine, UGN-101 gradually dissolves and releases the active drug, mitomycin, over a period of several hours versus several minutes for mitomycin in its water-based formulation. We believe that this substantial increase in dwell time of mitomycin positions UGN-101 as a potential first-line chemoablation treatment for LG UTUC, potentially sparing patients from repeated tumor resection surgeries and potentially reducing the need for bladder and upper urinary tract surgeries, including upper urinary tract removal.

The Orphan Drug Designation granted to UGN-101 for the treatment of UTUC potentially entitles us to regulatory exclusivity for UGN-101 for seven years following approval by the FDA, if granted. We believe Breakthrough Designation may allow us to obtain priority review of our NDA submission. We have initiated a rolling review of the NDA through submission of nonclinical data to the FDA in December 2018, we expect to complete the NDA submission process in 2019.

Initial Clinical Results for UGN-101

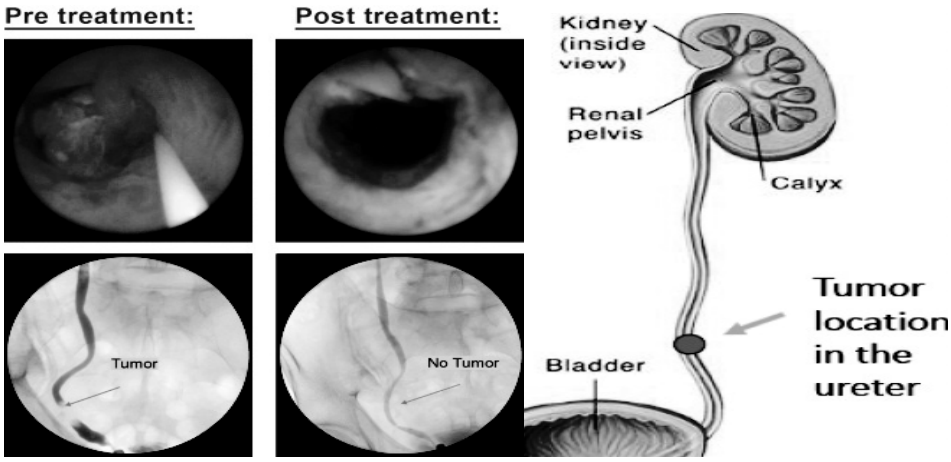
UGN-101 was evaluated in an investigator-initiated Compassionate Use program for the treatment of severe, non-resectable UTUC, which commenced in September 2014. The Compassionate Use program, which was conducted in the United States, Europe and Israel, included patients diagnosed with unilateral and bilateral low- and high-grade UTUC, as well as patients with a solitary kidney. Patients in the Compassionate Use program received six weekly instillations of UGN-101 administered directly to the upper urinary tract. Consistent with the nature of Compassionate Use programs, which are investigator-initiated programs, a statistical plan or primary endpoint was not used as in a regular clinical trial. Approximately four weeks following the completion of treatment, the patients were evaluated for response. Patients were visually evaluated endoscopically or through the use of a nonsurgical viewing instrument, with additional confirmation through urine cytology, or examination of cells collected from a urine specimen. At the evaluation time, which was approximately four weeks following the completion of the treatment course, patients were deemed to have achieved a complete response if, in the judgment of the physician, no tumors initially diagnosed by the physician were detected and a partial response if, in the judgment of the physician, the size or number of tumors had decreased or if, following an initial complete response, there is tumor recurrence within three months after the evaluation time. Safety and feasibility of treatment with UGN-101 were also evaluated. Twenty-two patients were treated in the study, with more than 130 instillations of UGN-101 performed. Of the 22 patients treated, 18 were assessed as having LG UTUC. Of the 18 patients assessed as having low-grade disease, 14 completed six instillations of UGN-101. Of these 14 patients, 13 were evaluated for response and one could not be evaluated to confirm response. Of the 13 patients who were evaluated for response, eight achieved a complete response and five, achieved a partial response at the primary evaluation time. One of the patients who received a partial response subsequently received an additional three courses of UGN-101 and thereafter achieved a complete response.

Of the eight patients who have achieved a complete response at the primary evaluation time, we are aware of three patients who have subsequently experienced recurrences to date. Recurrences were generally of small tumors, a few millimeters in diameter, and were manageable by endoscopic tumor resection. To our knowledge, five of the eight patients have not recurred to date, with three of the five patients having achieved durability of 12 months or greater to date. The median durability for these eight patients is still ongoing and is now greater than twelve months, based on investigator reports. The follow-up evaluation plan for patients in our Compassionate Use program is determined by each individual investigator and varies from patient to patient, and some patients have not undergone follow-up evaluation or have been lost to follow-up. As part of the ongoing single pivotal Phase 3 clinical trial, in order to potentially further extend durability, patients who achieve a complete response at the primary disease evaluation visit will be followed for durability of response and may receive monthly maintenance UGN-101 instillations for up to 12 months.

UGN-101 was observed to be well-tolerated in the Compassionate Use Program. The main observed adverse events, or AEs, related to UGN-101 have been fatigue, allergic reaction, nausea, fever, and dysuria, which is pain or difficulty while urinating. All of the AEs that have been observed to date are known side effects associated with the use of mitomycin and appear on the mitomycin label as potential side effects. Various serious adverse events, or SAEs, were also reported most of which were determined to be unrelated to treatment with UGN-101. These SAEs include acute pyelonephritis, a kidney infection caused by bacteria; hydronephrosis, which is the swelling of the upper urinary tract due to a build-up of urine caused by some degree of obstruction; severe arrhythmia, which is a severe abnormal heart rhythm; cardiac asthma, which is a medical diagnosis of wheezing, coughing or shortness of breath due to congestive heart failure; aggravation of renal function; hyperkalemia, which is a condition of elevated levels of potassium in the blood; pancytopenia, which is a deficiency of red cells, white cells and platelets in the blood; scarring and narrowing of the calyceal infundibulum, which was most probably present at baseline; asymptomatic extravasation from the upper tract, which is leakage of fluids from the upper tract to the surrounding tissue; and death.

This Compassionate Use program was allowed by the FDA to accumulate safety and efficacy data. In the first quarter of 2017, we commenced a pivotal, open-label, single-arm Phase 3 clinical trial of UGN-101 for the treatment of LG UTUC.

The following images show pre-treatment and post- UGN-101 treatment results from one LG UTUC patient in the Compassionate Use program.



(Courtesy of Dr. J. Gregory Wirth, Geneva Hospital, Switzerland)

The top left image is a pre-treatment ureteroscopic view of a tumor located in the ureter. The bottom left image is a pre-treatment x-ray revealing an obstruction within the ureter in which no contrast (black) can be visualized in the distal ureter (denoted by arrow). The top right image is a post-treatment ureteroscopic view of the same location following UGN-101 chemoablation treatment. The bottom right image is a post-treatment x-ray of the ureter which reveals no obstruction within the ureter.

FDA Pathway for UGN-101

As part of our IND-enabling work for UGN-101, we completed a large-scale good laboratory practices, or GLP, toxicity study in an upper urinary tract swine model in which more than 250 instillations of UGN-101 were performed. This study evaluated the safety of the procedure and UGN-101 administration, also utilizing higher dosage levels than those used in the clinical settings. In this GLP toxicology study, the instillation of UGN-101 was found to be safe. We are also conducting chemistry, manufacturing and controls, or CMC, studies as part of our development process.

Next Steps in the Clinical Development of UGN-101

Based on discussions with the FDA, we intend to develop UGN-101 through the FDA's 505(b)(2) regulatory pathway. We submitted an IND for UGN-101 in November 2016, which was accepted by the FDA in December 2016. We commenced a pivotal, open-label, single-arm Phase 3 clinical trial of UGN-101 for the treatment of LG UTUC in the first quarter of 2017. The company completed recruitment in the fourth quarter of 2018, and is currently in a rolling NDA submission process which is expected to be completed in the second half of 2019. Based on UGN-101's Breakthrough Therapy Designation, the company expects a six-month priority review process from the completion and FDA's acceptance for filing of the NDA submission.

This Phase 3 clinical trial is being conducted in the United States and Israel with enrollment of 71 patients. We expect this clinical trial, if successfully completed, to support an NDA for LG UTUC for UGN-101. The patients will initially receive six weekly instillations of UGN-101. The primary efficacy endpoint is the complete response rate, defined as the percentage of patients with a complete response (CR) at the primary disease evaluation (PDE) visit, which occurs approximately four to five weeks following the sixth weekly instillation. In addition, patients who achieve a CR at the PDE visit will be followed for durability of response. Such patients may also receive monthly UGN-101 maintenance instillations for up to 12 months. We anticipate submitting the clinical data to the NDA for UGN-101 in the second half of 2019. In the Phase 3 trial, to date, UGN-101 therapy has been well tolerated. Adverse events encountered in treated subjects include the expected effects of mitomycin administration to the upper urinary tract (ureteral inflammation and stenosis, pain and urinary tract irritation). In addition, perturbation of laboratory measures of renal and hematopoietic function has been observed.

UGN-102: Our Product Candidate for the Treatment of Low-Grade Non-Muscle Invasive Bladder Cancer

UGN-102 is our novel sustained-release formulation of high dose mitomycin that we are developing for the treatment of LG NMIBC as a first-line non-surgical chemoablation alternative to TURBT. We recently completed a Phase 2a randomized, open-label, three arm, active-controlled clinical trial in Europe and Israel that evaluated the safety and efficacy of UGN-102 (40mg and 80mg mitomycin) compared to 40mg mitomycin in water in patients with LG NMIBC. We commenced the trial in September 2013 and the last patient was enrolled in March 2016. For the primary endpoint, 19 of 22, or approximately 86%, of the patients with confirmed LG NMIBC in the 80mg mitomycin dose group of UGN-102 achieved a complete response.

We have submitted an IND for UGN-102 in June 2018, as well as commenced a Phase 2b clinical trial in patients with LG NMIBC at intermediate risk of recurrence in the US and in Israel.

Limitations of Current Therapies for Non-Muscle Invasive Bladder Cancer

Tumor grade and stage are the most important variables for determining the likelihood of progression from NMIBC to MIBC. The three stages of NMIBC are: Ta (70%), T1 (20%) and CIS or Tis (10%). Approximately 70% of NMIBC patients have a tumor that is classified as low-grade upon diagnosis. Ta and CIS are limited to the urothelial layer, and T1 is limited to the layer below, which is the lamina propria.

Recurrence, which occurs in approximately 80% of patients, is the primary threat for NMIBC patients. Multiplicity, or number of tumors, tumor size and prior recurrence rate are the most important variables in determining the likelihood and potential severity of recurrence. In T1 and CIS NMIBC patients, progression, which occurs in approximately 45% of patients, is the main threat. Treatment ranges from one or more TURBT procedures followed by adjuvant chemotherapy or immunotherapy instillation(s) in NMIBC patients with a low risk of recurrence to cystectomy for the treatment of NMIBC patients with a high risk of recurrence.

TURBT is conducted in a hospital setting under general anesthesia and can often have side effects and complications. The most common complications, risks and limitations of TURBT include:

- bleeding at the time of surgery that requires clot irrigation and mild burning;
- infection of the bladder;
- injury to the urethra and bladder perforation with potential intra-abdominal leakage;
- reimplantation and cell migration;
- repeat TURBT procedures, which are necessary for approximately 10% of patients within three months;
- complete removal of tumor tissue often not being feasible;
- potential recurrence of up to 25% of the tumors at the original treatment site; and
- some tumors not being detectable.

Post-operative adjuvant treatments for NMIBC, which are given to prevent reimplantation of the cancerous cells, consist primarily of chemotherapy in the case of low-grade tumors and immunotherapy in the case of high-grade tumors, and are administered intravesically via catheter. Adjuvant intravesical chemotherapy is used primarily in low-grade tumors following TURBT in order to try to delay tumor recurrence but is not used as a chemoablation agent. The rationale is to expose tumors to high local drug concentrations while minimizing the systemic exposure, thereby enhancing the treatment effect and reducing the drug toxicity. However, these traditional adjuvant treatments to treating bladder cancer have been limited because, after instillation, the drug concentration is reduced, and the drug is washed out due to urine voiding. As a result, the cancerous tissue is not exposed to the chemotherapy drug for the optimal length of time.

No drugs have been approved by the FDA as first-line treatment for NMIBC and only three drugs have been approved for NMIBC, all used as adjuvant treatment: Thiotepa, which was approved in 1959; bacille Calmette-Guerin, or BCG, which was approved in 1989; and Valstar, which was approved in 1998. Mitomycin is the drug used most often for intravesical chemotherapy. It is used off-label as an adjuvant treatment in the post-operative setting for low-grade tumors with high risk of recurrence. Other drugs that can be used include docetaxel and gemcitabine. BCG, an immunotherapy-based drug, is used as an adjuvant treatment for patients with high-grade NMIBC. Upon recurrence, which occurs in approximately 35% of patients, the patients undergo another round of BCG therapy with a response rate of 30% to 50%. Radical cystectomy, or surgical removal of the bladder, is also a common treatment option for patients who fail multiple intravesical BCG therapies. However, treatment with BCG is associated with severe side effects, as evidenced by a boxed warning on the label, which is a warning placed on a prescription drug's label by the FDA and is designed to call attention to serious or life-threatening risks.

We are not aware of any drugs currently in development for the treatment of NMIBC that take into consideration bladder physiology, specifically the fact that urine is produced and voided frequently, thus diluting the concentration of the active drug almost immediately.

Our Solution: UGN-102

UGN-102, an RTGel-based formulation of high dose mitomycin, is our product candidate for the treatment of LG NMIBC. UGN-102 is administered locally using standard catheters and is designed to conform to the bladder's anatomy and persist in the bladder despite urine flow and bladder movement. Once instilled, UGN-102 converts into gel form at body temperature. Subsequently, upon contact with urine, UGN-102 gradually dissolves and releases the active drug, mitomycin, over a period of several hours versus the time until first voiding,

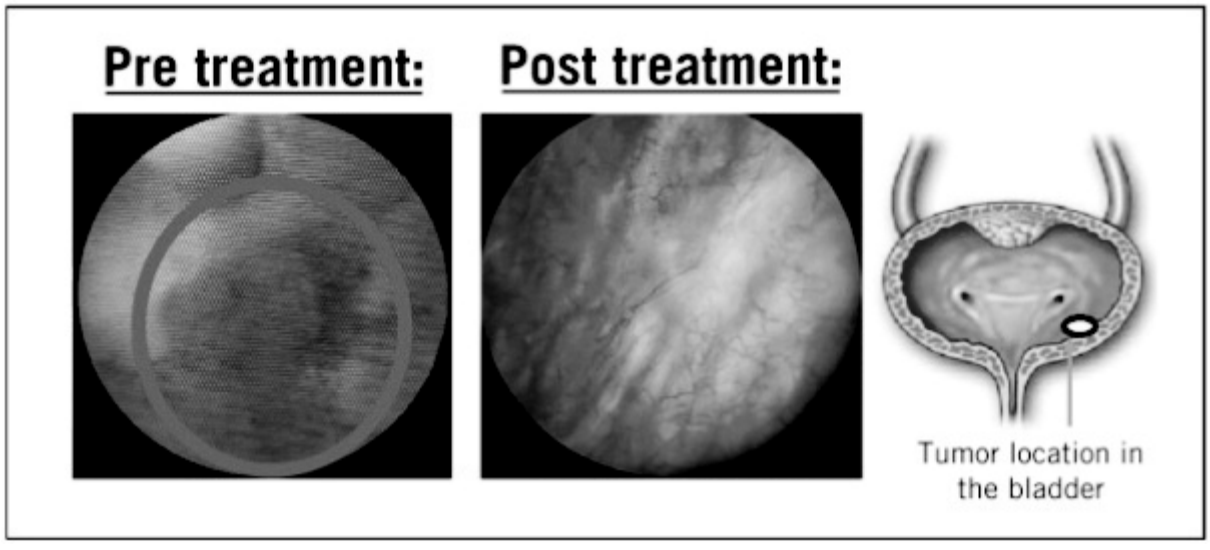
often less than an hour, for mitomycin in its current water-based formulation, without compromising the safety of the patient or interfering with the natural flow of urine out of the bladder. We believe that the resulting significantly increased dwell time of mitomycin in the bladder prolongs exposure of mitomycin to the tissue and therefore has the potential to chemoablate visible and unseen tumors. As a result of these properties, our goal is to develop UGN-102 as a first-line chemoablation non-surgical alternative to TURBT for the treatment of LG NMIBC.

Phase 2a Clinical Trial

We completed a Phase 2a randomized, open-label, single-arm, active-controlled clinical trial in Europe and Israel that evaluated the safety and efficacy of UGN-102 0.06% (40 mg mitomycin in 64 ml gel) and UGN-102 0.12% (80 mg mitomycin in 64 ml gel) in LG NMIBC compared to the intravesical instillation of 40 mg of mitomycin in water (mitomycin 0.1%). We commenced the trial in September 2013 and the last patient was enrolled in March 2016. In this trial, patients underwent six weekly instillations according to their assigned treatment arm. The primary endpoint of the trial used for observational purposes only is the complete response rate at the primary disease endpoint, which is evaluated approximately four weeks after the sixth weekly installation. Safety, feasibility of local treatment with UGN-102 and durability of response were also evaluated. 81 patients were enrolled, 65 of whom have been evaluated for response. Of the 65 evaluable patients in the study, 20, 22 and 23 patients were in the UGN-102 40mg mitomycin, UGN-102 80mg MCC and the water-based 40mg mitomycin control arm, respectively. The results indicate complete response rates at the primary evaluation time of 45%, 86% and 70% for UGN-102 40mg mitomycin, UGN-102 80mg mitomycin and water-based 40mg mitomycin control arm, respectively. Durability at 12 months in patients who were CR demonstrated numerical differences across the treatment arms and was higher in the 80mg UGN-102 arm than in the 40mg UGN-102 arm or the 40 mg MMC + water (control) arm (30.8% vs. 12.5% and 14.3%, respectively). This can be explained at least in part by imbalances in the baseline tumor characteristics in patients across treatment arms, whereby more patients in the 80 mg UGN-102 arm were at increased risk of recurrence compared to the other treatment arms.

In treating LG NMIBC, resection of small tumors is primarily conducted in the outpatient setting, typically without anesthesia using fulguration, a procedure that destroys the diseased area in the lining of the bladder by burning using electric current. The effectiveness of tumor resection in these cases is high and the one-year recurrence rate is estimated to be only 10%. However, in patients with larger tumors and multiple tumors, standard management includes surgical removal using TURBT, a procedure conducted in the operating room in a hospital setting under general anesthesia, which may require at least an overnight stay. TURBT is associated with increased risks and costs and higher recurrence rates that can reach up to 60%.

The following images show cytoscopic views of complete responses in a LG NMIBC patient treated with UGN-102.



The image to the left is a pre-treatment cystoscopic view of a tumor located in the bladder. The image to the right is a post-treatment cystoscopic view of the same location following UGN-102 chemoablation treatment.

Next Steps in the Clinical Development of UGN-102

We completed the Phase 2a clinical trial in the first half of 2017. We have met with the FDA to discuss next steps in the clinical development program for UGN-102. We submitted an IND for UGN-102 in June 2018 and commenced a U.S. based Phase 2b clinical trial for UGN-102 In NMIBC.

UGN-201: Our Product Candidate for the Treatment of High-Grade NMIBC

We are developing UGN-201, our immune-modulation product candidate, for the treatment of high-grade NMIBC. A Phase 1 dose escalation study was conducted in 23 NMIBC patients and UGN-201 appeared to be well-tolerated in the study. This was followed by a Phase 2 pilot study under an IND in 12 patients with CIS bladder cancer in the United States. 20% of the 10 patients evaluated for efficacy achieved a complete response, and UGN-201 was observed to be well-tolerated in the trial. We intend to further investigate the use of UGN-201 for the treatment of high-grade NMIBC, as a single agent or possibly combining it with UGN-102, UGN-101 or with immune checkpoint inhibitors.

Limitations of Current Therapies for High-Grade NMIBC

High-grade NMIBC is a highly aggressive form of bladder cancer. TURBT is the initial treatment of choice for high-grade NMIBC; however, the high rates of recurrence and significant risk of progression to muscle-invasive tumors are particularly dangerous. Bladder removal can be the first treatment of choice for young, otherwise healthy patients with high-grade disease or for patients who cannot tolerate BCG. BCG, an immunotherapy-based drug, is the current standard of care as an adjuvant therapy post-resection in high-grade tumors. However, treatment with BCG is associated with severe side effects, as evidenced by a boxed warning on the label.

Our Solution: UGN-201

We believe that UGN-201 our immune-modulation product candidate, could represent a valid alternative to the current standard of care for the BCG adjuvant, post-TURBT treatment of high-grade NMIBC. UGN-201's active ingredient is imiquimod, an imidazoquinoline, synthetic immune modulator, which specifically targets TLR7, which is expressed in bladder cancer cells. Toll-like receptors are pattern recognition receptors whose importance in stimulating innate and adaptive immunity has been established by recent studies. Toll-like receptors are able to sense microbial components as well as host-derived endogenous molecules released by injured tissues and play a critical role in defending against invading pathogens.

Imiquimod, in its topical formulation, is FDA approved for several indications, including superficial basal cell carcinoma. UGN-201 is a liquid formulation of imiquimod for intravesical administration that has been optimized for delivery in the urinary tract. UGN-201 does not use our RTGel technology. We believe that UGN-201 may elicit an adaptive immune response in the presence of released bladder cancer antigens, which may translate into a long lasting acquired immune response. We also believe the combination of UGN-201 with immune checkpoint inhibitors could further increase the adaptive immune response and potentially represent a viable alternative to BCG for the adjuvant treatment of high-grade NMIBC or UTUC.

We have obtained Orphan Drug Designation for UGN-201 for the treatment of CIS in the bladder. We have an active IND for UGN-201, which has been effective since 2013.

We acquired UGN-201 from Telormedix SA, a private Swiss-based biotechnology company, in the fourth quarter of 2015. Telormedix conducted all of the previous studies related to UGN-201, including the Phase 1 and Phase 1b studies.

UGN-201 Clinical Results

UGN-201 was evaluated in a Phase 1 dose escalation study that enrolled 23 patients diagnosed with NMIBC. UGN-201 was well-tolerated at the doses used. Subsequently, a Phase 2 study of UGN-201 was conducted under an IND in patients with CIS bladder cancer in the United States. The Phase 2 study was commenced in April 2013 and completed in February 2014. Patients were dosed with UGN-201 0.4% weekly for six weeks. The study was designed to evaluate the safety and preliminary efficacy of UGN-201 in CIS patients. The primary efficacy endpoint for observational purposes only was the rate of complete response at five to seven weeks after the sixth weekly instillation. Twelve patients were enrolled into the pilot study, of whom 10 patients were evaluable for response. As per the publication, two of the 10 patients, or 20%, achieved a complete response. UGN-201 was observed to be well tolerated in this trial. The most common AEs related to UGN-201 were urination urgency, dysuria, fatigue, urinary tract infections and hematuria. One SAE, a urinary tract infection, was observed and was resolved.

Next Steps in the Clinical Development of UGN-201

We intend to further investigate the use of UGN-201 for the treatment of high-grade NMIBC, as a single agent or possibly combined with UGN-101, UGN-102 or other immunotherapy agents. Such a combination study would evaluate whether this multimodality approach, harnessing the power of the immune system together with the chemoablation properties of UGN-102 or UGN-101, can provide a safe and effective approach for the treatment of high-grade urothelial tumors.

Preclinical Programs

Using our proprietary RTGel formulation technology, we are pursuing additional preclinical programs to expand and enhance our uro-oncology product portfolio. In particular, we are pursuing preclinical programs for high-grade bladder cancer and high-grade UTUC using checkpoint inhibitors such as an anti PD-L1 or an anti CTLA-4.

License Agreement with Allergan

In October 2016, we entered into the Allergan Agreement with Allergan and 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, to which we refer as the Licensed Products, which are approved for the treatment of adults with overactive bladder who cannot use or do not adequately respond to anticholinergics. Additionally, we granted Allergan a non-exclusive, worldwide license to use certain of our trademarks as required for Allergan to practice its exclusive license with respect to the Licensed Products.

Under the Allergan Agreement, Allergan is solely responsible, at its expense, for developing the Licensed Products and obtaining all regulatory approvals for Licensed Products worldwide. Allergan is also solely responsible, at its expense, for commercializing the Licensed Products worldwide after receiving the regulatory approval to do so. Allergan is required to use commercially reasonable efforts to develop and commercialize the Licensed Products for overactive bladder in certain major market countries.

We will supply Allergan with certain quantities of RTGel for development of Licensed Products through Phase 2 clinical trials using BOTOX® together with RTGel in patients with overactive bladder, at Allergan's request and expense. Allergan has the right to reduce the next milestone payment to us if there is a material supply failure from us. Prior to completion of the first Phase 2 clinical trial, Allergan has the right to request that we transfer to Allergan our manufacturing process for RTGel and Allergan will assume the responsibility to manufacture RTGel and Licensed Product for its own development and commercialization activities.

Allergan paid us a nonrefundable upfront license fee of $17.5 million upon signing the agreement, and, in the third quarter of 2017, we received an additional $7.5 million milestone payment upon the submission by Allergan of an IND to the FDA for a Licensed Product. In October 2017, we announced that Allergan had begun a Phase 2 study of RTGel in combination with BOTOX® for the treatment of overactive bladder.

Further, we are eligible to receive additional material milestone payments of up to an aggregate of $200.0 million upon the successful completion of certain development, regulatory and commercial milestones, including $20.0 million upon initiation of a Phase 3 clinical trial for a Licensed Product for overactive bladder; $15.0 million upon initiation of a Phase 3 clinical trial for a Licensed Product for a specified second indication; $50.0 million and $25.0 million upon the first commercial sale of a Licensed Product for overactive bladder in the United States and the European Union, respectively; $25.0 million and $15.0 million upon the first commercial sale of a Licensed Product for a specified second indication in the United States and the European Union, respectively; and $50.0 million upon net sales of all Licensed Products of $500.0 million. Allergan will pay us a tiered royalty in the low single digits based on worldwide annual net sales of Licensed Products, subject to certain reductions for the market entry of competing products and/or loss of our patent coverage of Licensed Products. We are responsible for payments to any third party for certain RTGel-related third party intellectual properties.

Under the Allergan Agreement, Allergan granted us a non-exclusive, sublicensable, fully paid-up, perpetual, worldwide license under any improvements Allergan makes to the composition, formulation, or manufacture of RTGel for the research, development, manufacture and commercialization of any product containing RTGel and any active ingredient (other than a clostridial toxin) for all indications other than indications covered by the agreement and an exclusive, sublicensable, royalty-bearing (in low single digits), perpetual worldwide license under such improvements for use in the prevention or treatment of oncology indications.

We plan to continue to research, develop and commercialize other products combining RTGel with other active ingredients, except that there are certain restrictions with respect to the overactive bladder and neurogenic detrusor overactivity indications. Neurogenic detrusor overactivity is when a known neurologic abnormality impairs the signaling systems between the bladder and the central nervous system, and the brain is unable to inhibit the detrusor muscles controlling urination.

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.

Intellectual Property

Our patent estate includes patents and applications with claims directed to our UGN-101, UGN-102, RTGel, BotuGel and UGN-201 product candidates, as well as broader claims for potential future product candidates. On a worldwide basis, our patent estate includes more than 70 patent filings and pending patent applications for our product candidates claiming new treatment methods, manufacturing process, novel intravesical devices and future combination products that are mainly designed to treat internal cavity cancers. In the United States, we currently have 15 issued patents and more than 45 patent applications filed worldwide that are directed to methods, systems and compositions for treating internal cavity cancers, and in particular, urinary tract cancer and bladder cancer. These U.S.-issued patents are expected to remain in effect until between 2024 and 2035.

Our worldwide intellectual property portfolio includes patents and patent applications filed in many jurisdiction such as the United States, European Union, Canada, Israel, Australia, China, Japan, Mexico of which are expected to remain in effect until 2035:

- hydrogel-based pharmaceutical compositions for optimal delivery of various therapeutic agents to the internal cavity such as a bladder and/or urinary tract
- The method for treating bladder cancer, upper urinary tract cancer, and urothelial cancer using hydrogel-based composition
- The method for treating overactive bladder and IC topically without a need for injections
- Special catheters and in-dwelling ureter-catheter systems for optimal delivery of a drug into the renal cavity
- Pharmaceutical compositions comprising an imidazoquinolin-amine (specifically imiquimod) and lactic acid for treating bladder cancer diseases
- Novel phospholipid drug analogs (new chemical entities) for treating cancer or infections.

In addition to patents, we have filed applications for trademark registration with the United States Patent and Trademark Office, or the USPTO, for “Jelmyto,” “VesiGel,” “RTGel,” “BotuGel” and for certain other tradenames and logos. Furthermore, we rely upon trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position. Preparing and filing patent applications is a joint endeavor of our research and development team and our in-house and external patent attorneys. Our patent attorneys conduct patent prior-art searches and then analyze the data in order to provide our research and development team with recommendations on a routine basis. This results in:

- protecting our product candidates that are under development;
- encouraging pharmaceutical companies to negotiate development agreements with us; and
- preventing competitors from attempting to design-around our inventions.

Competition

The standard of care for treating NMIBC patients is the TURBT procedure for tumor resection, followed by post-operative adjuvant chemotherapy or immunotherapy instillations, administered to prevent reimplantation of the cancerous cells. The adjuvant agents used are predominately generic treatments and regimens. Only three drugs have been approved for the treatment of non-muscle invasive bladder cancer (NMIBC: Thiotepa, which was approved by the FDA in 1959; BCG, which was approved by the FDA in 1989; Valstar, which was approved by the FDA in 1998. Despite the approval of these drugs, there remain high unmet needs in the bladder cancer market. BCG has been used to treat patients with CIS and high-grade T1 since 1990. Valstar is indicated for patients with CIS (High Grade NMIBC) that do not respond to BCG treatment and Thiotepa is an over 50-year-old drug, rarely used, indicated for superficial papillary carcinoma of the bladder. Mitomycin is used off-label as the standard adjuvant treatment in the post-TURBT setting for LG NMIBC patients. Off-label means that while the FDA has not approved mitomycin as adjuvant treatment in the post-TURBT setting for LG NMIBC patients, physicians are permitted to utilize it as standard of care for this indication as part of medical practice. However, off-label usage as a standard of care does not change the FDA’s approval criteria and does not suggest that FDA approval is more likely than for other investigational drugs. In the UTUC space, there are no approved drugs used to treat the disease. Tumor resection surgeries are conducted in some cases of LG UTUC; however, complete kidney and upper urinary tract removal is the standard of care for frequently recurring UTUC.

There are several products in the development pipeline, most of which are second- or third line-treatments mainly targeted for high-grade NMIBC patients who have failed BCG treatment. All are targeted to reduce recurrence, but none are developed to reduce the need for TURBT and other tumor resection therapies.

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, Viralytics 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, LG 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 LG 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 TURBT, which is 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 to replace the existing standard of care, which is a first-line tumor surgical procedure for both bladder cancer and UTUC.

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.

These potential competitors may therefore introduce competing products without our prior knowledge and without our ability to take preemptive measures in anticipation of their commercial launch. 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 exclusively licensing products that are more effective, easier to administer or less costly than our product candidates.

Government Regulation

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, packaging, recordkeeping, tracking, approval, import, export, distribution, advertising and promotion of our products.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- nonclinical laboratory and animal tests that must be conducted in accordance with good laboratory practices, or GLPs;
- submission of an IND, which must become effective before clinical trials may begin;
- approval by an independent institutional review board, or IRB, for each clinical site or centrally before each trial may be initiated;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed product candidate for its intended use, performed in accordance with good clinical practices, or GCPs;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with cGMP and GCPs; and
- FDA approval of an NDA to permit commercial marketing for particular indications for use.

Prior to the commencement of marketing of controlled substances, the U.S. Drug Enforcement Agency, or DEA, must also determine the controlled substance schedule, taking into account the recommendation of the FDA.

The testing and approval process requires substantial time, effort and financial resources. Preclinical studies include laboratory evaluation of drug substance chemistry, pharmacology, toxicity and drug product formulation, as well as animal studies to assess potential safety and efficacy. Prior to commencing the first clinical trial with a product candidate, we must submit the results of the preclinical tests and preclinical literature, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical studies may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the conduct of the clinical trial by imposing a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may not result in FDA authorization to

commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, as well as amendments to previously submitted clinical trials. Further, an independent IRB for each study site proposing to conduct the clinical trial must review and approve the plan for any clinical trial, its informed consent form and other communications to study subjects before the clinical trial commences at that site. The IRB must continue to oversee the clinical trial while it is being conducted, including any changes to the study plans. Regulatory authorities, an IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, the clinical trial is not being conducted in accordance with the FDA's or the IRB's requirements, if the drug has been associated with unexpected serious harm to subjects, or based on evolving business objectives or competitive climate. Some studies also include a data safety monitoring board, which receives special access to unblinded data during the clinical trial and may advise us to halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

In general, for purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1—Studies are initially conducted to test the product candidate for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution and excretion in healthy volunteers or subjects with the target disease or condition. If possible, Phase 1 trials may also be used to gain an initial indication of product effectiveness.
- Phase 2—Controlled studies are conducted with groups of subjects with a specified disease or condition to provide enough data to evaluate the preliminary efficacy, optimal dosages and dosing schedule and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3—These clinical trials are undertaken in larger subject populations to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded subject population at multiple clinical trial sites. Evidence is considered to be statistically significant when the probability of the result occurring by random chance, rather than from the efficacy of the treatment, is sufficiently low. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. These trials may be done globally to support global registrations so long as the global sites are also representative of the U.S. population and the conduct of the study at global sites comports with FDA regulations and guidance, such as compliance with GCPs.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information.

Clinical trials must be conducted under the supervision of qualified investigators in accordance with GCP requirements, which includes the requirements that all research subjects provide their informed consent in writing for their participation in any clinical trial, and the review and approval of the study by an IRB. Investigators must also provide information to the clinical trial sponsors to allow the sponsors to make specified financial disclosures to the FDA. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the trial procedures, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated and a statistical analysis plan. Information about some clinical trials, including a description of the trial and trial results, must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their ClinicalTrials.gov website.

The manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and active pharmaceutical ingredients imported into the United States are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the Federal Food, Drug and Cosmetic Act, or the FDCA. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and the IRB and more frequently if SAEs occur.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

505(b)(2) Regulatory Approval Process

Section 505(b)(2) of the FDCA, or 505(b)(2), provides an alternate regulatory pathway to FDA approval for new or improved formulations or new uses of previously approved drug products. Specifically, 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. The applicant may rely upon the

FDA's prior findings of safety and efficacy for an approved product that acts as the reference listed drug for purposes of a 505(b)(2) NDA. The FDA may also require 505(b)(2) applicants to perform additional studies or measurements to support any changes from the reference listed drug. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Orange Book Listing

Section 505 of the FFDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy, but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product. ANDAs are termed "abbreviated" because they are generally not required to include preclinical and clinical data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA patents whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in Approved Drug Products with Therapeutic Equivalence Evaluations, also known as the Orange Book. These products may be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA.

Any applicant who submits an ANDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. This last certification is known as a Paragraph IV certification. Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through a Paragraph IV certification. If the applicant does not challenge the listed patents or does not indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired.

If the competitor has provided a Paragraph IV certification to the FDA, the competitor must also send notice of the Paragraph IV certification to the holder of the NDA for the reference listed drug and the patent owner once the application has been accepted for filing by the FDA. The NDA holder or patent owner may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification prevents the FDA from approving the application until the earlier of 30 months from the date of the lawsuit, expiration of the patent, settlement of the lawsuit, a decision in the infringement case that is favorable to the applicant or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a Paragraph IV certification, the NDA holder or patent owner regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation. The applicant may also elect to submit a statement certifying that its proposed label does not contain, or carves out, any language regarding the patented method-of-use rather than certify to a listed method-of-use patent.

Exclusivity

The FDA provides periods of regulatory exclusivity, which provides the holder of an approved NDA limited protection from new competition in the marketplace for the innovation represented by its approved drug for a period of three or five years following the FDA's approval of the NDA. Five years of exclusivity are available to NCEs. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt, including a salt with hydrogen or coordination bonds, or other noncovalent, or not involving the sharing of electron pairs between atoms, derivatives, such as a complex (i.e., formed by the chemical interaction of two compounds), chelate (i.e., a chemical compound), or clathrate (i.e., a polymer framework that traps molecules), of the molecule, responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review or approve an ANDA or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. An ANDA or 505(b)(2) application, however, may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed.

If a product is not eligible for the NCE exclusivity, it may be eligible for three years of exclusivity. Three-year exclusivity is available to the holder of an NDA, including a 505(b)(2) NDA, for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical trials, other than bioavailability or bioequivalence trials, was essential to the approval of the application and was conducted or sponsored by the applicant. This three-year exclusivity period protects against FDA approval of ANDAs and 505(b)(2) NDAs for the condition of the new drug's approval. As a general matter, three-year exclusivity does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

The Orphan Drug Act

Under the Orphan Drug Act, the FDA may grant Orphan Drug Designation to drugs intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan Drug Designation must be requested before submitting an NDA. After the FDA grants Orphan Drug Designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA Orphan Drug Designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of Orphan Drug Designation are tax credits for certain research and a waiver of the NDA application user fee.

Fast Track and Breakthrough Therapy Designations

The FDA is required to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment, and which demonstrate the potential to address unmet medical needs for the condition. Under the Fast Track program, the sponsor of a new product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the submission of the IND for the product candidate. The FDA must determine if the product candidate qualifies for Fast Track and Breakthrough Therapy designations within 60 days after receipt of the sponsor's request.

For Fast Track and Breakthrough Therapy products, the sponsor may have more frequent interactions with the FDA and the FDA may initiate review of sections of a Fast Track or Breakthrough Therapy product's NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a Fast Track or Breakthrough Therapy application does not begin until the last section of the NDA is submitted. In addition, the Fast Track and Breakthrough Therapy designations may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process. A Fast Track and Breakthrough Therapy designated product candidate would ordinarily meet the FDA's criteria for priority review.

NDA Submission and Review by the FDA

Assuming successful completion of the required clinical and preclinical testing, among other items, the results of product development, including chemistry, manufacture and controls, nonclinical studies and clinical trials are submitted to the FDA, along with proposed labeling, as part of an NDA. The submission of an NDA requires payment of a substantial user fee to the FDA. These user fees must be paid at the time of the first submission of the application, even if the application is being submitted on a rolling basis. Fee waivers or reductions are available in some circumstances. One basis for a waiver of the application user fee is if the applicant employs fewer than 500 employees, including employees of affiliates, the applicant does not have an approved marketing application for a product that has been introduced or delivered for introduction into interstate commerce, and the applicant, including its affiliates, is submitting its first marketing application.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA for a new active ingredient, indication, dosage form, dosage regimen or route of administration must contain data that are adequate to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDA may refer applications for drugs that contain active ingredients, including any ester or salt of the active ingredients, that have not previously been approved by the FDA to an advisory committee or provide in an action letter a summary of the reasons for not referring it to an advisory committee. The FDA may also refer drugs which present difficult questions of safety, purity or potency to an advisory committee. An advisory committee is typically a panel that includes clinicians and other experts who review, evaluate and make a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA reviews applications to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities, including contract manufacturers and subcontracts, are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs.

Once the FDA receives an application, it has 60 days to review the NDA to determine if it is substantially complete to permit a substantive review, before it accepts the application for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The FDA's NDA review times may differ based on whether the application is a standard review or priority review application. The FDA may give a priority review designation to drugs that are intended to treat serious conditions and provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has set the review goal of 10 months from the 60-day filing date to complete its initial review of a standard NDA for an NME and make a decision on the application. For non-NME standard applications, the FDA has set the review goal of 10 months from the submission date to complete its initial review and to make a decision on the application. For priority review applications, the FDA has set the review goal of reviewing NME NDAs within six months of the 60-day filing date and non-NME applications within six months of the submission date. Such deadlines are referred to as the PDUFA date. The PDUFA date is only a goal and the FDA does not always meet its PDUFA dates. The review process and the PDUFA date may also be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding the submission.

Once the FDA's review of the application is complete, the FDA will issue either a Complete Response Letter, or CRL, or approval letter. A CRL indicates that the review cycle of the application is complete, and the application is not ready for approval. A CRL generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing, or other information or analyses in order for the FDA to reconsider the application. The FDA has the goal of reviewing 90% of application resubmissions in either two or six months of the resubmission date, depending on the kind of resubmission. Even with the submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product, or impose other conditions, including distribution restrictions or other risk management mechanisms. For example, the FDA may require a risk evaluation and mitigation strategy, or REMS, as a condition of approval or following approval to mitigate any identified or suspected serious risks and ensure safe use of the drug. The FDA may prevent or limit further marketing of a product, or impose additional post-marketing requirements, based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements, FDA notification and FDA review and approval. Further, should new safety information arise, additional testing, product labeling or FDA notification may be required.

If regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed or may include contraindications, warnings or precautions in the product labeling, which has resulted in a boxed warning. The FDA also may not approve the inclusion of labeling claims necessary for successful marketing. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require Phase 4 post-marketing studies to monitor the effect of approved products and may limit further marketing of the product based on the results of these post-marketing studies.

Post-approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including manufacturing, periodic reporting, product sampling and distribution, advertising, promotion, drug shortage reporting, compliance with any post-approval requirements imposed as a conditional of approval such as Phase 4 clinical trials, REMS and surveillance, recordkeeping and reporting requirements, including adverse experiences.

After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual program user fee requirements for any approved products, as well as new application fees for supplemental applications with clinical data. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and to list their drug products and are subject to periodic announced and unannounced inspections by the FDA and these state agencies for compliance with cGMPs and other requirements, which impose procedural and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP regulations and other FDA regulatory requirements.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented, or FDA notification. FDA regulations also require investigation and correction of any deviations from cGMPs and specifications and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in withdrawal of marketing approval, mandatory revisions to the approved labeling to add new safety information or other limitations, imposition of post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS program, among other consequences.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA. Physicians, in their independent professional medical judgement, may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. We, however, are prohibited from marketing or promoting drugs for uses outside of the approved labeling but may share truthful and not misleading information that is otherwise consistent with the product's approved labeling.

In addition, the distribution of prescription pharmaceutical products, including samples, is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. The Drug Supply Chain Security Act also imposes obligations on manufacturers of pharmaceutical products related to product and tracking and tracing.

Failure to comply with any of the FDA's requirements could result in significant adverse enforcement actions. These include a variety of administrative or judicial sanctions, such as refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, cyber letters, modification of promotional materials or labeling, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, debarment, injunctions, fines, consent decrees, corporate integrity agreements, refusals of government contracts and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement or civil or criminal penalties, including fines and imprisonment. Any of these sanctions could result in adverse publicity, among other adverse consequences.

Other Healthcare Regulations

Our business activities, including but not limited to, research, sales, promotion, distribution, medical education and other activities following product approval will be subject to regulation by numerous regulatory and law enforcement authorities in the United States in addition to the FDA, including potentially the Department of Justice, the Department of Health and Human Services, or HHS, and its various divisions, including the Centers for Medicare & Medicaid Services, or CMS, and the Health Resources and Services Administration, the Department of Veterans Affairs, the Department of Defense and state and local governments. Our business activities must comply with numerous healthcare laws and regulations, including those described below.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, the referral of an individual for, or purchasing, leasing, ordering, or arranging for the purchase, lease or order of, any good, facility, item or service reimbursable, in whole or in part, by Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value, including unlawful financial inducements paid to prescribers and beneficiaries, as well as impermissible promotional practices. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but the exceptions and safe harbors are drawn narrowly. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Additionally, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, amended the intent requirement of the federal Anti-Kickback Statute so that a person or entity no longer needs to have actual knowledge of the federal Anti-Kickback Statute, or the specific intent to violate it, to have violated the statute. The ACA also provided that a violation of the federal Anti-Kickback Statute is grounds for the government or a whistleblower to assert that a claim for payment of items or services resulting from such violation constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

The federal civil and criminal false claims laws, including the federal civil False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or for approval by, the federal government, including the Medicare and Medicaid programs, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government.

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

As a condition of receiving Medicaid coverage for prescription drugs, the Medicaid Drug Rebate Program requires manufacturers to calculate and report to CMS their Average Manufacturer Price, or AMP, which is used to determine rebate payments shared between the states and the federal government and, for some multiple source drugs, Medicaid payment rates for the drug, and for drugs paid under Medicare Part B, to also calculate and report their average sales price, which is used to determine the Medicare Part B payment rate for the drug. In January 2016, CMS issued a final rule regarding the Medicaid Drug Rebate Program, effective April 1, 2016, that, among other things, revises the manner in which the AMP is to be calculated by manufacturers participating in the program and implements certain amendments to the Medicaid rebate statute created under the ACA. Drugs that are approved under a biologics license application, or BLA, or an NDA, including a 505(b)(2) NDA, are subject to an additional requirement to calculate and report the manufacturer's best price for the drug and inflation penalties which can substantially increase rebate payments. For BLA and NDA drugs, the Veterans Health Care Act requires manufacturers to calculate and report to the Department of Veterans Affairs a different price called the Non-Federal AMP, offer the drugs for sale on the Federal Supply Schedule, and charge the government no more than a statutory price referred to as the Federal Ceiling Price, which includes an inflation penalty. A separate law requires manufacturers to pay rebates on these drugs when paid by the Department of Defense under its TRICARE Retail Pharmacy Program. Knowingly submitting false pricing information to the government creates potential federal civil False Claims Act liability.

The Federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal civil and criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including public and private payors, or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. The ACA amended the federal health care fraud criminal statute implemented under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have violated the statute.

Additionally, the federal Open Payments program pursuant to the Physician Payments Sunshine Act, created under Section 6002 of the ACA and its implementing regulations, require some manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with specified exceptions) to report annually information related to specified payments or other transfers of value provided to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, physicians and teaching hospitals and to report annually specified ownership and investment interests held by physicians and their immediate family members.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, impose requirements relating to the privacy, security and transmission of individually identifiable health information on HIPAA covered entities, which include certain healthcare providers, health plans and healthcare clearinghouses, and their business associates, including mandatory contractual terms and the 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 the federal HIPAA laws 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.

In addition, the European Union, or EU, has established its own data security and privacy legal framework, including but not limited to the European General Data Protection Regulation, or GDPR, which contains provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures intended to bring non-EU companies under the regulation. We anticipate that over time we may expand our business to include additional operations outside of the United States and Israel. With such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR.

Additionally, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. When it goes into effect on January 1, 2020, the CCPA will require covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Legislators have stated that amendments will be proposed to the CCPA before it goes into effect, but it remains unclear what, if any, modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA will likely impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.[1]

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. We may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and/or state laws that require drug manufacturers to report information related to marketing expenditures or payments and other transfers of value to physicians and other healthcare providers, and drug pricing. Certain state and local laws also require the registration of pharmaceutical sales representatives.

Enforcement actions can be brought by federal or state governments or, in some cases, as "qui tam" actions brought by individual whistleblowers in the name of the government. Depending on the circumstances, failure to comply with these laws can result in significant penalties, including criminal, civil and administrative penalties, damages, fines, disgorgement, debarment from government contracts, 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, exclusion from government programs, refusal to allow us to enter into supply contracts, including government contracts, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations, any of which could adversely affect our business.

Coverage and Reimbursement

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for our products, once approved, and related treatments will be available from third-party payors, such as government health administration authorities, private health insurers and managed care organizations. Third-party payors determine which medications they will cover and separately establish reimbursement levels. Even if we obtain coverage for a given product by a third-party payor, the third-party payor's reimbursement rates may not be adequate to make the product affordable to patients or profitable to us, or the third-party payors 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.

Government authorities and other third-party payors are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices as a condition of coverage, are using restrictive formularies and preferred drug lists to leverage greater discounts in competitive classes and are challenging the prices charged for medical products. Further, no uniform policy for determining 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 is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, that the level of reimbursement will be adequate. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available, or if reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

Healthcare Reform Measures

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals designed 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 and/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, the ACA was passed, which has changed health care financing by both governmental and private insurers and significantly affected the U.S. pharmaceutical industry. The ACA, among other things, subjected manufacturers to new annual fees and taxes for specified branded prescription drugs, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, expanded health care fraud and abuse laws, revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs under the Medicaid Drug Rebate Program are calculated, imposed an additional rebate similar to an inflation penalty on new formulations of drugs, extended the Medicaid Drug Rebate Program to Medicaid managed care organizations, expanded the 340B program, which caps the price at which manufacturers can sell covered outpatient pharmaceuticals to specified hospitals, clinics and community health centers, and provided incentives to programs that increase the federal government's comparative effectiveness research.

However, some provisions of the ACA have yet to be fully implemented and certain provisions have been subject to judicial and Congressional challenges, as well as efforts by the Trump Administration 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 has been signed into law. Legislation enacted in 2017 (H.R. 1, "An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018"), informally titled the Tax Cuts and Jobs Act of 2017, or Tax Act, included a provision which 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, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." 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 inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax 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.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional U.S. Congressional action is taken. In addition, 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.

Further, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, 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. Further, the Trump administration released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug 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. HHS has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. On January 31, 2019, the HHS Office of Inspector General, proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations. While some of these and other proposed measures may require authorization through additional legislation to become effective, Congress and the Trump Administration have both stated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Additional health reform measures may continue and affect our business in unknown ways.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the companies to maintain books and records that accurately and fairly reflect all transactions of the companies, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to develop or sell any products outside of the United States. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Manufacturing, Supply and Production

We do not own or operate manufacturing facilities for the production of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials, active ingredients and finished products for our preclinical research and clinical trials. The company is in the process of negotiating commercial supply agreements with its primary third-party vendors. We anticipate that these agreements will be executed in advance of commercial approval for UGN-101. The company also intends on negotiating back-up supply agreements with other third-party manufacturers for the commercial production of those products.

Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval. We currently employ internal resources to manage our manufacturing contractors. The relevant manufacturers of our drug products for our current preclinical and clinical trials have advised us that they are compliant with both current good laboratory practice, or cGLP, and cGMP.

Our product candidates, if approved, may not be producible in sufficient commercial quantities, in compliance with regulatory requirements or at an acceptable cost. We and our contract manufacturers are, and will be, subject to extensive governmental regulation in connection with the manufacture of any pharmaceutical products or medical devices. We and our contract manufacturers must ensure that all of the processes, methods and equipment are compliant with cGMP and cGLP for drugs on an ongoing basis, as mandated by the FDA and foreign regulatory authorities, and conduct extensive audits of vendors, contract laboratories and suppliers.

Marketing, Sales and Distribution

Given our stage of development, we do not have any internal sales, marketing or distribution infrastructure or capabilities, and our marketing department currently consists only of a marketing director, whose main responsibility is to produce marketing and communication materials, exhibitions, website content and to identify unmet needs in the urology market, assess their commercial potential and advise on the prioritization of the development of our future product candidates accordingly. The Company's U.S. subsidiary, Urogen Pharma, Inc., was formed to support our U.S. development and potential commercialization efforts.

In the event that we receive regulatory approvals for our products in markets outside of the United States, we intend, where appropriate, to pursue commercialization relationships, including strategic alliances and licensing, with pharmaceutical companies and other strategic partners, which are equipped to market or sell our products through their well-developed sales, marketing and distribution organizations in such countries.

In addition, we may out-license some or all of our worldwide patent rights to more than one party to achieve the fullest development, marketing and distribution of any products we develop.

Employees

As of February 22, 2019, we had 78 employees worldwide, 19 of whom hold PhD, PharmD, or M.D. degrees. None of our employees is subject to a collective bargaining agreement. We have never experienced any employment-related work stoppages and consider our relationships with our employees are good.

Israeli labor laws govern the length of the workday and workweek, minimum wages for employees, procedures for hiring and dismissing employees, determination of severance pay, annual leave, sick days, advance notice of termination, payments to the National Insurance Institute, and other conditions of employment and include equal opportunity and anti-discrimination laws. While none of our employees is party to any collective bargaining agreements, certain provisions of the collective bargaining agreements between the Histadrut (General Federation of Labor in Israel) and the Coordination Bureau of Economic Organizations (including the Industrialists' Associations) are applicable to our employees in Israel by order of the Israeli Ministry of Economy and Industry. These provisions primarily concern pension fund benefits for all employees, insurance for work-related accidents, recuperation pay and travel expenses. We generally provide our employees with benefits and working conditions beyond the required minimums.

Corporate Information

Our legal and commercial name is UroGen Pharma Ltd, with registered offices at 9 Ha'Ta'asiya St., Ra'anana 4365007, Israel. We are a company organized under the laws of State of Israel. We were formed in 2004 with an indefinite duration. We are registered with the Israeli Registrar of Companies. Our principal executive offices are located at 499 Park Ave 12th Floor, New York, New York 10022. Our telephone number is (646) 768-9780. Investors should contact us for any inquiries through the address and telephone number of our principal executive office. We maintain a web site at http://www.urogen.com. The reference to our website is an inactive textual reference only and the information contained in, or that can be accessed through, our website is not incorporated into this Annual Report.

For all documents filed after January 1, 2019, we file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and other information with the SEC. Our filings with the SEC are available free of charge on the SEC's website at *www.sec.gov* and on our website under the "Investors" tab as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Unless the context requires otherwise, references in this Annual Report to "we," "us", "our" and "UroGen" refer to UroGen Pharma, Ltd. and its subsidiaries.

Item 1A. Risk Factors

An investment in shares of our ordinary shares involves a high degree of risk. You should carefully consider all of the information set forth in this Annual Report 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 report 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 Annual Report. 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 $75.7 million and $20.0 million for the years ended December 31, 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. In January 2019, we completed an underwritten public offering in which we received net proceeds of approximately $161.8 million, after deducting the underwriting discounts and commissions and payment of other offering expenses.

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 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, their sufficiency 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;
- if applicable, 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 determination of 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 or procedure-related adverse events and many are

indicated as potential side effects of mitomycin usage on the mitomycin label. However, we cannot assure you that adverse events related to UGN-101 and UGN-102 that are not directly attributable to mitomycin 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 this Annual Report and our other filings with the SEC. 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 LG UTUC and of UGN-102 for the first-line treatment of LG 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 mitomycin 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 mitomycin or procedure-related adverse events and many are indicated as potential side effects of mitomycin usage on the mitomycin 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 boxed 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 LG UTUC, and in the case of UGN-102, for the first-line treatment of LG NMIBC, and for other therapeutic indications that we may seek to pursue with any of our product candidates. Physicians treating LG UTUC and LG 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 LG UTUC with UGN-101 and the treatment of LG 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 LG UTUC and UGN-102 for the treatment of LG 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 (durbalumab) 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, Viralytics 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, LG 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 LG 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 Annual Report 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 mitomycin 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 mitomycin API in the quantities and on the timeline required, it is possible that the restructuring could adversely affect our ability to obtain mitomycin in any given period and could require us to expend funds and effort to identify and engage one or more alternate suppliers of mitomycin. 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 mitomycin drug product, or final mitomycin formulation, necessary for our clinical trial and commercial requirements. We have yet to complete the mitomycin 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 mitomycin through this drug product manufacturer, we plan to continue to rely on third parties for such production of mitomycin 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 mitomycin, through a third-party manufacturer of mitomycin, 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 mitomycin.

Even if we are successful in being approved as a commercial supplier of mitomycin, 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 mitomycin, 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 mitomycin 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 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 LG 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 LG 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 but we are permitted to share truthful and not misleading information that is otherwise consistent with the product's FDA approved labeling. 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 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, 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 mitomycin, 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 included 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 of 2017, or Tax Act, included 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, or HHS, 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 inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax 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. HHS 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. On January 31, 2019, the HHS Office of Inspector General, proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations. Although a number of these, and other proposed measures may 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 civil and 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, 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.

The European Union, or EU, has established its own data security and privacy legal framework, including but not limited to the European General Data Protection Regulation, or GDPR, which contains provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures intended to bring non-EU companies under the regulation. We anticipate that over time we may expand our business to include additional operations outside of the United States and Israel. With such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR.

Additionally, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. When it goes into effect on January 1, 2020, the CCPA will require covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Legislators have stated that amendments will be proposed to the CCPA before it goes into effect, but it remains unclear what, if any, modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA will likely impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

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 to CMS 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, drug pricing, 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. Certain state and local laws also require the registration of pharmaceutical sales representatives.

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 significant administrative, civil and criminal penalties, damages, monetary fines, disgorgement, 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 the structure of healthcare payment systems;
- 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 this Annual Report, the holders of up to approximately 4.5 million 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℠ 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 year ended December 31, 2018 and taxable year ending 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 below) 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." For purposes of this discussion, a "U.S. Holder" is a beneficial owner of our ordinary shares that, for U.S. federal income tax purposes, is or is treated as any of the following: (a) an individual who is a citizen or resident of the United States; (b) a corporation, or entity treated as a corporation for U.S. federal income tax purposes, created or organized under the laws of the United States, any state thereof, or the District of Columbia; (c) an estate, the income of which is subject to U.S. federal income tax regardless of its source; or (d) a trust that (1) is subject to the supervision of a U.S. court and the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

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 Act was signed into law and significantly revised the U.S. Internal Revenue Code of 1986, as amended, or the Code. The Tax 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 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 Global 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. 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.

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.

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. As of December 31, 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 year ended December 31, 2018. 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. 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.

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. One of our directors resides outside of the United States, and most of our assets and most of the assets of this director are located outside of the United States. Therefore, a judgment obtained against us, or this director, 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 this director 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 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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease an approximately 11,495 square foot facility in Israel, which is used primarily as research and development laboratories as well as for administrative purposes. We lease approximately 9,336 square feet of space in New York, which serves as our principal executive offices and is used for marketing as well as general and administrative purposes. We lease approximately 4,906 square feet of space in Los Angeles, which is used for general and administrative purposes. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional or alternative spaces will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings

From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities

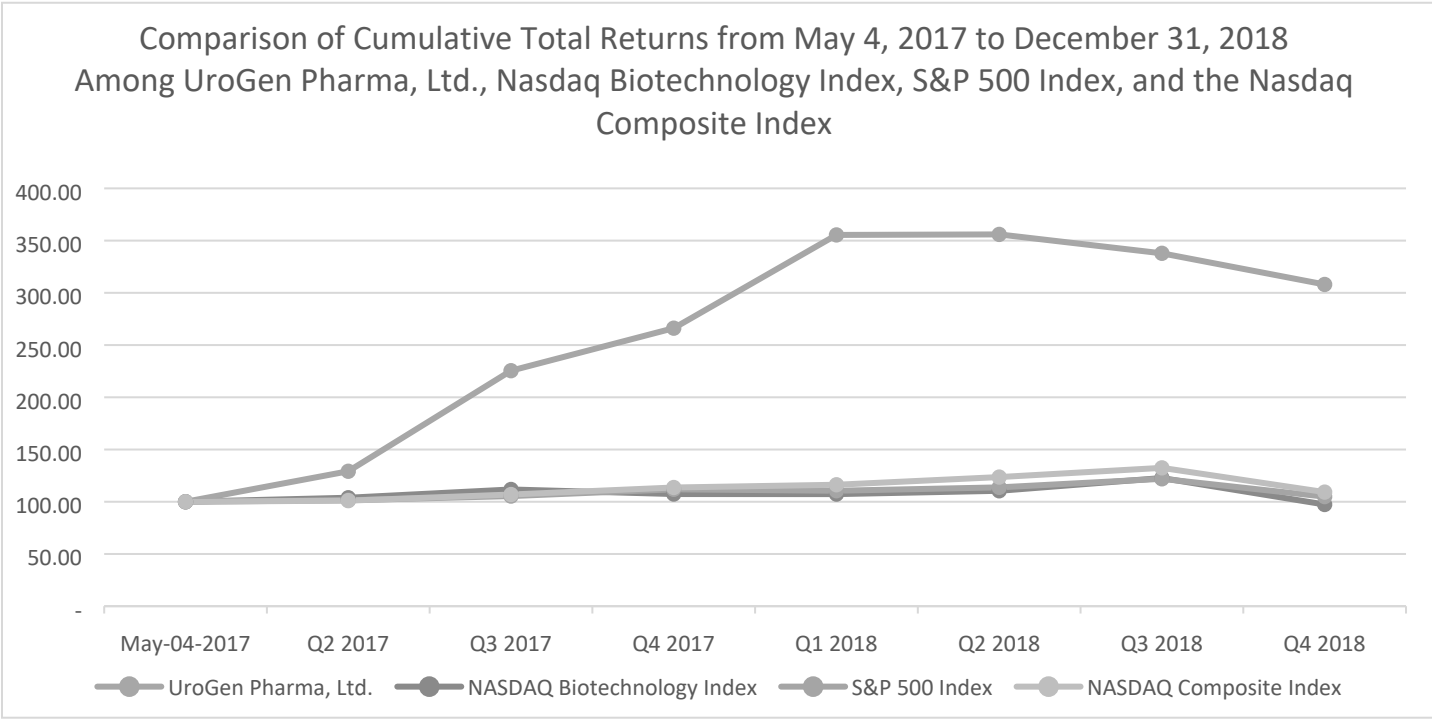
Recent Sales of Unregistered Securities

None.

Stock Performance Graph

This performance graph shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or incorporated by reference into any of our filings under the Securities Act or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Our ordinary shares has been traded on The Nasdaq Global Market since May 4, 2017 under the symbol URGN. Prior to such time, there was no public market for our ordinary shares. The following graph shows the value of an investment of $100 from May 4, 2017 (the date our ordinary shares commenced trading on The Nasdaq Global Market) through December 31, 2018, in our ordinary shares, the Nasdaq Biotechnology Index, the Standard & Poor's 500 Index (S&P 500), and Nasdaq Composite Index. The historical share price performance of our common shares shown in the performance graph is not necessarily indicative of future stock price performance.



	Cumulative Total Return date ended							
	5/4/2017 (Inception)	6/30/2017	9/30/2017	12/31/2017	3/31/2018	6/30/2018	9/30/2018	12/31/2018
Urogen Pharma	$ 100.00	$ 129.18	$ 225.46	$ 266.17	$ 355.44	$ 355.94	$ 337.84	$ 308.01
Nasdaq Biotechnology	100.00	103.83	111.75	107.38	107.31	110.48	122.70	97.37
S&P	100.00	101.42	105.43	111.89	110.52	113.76	121.95	104.91
Nasdaq Composite	100.00	101.07	106.92	113.63	116.26	123.62	132.44	109.22

Holders

As of February 22, 2019 there were approximately 27 registered holders of record of our ordinary shares.

Dividend Policy

We have not paid any dividends on our ordinary shares since our inception and do not expect to pay dividends on our ordinary shares in the foreseeable future. We currently intend to retain all available funds as well as future earnings, if any, to fund the development and expansion of our operations. Any future determination to pay dividends will be made at the discretion of our board of directors.

Use of Proceeds from Initial Public Offering of Ordinary Shares

In May 2017, we completed our initial public offering, or IPO, and sold 5,144,378 shares of our ordinary shares at a price of $13.00 per share. The net offering proceeds to us, after deducting underwriting discounts and commissions and offering expenses, were approximately $60.8 million. The offering commenced on May 1, 2017 and did not terminate before all of the securities registered in the registration statement were sold. The effective date of the registration statement, File No. 333-217201, for our ordinary shares was May 3, 2017. Jefferies LLC and Cowen and Company, LLC acted as joint book-running managers for the IPO, Raymond James & Associates, Inc. and Oppenheimer & Co. Inc acted as co-managers.

None of the net proceeds of our offering were paid directly or indirectly to any of our directors or executive officers, to their associates, persons owning ten percent or more of any class of our equity securities, or to any of our affiliates.

As of December 31, 2018, we have used approximately $35.8 million of the net proceeds from our IPO primarily to fund our UGN-101 clinical program and other programs as well as working capital, including general operating expenses, as further described under the "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this Annual Report.

The remaining net proceeds from our IPO will be used, together with our cash and cash equivalents and marketable securities, to fund continued advancement of our product pipeline, with the balance to be used to fund working capital and other general corporate purposes, which may include licensing, acquiring or investing in additional businesses, technologies, products, or assets of other products, businesses or technologies.

Purchases of Equity Securities by the Issuer or Affiliated Purchasers

None.

Item 6. Selected Financial Data

The following selected financial data has been derived from our audited financial statements, including the consolidated balance sheets at December 31, 2018 and 2017 and the related consolidated statements of operations for each of the three years ended December 31, 2018 and related notes appearing elsewhere in this Annual Report. The consolidated statement of operations data for the years ended December 31, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016, 2015 and 2014 are derived from our audited consolidated financial statements that are not included in this Annual Report. Our historical results are not necessarily indicative of the results that can be expected in the future. The selected historical financial data below should be read in conjunction with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and related notes appearing elsewhere in this Annual Report.

	Years Ended December 31,				
	2018	2017	2016	2015	2014
Statements of operations data:	(in thousands, except share and per share data)				
Revenues	$ 1,128	$ 8,158	$ 17,530	$ —	$ —
Cost of revenue	1,803	600	28	—	—
Gross profit	(675)	7,558	17,502	—	—
Research and development expenses, net	36,934	18,697	10,287	10,515	3,479
General and administrative expenses	39,571	8,811	6,417	1,895	890
Operating (loss) income	(77,180)	(19,950)	798	(12,410)	(4,369)
Finance (income) expenses, net	(1,648)	31	2,739	279	107
Loss before income taxes	(75,532)	(19,981)	(1,941)	(12,689)	(4,476)
Income tax expense	125	19	—	—	—
Net loss	$ (75,657)	$ (20,000)	$ (1,941)	$ (12,689)	$ (4,476)
Loss per ordinary share, basic and diluted	$ (4.80)	$ (2.14)	$ (1.91)	$ (5.88)	$ (6.34)
Weighted average number of ordinary shares outstanding used in computing loss per share	15,754,193	9,716,790	2,305,503	2,300,959	719,059

	As of December 31,				
	2018	2017	2016	2015	2014
			(in thousands)		
Balance sheet data:					
Cash and equivalents, short-term investments	$ 101,318	$ 73,000	$ 21,362	$ 17,975	$ 3,870
Working capital	88,778	67,437	18,904	16,894	3,397
Total assets	103,559	75,550	23,056	19,930	4,359
Total liabilities	13,465	7,035	6,749	3,109	1,196
Total shareholders' equity	$ 90,094	$ 68,515	$ 16,307	$ 16,281	$ 3,163

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion contains management's discussion and analysis of our financial condition and results of operations and should be read together with "Selected Financial Data" and the historical consolidated financial statements and the notes thereto included in "Financial Statements and Supplementary Data". This discussion contains forward-looking statements that reflect our plans, estimates and beliefs and involve numerous risks and uncertainties, including but not limited to those described in the "Risk Factors" section of this Annual Report. Actual results may differ materially from those contained in any forward-looking statements. You should carefully read "Special Note Regarding Forward-Looking Statements" and "Risk Factors."

Overview

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, 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 LG 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.

We estimate that the prevalence of LG UTUC in the United States is approximately 6,000 to 8,000; the prevalence of LG NMIBC is approximately 80,000; and the prevalence of carcinoma in situ (CIS) bladder cancer is approximately 2,000.

Our lead product candidates, UGN-101 and UGN-102, are formulated using our proprietary reverse thermally triggered hydrogel, or RTGel, technology. We believe that RTGel-based drug formulations, which provide for the sustained release of an active drug, may improve the efficacy of treatment of various types of urothelial cancer without compromising the safety of the patient or interfering with the natural flow of fluids from the urinary tract to the bladder. Our formulations are designed to achieve this by increasing the dwell time as well as the tissue coverage of the active drug throughout the organ. Consequently, we believe that RTGel-based drug formulations may enable us to overcome the anatomical and physiological challenges that have historically contributed to the lack of drug development for the treatment of urothelial cancer. No drugs have been approved by the U.S. Food and Drug Administration, or the FDA, for the treatment of non-muscle invasive bladder cancer, or NMIBC, in more than 15 years.

Our clinical stage pipeline also includes UGN-201, our proprietary immunotherapy product candidate for the treatment of high-grade NMIBC, which may include Carcinoma in Situ, or CIS. UGN-201 is a novel, liquid formulation of Imiquimod, a generic toll-like receptor 7, or TLR7, agonist. Toll-like receptor agonists play a key role in initiating the innate immune response system. We believe that the combination of UGN-201 with additional immunotherapy drugs, such as immune checkpoint inhibitors or chemotherapy drugs like UGN-102, could represent a valid alternative to the current standard of care for the post-TURBT adjuvant treatment of high-grade NMIBC.

BotuGel is our proprietary novel RTGel-based formulation of BOTOX, a branded drug, that we believe can potentially serve as an effective treatment option for patients suffering from overactive bladder. In October 2016, we announced the licensing of the worldwide rights to RTGel in combination with neurotoxins, including BOTOX, to Allergan Pharmaceuticals International Limited, or Allergan, a wholly owned subsidiary of Allergan plc, or the Allergan Agreement. In August 2017, we announced that Allergan had submitted an IND to the FDA in order to be able to commence clinical trials in the United States using the RTGel in combination with BOTOX. In October 2017, Allergan commenced a Phase 2 clinical trial of BotuGel for the treatment of overactive bladder.

Our Research and Development and License Agreements

We entered into an exclusive license agreement with Allergan Pharmaceuticals International Limited, or Allergan, a wholly owned subsidiary of Allergan plc in October 2016, which we refer to as the Allergan Agreement. Allergan paid us a nonrefundable upfront license fee of $17.5 million, and we are eligible to receive additional milestone payments upon the successful completion of certain development, regulatory and commercial milestones. Under the Allergan Agreement, Allergan is solely responsible, at its expense, for developing, obtaining regulatory approvals for and commercializing, on a worldwide basis, 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. Allergan is obligated to pay us a tiered royalty in the low single digits based on worldwide annual net sales of Licensed Products, subject to certain reductions for the market entry of competing products and/or loss of our patent coverage of Licensed Products. We are responsible for payments to any third party for certain RTGel-related third-party intellectual properties. In July 2017, Allergan notified us that they had submitted their Investigational New Drug, or IND, application for BotuGel, our proprietary novel RTGel-based formulation of BOTOX for the treatment of overactive bladder, to the FDA. The submission of the IND triggered the second milestone under the Allergan Agreement, pursuant to which we received a payment of $7.5 million in August 2017. Allergan commenced a Phase 2 clinical trial of BotuGel in October 2017, pursuant to Allergan Agreement.

For additional information regarding our research and development and license agreements, see Note 6 to our financial statements appearing elsewhere in this Annual Report.

Components of Operating Results

Revenues

We do not currently have any products approved for sale and, to date, we have not recognized any revenues from sales of UGN-101, UGN-102 or UGN-201. For the year ended December 31, 2018, we recognized revenues of $1.1 million from RTGel sales under the Allergan Agreement. For the year ended December 31, 2017, we recognized revenues of $7.5 million under the Allergan Agreement upon the achievement of a milestone in August 2017 as well as sales of RTGel to Allergan, per the Allergan Agreement. In the future, we may generate revenue from a combination of product sales, reimbursements, up-front payments, milestone payments and royalties in connection with the Allergan Agreement and future collaborations. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of license fees, milestone and other payments, and the amount and timing of payments that we receive upon the sale of our products, to the extent any are successfully commercialized. If we fail to achieve clinical success and/or to obtain regulatory approval of any of our product candidates in a timely manner, our ability to generate future revenue will be impaired.

Research and Development Expenses, Net

Research and development expenses consist primarily of:

- salaries and related costs, including share-based compensation expense, for our personnel in research and development functions;
- expenses incurred under agreements with third parties, including CROs, subcontractors, suppliers and consultants, preclinical studies and clinical trials;
- expenses incurred to acquire, develop and manufacture preclinical study and clinical trial materials; and
- facility and equipment costs, including depreciation expense, maintenance and allocated direct and indirect overhead costs.

We expense all research and development costs as incurred. In light of the fact that our employees and internal resources may be engaged in projects for multiple programs at any time, our focus is on total research and development expenditures, and we do not allocate our internal research and development expenses by project.

We estimate preclinical study and clinical trial expenses based on the services performed pursuant to contracts with research institutions and contract research organizations that conduct and manage preclinical studies and clinical trials on our behalf based on actual time and expenses incurred by them.

We accrue for costs incurred as the services are being provided by monitoring the status of the trial or project and the invoices received from our external service providers. We adjust our accrual as actual costs become known. Where at risk contingent milestone payments are due to third parties under research and development and collaboration agreements, the milestone payment obligations are expensed when the milestone results are achieved.

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.

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.

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 in whole or in part with IIA-funded technology, up to the amount of the grant related to any such products plus accrued interest. As of December 31, 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 year ended December 31, 2018. 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. 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. Under applicable accounting rules, we deduct the IIA grants from research and development expenses as the applicable costs are incurred. We also had a preclinical collaboration for BotuGel with Allergan into which we initially entered into in February 2014. We deduct amounts received from the preclinical collaboration with Allergan from our research and development expenses as the applicable costs are incurred. As a result, our research and development expenses are shown on our financial statements net of the IIA grants and amounts received from the preclinical collaboration.

We are currently focused on advancing our product candidates, and our future research and development expenses will depend on their clinical success. Research and development expenses will continue to be significant and will increase over at least the next several years as we continue to develop our product candidates and conduct preclinical studies and clinical trials of our product candidates.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We do not believe that it is possible at this time to accurately project total expenses required for us to reach commercialization of our product candidates. Due to the inherently unpredictable nature of preclinical and clinical development, we are unable to estimate with certainty the costs we will incur and the timelines that will be required in the continued development and approval of our product candidates. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. In addition, we cannot forecast which product candidates may be subject to future collaborations, if and when such arrangements will be entered into, if at all, and to what degree such arrangements would affect our development plans and capital requirements. We expect our research and development expenses to increase over the next several years as our clinical programs progress and as we seek to initiate clinical trials of additional product candidates. We also expect to incur increased research and development expenses as we selectively identify and develop additional product candidates.

The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors that include, but are not limited to, the following:

- per patient trial costs;
- the number of patients that participate in the trials;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up; and
- the efficacy and safety profile of the product candidates.

In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability. We will determine which programs to pursue and how much to fund each program in response to the scientific and clinical success of each product candidate, as well as an assessment of each product candidate’s commercial potential.

Because UGN-101 and UGN-102 are still in clinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of product candidates or whether, or when, we may achieve profitability. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, including share-based compensation, related to directors, executive, finance, business development, investor relations, and human resource functions, facility costs and external professional service costs, including legal, accounting and audit services and other consulting fees.

We anticipate that our general and administrative expenses will increase in the future as we increase our administrative headcount and infrastructure to support our continued research and development programs and the potential approval and commercialization of our product candidates. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. The increased costs associated with being a public company include expenses related to services associated with maintaining compliance with Nasdaq listing rules and SEC requirements, insurance, executive compensation, investor relations costs, and other costs associated with being a public company.

In addition, if any of our product candidates receives regulatory approval and if we invest in building a commercial infrastructure to support the marketing of our products, we expect to incur greater expenses.

Finance Expenses, Net

Finance expenses, net, consisted primarily of finance expenses on warrants offset by interest income.

Income Taxes

We have yet to generate taxable income in Israel. We have historically incurred operating losses resulting in carry forward tax losses totaling approximately $72.1 million as of December 31, 2018. We anticipate that we will continue to generate tax losses for the foreseeable future and that we will be able to carry forward these tax losses indefinitely to future taxable years. Accordingly, we do not expect to pay taxes in Israel until we have taxable income after the full utilization of our carry forward tax losses. We have provided a full valuation allowance with respect to the deferred tax assets related to these carry forward losses.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

The following table sets forth our results of operations for the years ended December 31, 2018 and 2017.

	Year Ended December 31,		
	2018	2017	Change
		(in thousands)	
Revenues	$ 1,128	$ 8,158	$ (7,030)
Cost of revenue	1,803	600	1,203
Gross profit	(675)	7,558	(8,233)
Operating expenses:			
Research and development	36,934	18,697	18,237
General and administrative	39,571	8,811	30,760
Total operating expenses	76,505	27,508	48,997
Operating (loss) income	(77,180)	(19,950)	(57,230)
Finance (income) expenses, net	(1,648)	31	(1,679)
Loss before income taxes	(75,532)	(19,981)	(55,551)
Income tax expense	125	19	106
Net loss	$ (75,657)	$ (20,000)	$ (55,657)

Revenues

Revenues were $1.1 million and $8.2 million for the years ended December 31, 2018 and 2017, respectively. The decrease of $7.0 million was primarily due to the decreased revenue recognized under the Allergan Agreement.

Research and Development Expenses

Research and development expenses increased by $18.2 million to $36.9 million in the year ended December 31, 2018 from $18.7 million in the year ended December 31, 2017. Approximately $8.1 million of the increase was attributable to share-based compensation, including $2.4 million in modification costs relating to senior management severance packages and $5.7 million in new grants to executive management and employees. The remaining increase of $10.1 million is mainly comprised of $4.1 million in increased headcount and related costs to support increased clinical trial activities, a $2.5 million increase in direct costs associated with the UGN-101 Phase 3 clinical trial, a $2.7 million increase due to increased clinical activity of the UGN-102 Phase 2b clinical trial and approximately a $0.6 million increase in allocated overhead costs to support the growth of our U.S. operations. Total non-cash research and development share-based compensation expense was $12.0 million and $3.9 million for the years ended December 31, 2018 and 2017, respectively.

General and Administrative Expenses

General and administrative expenses were $39.6 million and $8.8 million for the years ended December 31, 2018 and 2017, respectively. The increase in general and administrative expenses of $30.8 million resulted primarily from an increase in share-based compensation expense of $16.2 million, including $7.5 million in modification costs relating to senior management severance packages and $8.7 million in new grants to executive management and employees. The remaining increase resulted primarily from a $5.3 million increase in payroll and recruitment costs due to headcount and related costs to support our growing business, an increase of $4.4 million in commercial services, an increase of $3.2 million in consultant and directors' fees and an increase of $1.4 million to support the growth of our U.S. operations. Total non-cash general and administrative share-based compensation expense was $18.6 million and $2.4 million for the years ended December 31, 2018 and 2017, respectively.

Finance (Income) Expenses, Net

Finance (income) expenses, net was ($1.6 million) and $31,000 for the years ended December 31, 2018 and 2017, respectively. The increase of $1.7 million in finance income was primarily due to increased interest earned on our cash balances.

Comparison of the Years Ended December 31, 2017 and 2016

The following table sets forth our results of operations for the years ended December 31, 2017 and 2016.

	Year Ended December 31,		
	2017	2016	Change
Revenues	$ 8,158	$ 17,530	$ (9,372)
Cost of revenue	600	28	572
Gross profit	7,558	17,502	(9,944)
Operating expenses:			
Research and development	18,697	10,287	8,410
General and administrative	8,811	6,417	2,394
Total operating expenses	27,508	16,704	10,804
Operating (loss) income	(19,950)	798	(20,748)
Finance (income) expenses, net	31	2,739	(2,708)
Loss before income taxes	(19,981)	(1,941)	(18,040)
Income tax expense	19	—	19
Net loss	$ (20,000)	$ (1,941)	$ (18,059)

Revenues

Our total revenues decreased by $9.3 million to $8.2 million in the year ended December 31, 2017 from $17.5 million in the year ended December 31, 2016. This decrease is mainly due to the difference in proceeds of $7.5 million and $17.5 million received from Allergan upon the achievement of certain milestones under the Allergan Agreement in each of the years ended December 31, 2017 and 2016, respectively.

Research and Development Expenses

Research and development expenses increased by $8.4 million to $18.7 million in the year ended December 31, 2017 from $10.3 million in the year ended December 31, 2016. The increase was attributable mainly to an increase in direct costs associated with the UGN-101 Phase 3 clinical trial of approximately $3.1 million, an increase of approximately $2.8 million of share-based compensation expenses related to an increase in personnel and the grant date fair value of ordinary shares, and an increase of approximately $2.5 million in headcount, consulting and related costs to support increased clinical trial activities. Total non-cash research and development share-based compensation expense for the year ended December 31, 2017 was $3.9 million.

General and Administrative Expenses

General and administrative expenses increased by approximately $2.4 million to $8.8 million in the year ended December 31, 2017 from $6.4 million in the year ended December 31, 2016. The increase in general and administrative expenses resulted primarily from an increase in share-based compensation expense of approximately $1.6 million related to an increase in personnel and the grant date fair value of ordinary shares, an increase of $1.3 million in payroll and recruitment costs due to headcount and related costs to support our growing business, an increase of $0.9 million in professional service expenses, commercial services, director and officer insurance premiums, and other costs associated with being a public company, and an increase of $0.3 million in rent and office maintenance related to our new office in New York. These increases were offset by $1.7 million of initial public offering, or IPO, expenses in the statement of operations in 2016. Total non-cash general and administrative share-based compensation expense for the year ended December 31, 2017 was $2.4 million.

Finance Expenses, Net

Finance expenses, net were $31,000 and $2.7 million for the years ended December 31, 2017 and 2016, respectively. The decrease in finance expenses, net, was primarily due to the recording of the increase in fair value of the Preferred A-1 warrants to the income statement in 2016. The warrants converted to Preferred A-1 shares upon the closing of the IPO in May 2017. There was minimal change in the fair value of the warrants in 2017 prior to conversion.

Liquidity and Capital Resources

As of December 31, 2018, we had $101.3 million in cash, cash equivalents, and marketable securities. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation, and is held primarily in U. S. dollars. We believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operating and capital expenditure requirements for at least the next 12 months.

Through December 31, 2018, we funded our operations primarily through public equity offerings, private placements of equity securities and through the upfront payment received under the Allergan Agreement. In May 2017, we raised $60.8 million, net of issuance costs and underwriting discounts and commissions, in our IPO on the Nasdaq Global Market. In August 2017, we received $7.5 million from Allergan upon the achievement of a milestone under the Allergan Agreement. In addition, during the year ended December 31, 2016, we recorded $1.7 million in general and administrative expenses related to IPO costs, in accordance with SEC staff Bulletin Topic 5A.

In January 2018, we completed an underwritten public offering of 1,682,926 of our ordinary shares, including 219,512 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $41.00 per share. The net proceeds to us from the offering were approximately $64.0 million, after deducting the underwriting discounts and commissions and payment of other offering expenses.

In January 2019, we completed an underwritten public offering of 4,207,317 of our ordinary shares, including 548,780 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $41.00 per share. The net proceeds to us from the offering were approximately $161.8 million, after deducting the underwriting discounts and commissions and payment of other offering expenses.

We have incurred losses since our inception and negative cash flows from our operations, and as of December 31, 2018 we had an accumulated deficit of $122.9 million. We anticipate that we will continue to incur losses for at least the next several years. Our primary uses of capital are, and we expect will continue to be, research and development expenses, including third-party clinical research and development services, laboratory and related supplies, clinical costs, including manufacturing costs, legal and other regulatory expenses and general and administrative costs.

Because UGN-101 and UGN-102 are still in clinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of product candidates or whether, or when, we may achieve profitability. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements.

Cash Flows

The following table sets forth the significant sources and uses of cash for the periods set forth below:

	Year Ended December 31,		
	2018	2017	2016
		(in thousands)	
Net cash (used in) provided by:			
Operating activities	$ (37,334)	$ (9,568)	$ 4,189
Investing activities	35,287	(36,277)	(719)
Financing activities	66,421	61,585	(9)
Net change in cash and cash equivalents	$ 64,374	$ 15,740	$ 3,461

Operating Activities

Net cash used in operating activities was $37.3 million during the year ended December 31, 2018, compared to $9.6 million during the year ended December 31, 2017. The $27.7 million increase was attributable primarily to the increase of $55.7 million in the net loss for the year, partly offset by a $24.3 million increase in share-based compensation expense and a net increase in operating assets and liabilities of $3.6 million.

Net cash used in operating activities was $9.6 million during the year ended December 31, 2017, compared to $4.2 million provided by operating activities during the year ended December 31, 2016. The increase in cash used in operating activities was attributable primarily to the receipt of the different milestone payments from Allergan of $7.5 million in 2017 and $17.5 million in 2016 and an increase in expenditures related to the UGN-101 Phase 3 clinical trial of approximately $3.1 million, as well as an increase in personnel related costs to support our growing business and service provider costs related to becoming a public company. These increases were offset by the recording of $1.7 million of IPO expenses in 2016.

Investing Activities

Net cash provided by investing activities was $35.3 million during the year ended December 31, 2018, compared to $36.3 million used in investing activities during the year ended December 31, 2017. The increase of $71.6 million is primarily related to our investment in highly liquid, short term money market funds.

Net cash used in investing activities was $36.3 million during the year ended December 31, 2017, compared to $0.7 million during the year ended December 31, 2016. The increase of $35.6 million is primarily related to our investment in highly liquid, short term money market funds.

Financing Activities

Net cash provided by financing activities was $66.4 million during the year ended December 31, 2018, compared to $61.6 million during the year ended December 31, 2017. The increase is primarily related to the increased net proceeds received from our January 2018 underwritten offering as compared to the net proceeds received from our IPO in May 2017.

Net cash provided by financing activities was $61.6 million during the year ended December 31, 2017, compared to cash used in financing activities of $0.1 million during the year ended December 31, 2016. The difference is primarily related to the net proceeds received from our IPO in May 2017.

Funding Requirements

Our present and future funding requirements will depend on many factors, including, among other things:

- the progress, timing and completion of clinical trials for UGN-101 and UGN-102;
- preclinical studies and clinical trials for UGN-201 or any of our other product candidates;

- the costs related to obtaining regulatory approval for UGN-101, UGN-102 and UGN-201 and any of our other product candidates, and any delays we may encounter as a result of regulatory requirements or adverse clinical trial results with respect to any of these product candidates;
- selling, marketing and patent-related activities undertaken in connection with the commercialization of UGN-101 and UGN-102 and any of our other product candidates, and costs involved in the development of an effective sales and marketing organization;
- the costs involved in filing and prosecuting patent applications and obtaining, maintaining and enforcing patents or defending against claims or infringements raised by third parties, and license royalties or other amounts we may be required to pay to obtain rights to third party intellectual property rights;
- potential new product candidates we identify and attempt to develop; and
- revenues we may derive either directly or in the form of royalty payments from future sales of UGN-101, UGN-102, UGN-201, BotuGel and any other product candidates.

Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

Until such time, if ever, as we can generate substantial product revenue, we may finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. 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 any additional securities may include liquidation or other preferences that adversely affect your rights as a 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 dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish 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 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.

For more information as to the risks associated with our future funding needs, see "Item 1.A – Risk Factors." 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."

Contractual Obligations and Commitments

The obligations detailed below do not include grants received from the IIA pursuant to which we will owe royalties or reimbursement upon commercialization of our product candidates. As of December 31, 2018, the maximum royalty amount payable by us under these funding arrangements is $2.1 million, excluding 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. 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.

The following summarizes our significant contractual obligations as of December 31, 2018:

	Payments Due By Period				
	Less Than 1 Year	1 To 3 Years	3 To 5 Years	Greater Than 5 Years	Total
			(in thousands)		
Operating lease obligations [1]	$ 1,136	$ 1,927	$ 868	$ 58	$ 3,989

(1) Operating lease obligations consist of payments pursuant to lease agreements for our Israeli offices and laboratory facility and our New York offices. In November 2014, we entered into a lease agreement for our Israeli offices effective from February 1, 2015 for a period of three years, with an option to extend the lease agreement by an additional three years. In April 2016, we signed an addendum to the November 2014 lease agreement in order to increase the office space rented and extend the rental period. In November 2017, we signed an additional addendum to the November 2014 lease agreement in order to increase the office space rented. The lease agreement is effective until September 2019.

In September 2017, Urogen Pharma, Inc. entered into a new lease agreement for its current New York office for a period of approximately 41 months, which period commenced in October 2017. The new lease agreement will terminate on February 1, 2021, unless earlier terminated in accordance with its terms.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the dates of the balance sheets and the reported amounts of revenue and expenses during the reporting periods. In accordance with GAAP, we base our estimates on historical experience and on various other assumptions that we believe are reasonable under the circumstances at the time such estimates are made. Actual results may differ materially from our estimates and judgments under different assumptions or conditions. We periodically review our estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, are reflected in our financial statements prospectively from the date of the change in estimate.

We define our critical accounting policies as those accounting principles generally accepted in the United States that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. While our significant accounting policies are more fully described in Note 3 to our financial statements appearing elsewhere in this Annual Report, we believe the following are the critical accounting policies used in the preparation of our financial statements that require significant estimates and judgments.

Revenues

We derive virtually all of our revenues from a license and supply agreement with Allergan. Under the agreement, we grant Allergan an exclusive license to develop, commercialize, and otherwise exploit products that contain RTGel and agrees to supply Allergan with pre-clinical and clinical quantities of the RTGel product, also referred to as the RTGel vials. The license agreement contains up-front license fees, future supply fees, development, regulatory, and sales-based milestone payments, and sales-based royalty payments.

We determined that Allergan is our customer and the license and supply agreements are in scope of accounting standards codification ("ASC") 606, which we adopted as of January 1, 2018. We adopted ASC 606 under the modified retrospective method, which did not have a material impact on the Consolidated Statements of Operations. Previously, we analyzed revenues under ASC 605, which states that revenue is recognized only when all of the following conditions have been met: (i) there is persuasive evidence of an arrangement; (ii) delivery has occurred: (iii) the fee is fixed or determinable: and (iv) collectability of the fee is reasonably assured. The adoption of ASC 606 did not have a material impact on the timing and manner of recognized revenues.

Under ASC 606, in determining the appropriate amount of revenue to be recognized as it fulfills its obligations under the agreements with Allergan, we performed the following steps:

1) Identification of the contract;
2) Determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract;
3) Measurement of the transaction price, including the constraint on variable consideration;
4) Allocation of the transaction price to the performance obligations;
5) Recognition of revenue when or as the Company satisfies each performance obligation.

The license agreement contains two performance obligations: (a) the license component and (b) Allergan's right to require supply services of RTGel vials from us. The license component has standalone value (and therefore is accounted for separately from the supply services) since Allergan can use the license for its intended purposes without the Company's supply services.

In an arrangement with multiple goods and services, a good or service that is promised to a customer shall be considered a separate performance obligation if all of the following criteria are met:

1) The customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct); and
2) The entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract).

Allocating the Consideration in the Arrangement

Since the license to our intellectual property was determined to be functional and distinct from the other performance obligations identified in the arrangement, we recognized revenues from non-refundable, up-front fees allocated to the license when the license was transferred to Allergan and Allergan was able to use and benefit from the license. During the year ended December 31, 2016, we received consideration in an amount of $17.5 million for both the license of the intellectual property as well as Allergan's right to future supply services (which would be provided in consideration for future payments to us according to the pricing stipulated in the supply agreement). We determined that the pricing of the supply services represented their standalone selling price. Accordingly, we allocated the entire upfront fee of $17.5 million to the license performance obligation.

Development and Regulatory Milestone Payments

At the inception of an arrangement that includes development milestone payments, we evaluate whether the development milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated development milestone value is included in the transaction price. Development milestone payments that are not within our control or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The milestones are allocated entirely to the license performance obligation, as (1) the terms of milestone and royalty payments relate specifically to the license and (2) allocating milestones and royalties to the license performance obligation is consistent with the overall allocation objective, because management's estimate of the supply fee approximates the standalone selling price for RTGel vials and management's estimate of milestones and royalties approximates the standalone selling price of the license. During the year ended December 31, 2017, we recognized revenue of $7.5 million related to a development milestone payment resulting from Allergan's submission of an IND application for our RTGel in combination with Allergan's BOTOX for the treatment of overactive bladder to the U.S. FDA.

Royalties Based on Allergan's Revenue

We are also entitled to royalties based on Allergan's revenue from its product, however, these amounts would only be recognized when the conditions are met.

Supply of RTGel

We recognize revenue related to the supply of RTGel at a point in time, upon delivery to Allergan. During the years ended December 31, 2018 and 2017, we recognized $1.1 million and $0.7 million of revenue related to RTGel vials supplied to Allergan, respectively. There were no material RTGel vial sales during the year ended December 31, 2016.

Shipping and handling costs associated with supply of RTGel vials are accounted for as a fulfillment cost and are in included in cost of revenues.

See Note 6 appearing elsewhere in this Annual Report for further discussion regarding revenue recognized during the year ended December 31, 2018.

Research and Development

Research and development costs are expensed as incurred and consist primarily of the cost of salaries, share-based compensation expenses, payroll taxes and other employee benefits, subcontractors and materials used for research and development activities, including preclinical studies, clinical trials, manufacturing costs and professional services. The costs of services performed by others in connection with the research and development activities of an entity, including research and development conducted by others on behalf of the entity, shall be included in research and development costs. Grants received from the Israel Innovation Authority, f/k/a the Office of the Chief Scientist of Israel's Ministry of Industry, Trade and Labor (the "IIA") are recognized when the grant becomes receivable, provided there is reasonable assurance that we will comply with the conditions attached to the grant and there is reasonable assurance the grant will be received. The grant is deducted from the research and development expenses as the applicable costs are incurred. In the year ended December 31, 2016, research and development expenses increased by $0.2 million as a result of our decision not to pursue one of its research programs that had been approved as a result of other financing opportunities. For the year ended December 31, 2016 an amount of $0.1 million was received from Allergan, in connection with the pre-clinical collaboration agreement signed in August 2015 and deducted from the research and development expenses.

The costs of intangibles that are purchased from others for a particular research and development project and that have no alternative future uses (in other research and development projects or otherwise) and therefore no separate economic values are research and development costs at the time the costs are incurred.

Share-Based Compensation

We account for employees' and directors' share-based payment awards classified as equity awards using the grant-date fair value method. The fair value of share-based payment transactions is recognized as an expense over the requisite service period. As of December 31, 2016, we have early adopted the policy to account for forfeitures as they occur according to the FASB's Accounting Standards Update (ASU) 2016-09, Improvements to Employee Share-Based Payment Accounting. The adjustment for the beginning of the period was not material and therefore it was not reflected in the consolidated statements of changes in shareholders' equity.

We elected to recognize compensation costs for awards conditioned only on continued service that have a graded vesting schedule using the straight-line method and to value the awards based on the single-option award approach. Performance based awards are expensed over the requisite service period when the achievement of performance criteria is probable.

Equity awards granted to non-employees are re-measured at each reporting period at fair value until the commitment date had been reached which is usually the date the service is completed. The fair value of equity awards is charged to the statement of operations over the service period using the straight-line method.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements as defined under SEC rules.

Item 7A. Quantitative and Qualitative Disclosures about Market Risks

Interest Rate Fluctuation Risk

Some of the securities in which we invest have market risk in that a change in prevailing interest rates may cause the principal amount of the marketable securities to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash and cash equivalents. As of December 31, 2018, we had $101.3 million in cash and cash equivalents. We invest our cash primarily in money market accounts, but from time to time may invest in commercial paper and debt instruments of financial institutions, corporations, U.S. government-sponsored agencies and the U.S. Treasury. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our marketable securities without significantly increasing risk. We have established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity. If a 10% change in interest rates were to have occurred on December 31, 2018, this change would not have had a material effect on the fair value of our cash and cash equivalents as of that date.

Inflation Risk

Inflation generally may affect us by increasing our cost of labor and clinical trial costs. Inflation has not had a material effect on our business, financial condition or results of operations during the years ended December 31, 2018, 2017 or 2016.

Foreign Currency Exchange Risk

The U.S. dollar is our functional and reporting currency. However, a significant portion of our operating expenses are incurred in NIS. As a result, we are exposed to the risk 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, although the dollar appreciated against the NIS in 2018 by 8.1%, the level of devaluation of the dollar against the NIS in 2017 was 9.8%. If the dollar cost of our operations in Israel increases, our dollar-measured results of operations will be adversely affected. Our operations also could be adversely affected if we are unable to effectively hedge against currency fluctuations in the future.

We do not currently engage in currency hedging activities in order to reduce this currency exposure, but we may begin to do so in the future. Instruments that may be used to hedge future risks may include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that we will be fully protected against material foreign currency fluctuations.

Item 8. Financial Statements and Supplementary Data

UroGen Pharma, Ltd.

Index to financial statements

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of UroGen Pharma, Ltd.

Opinion on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of UroGen Pharma Ltd. and its subsidiary (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of operations, changes in shareholders equity and cash flows for each of the three years in the period ended December 31, 2018, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinion

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying *Management's Annual Report on Internal Control over Financial Reporting.* Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Tel Aviv, Israel
February 28, 2019

/s/Kesselman & Kesselman
Certified Public Accountants (Isr.)
A member of PricewaterhouseCoopers International Limited

We have served as the Company's auditor since 2010.

UROGEN PHARMA, LTD.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share amounts)

	December 31,	
	2018	2017
Assets		
CURRENT ASSETS:		
Cash and cash equivalents	$ 101,318	$ 36,999
Short-term investments	—	36,001
Restricted deposit	253	198
Inventory	—	316
Prepaid expenses and other current assets	672	958
TOTAL CURRENT ASSETS	102,243	74,472
NON-CURRENT ASSETS		
Property and equipment, net	948	805
Restricted deposit	51	29
Other non-current assets	317	244
TOTAL ASSETS	$ 103,559	$ 75,550
Liabilities and Shareholder's equity		
CURRENT LIABILITIES:		
Accounts payable and accrued expenses	$ 8,540	$ 4,435
Employee related accrued expenses	4,925	1,950
Deferred revenues	—	650
TOTAL CURRENT LIABILITIES	13,465	7,035
TOTAL LIABILITIES	13,465	7,035
COMMITMENTS AND CONTINGENCIES (Note 12)		
SHAREHOLDERS' EQUITY:		
Ordinary shares, NIS 0.01 par value; 100,000,000 shares authorized at December 31, 2018 and 2017; 16,214,883 and 13,751,390 shares issued and outstanding as of December 31, 2018 and 2017, respectively	44	37
Additional paid-in capital	212,921	115,692
Accumulated deficit	(122,871)	(47,214)
TOTAL SHAREHOLDERS' EQUITY	90,094	68,515
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$ 103,559	$ 75,550

The accompanying notes are an integral part of these consolidated financial statements.

UROGEN PHARMA, LTD.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2018	2017	2016
REVENUES	$ 1,128	$ 8,158	$ 17,530
COST OF REVENUES	1,803	600	28
GROSS (LOSS) PROFIT	(675)	7,558	17,502
OPERATING EXPENSES:			
RESEARCH AND DEVELOPMENT EXPENSES, NET	36,934	18,697	10,287
GENERAL AND ADMINISTRATIVE EXPENSES	39,571	8,811	6,417
OPERATING (LOSS) INCOME	(77,180)	(19,950)	798
FINANCE (INCOME) EXPENSES, NET	(1,648)	31	2,739
LOSS BEFORE INCOME TAXES	(75,532)	(19,981)	(1,941)
INCOME TAX EXPENSE	125	19	—
NET LOSS	$ (75,657)	$ (20,000)	$ (1,941)
LOSS PER ORDINARY SHARE BASIC AND DILUTED	$ (4.80)	$ (2.14)	$ (1.91)
WEIGHTED AVERAGE NUMBER OF SHARES OUTSTANDING USED IN COMPUTATION OF BASIC AND DILUTED LOSS PER ORDINARY SHARE	15,754,193	9,716,790	2,305,503

The accompanying notes are an integral part of these consolidated financial statements.

UROGEN PHARMA, LTD.
CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
(in thousands, except share amounts)

	Ordinary Shares		Preferred Shares		Additional paid-in capital	Accumulated Deficit	Total
	Number of Shares	Amount	Number of Shares	Amount		Amounts	
BALANCE AS OF JANUARY 1, 2016	2,300,959	$ 6	5,193,427	$ 13	$ 41,535	$ (25,273)	$ 16,281
CHANGES DURING 2016							
Exercise of options into ordinary shares	4,784	*			*		*
Share-based compensation					1,967		1,967
Net loss						(1,941)	(1,941)
BALANCE AS OF JANUARY 1, 2017	2,305,743	$ 6	5,193,427	$ 13	$ 43,502	$ (27,214)	$ 16,307
CHANGES DURING 2017							
Exercise of options into ordinary shares	743,806	2			402		404
Share-based compensation					6,300		6,300
Exercise of warrants into preferred shares			364,036	1	4,731		4,732
Exercise of preferred shares into ordinary shares	5,557,463	14	(5,557,463)	(14)			—
IPO, net of issuance expense and underwriters discounts of $6,105	5,144,378	15			60,757		60,772
Net loss						(20,000)	(20,000)
BALANCE AS OF JANUARY 1, 2018	13,751,390	$ 37	—	$ —	$ 115,692	$ (47,214)	$ 68,515
CHANGES DURING 2018							
Exercise of options into ordinary shares	780,567	2			2,399		2,401
Share-based compensation					30,642		30,642
Issuance of ordinary shares in public offering, net of issuance expenses	1,682,926	5			64,188		64,193
Net loss						(75,657)	(75,657)
BALANCE AS OF DECEMBER 31, 2018	16,214,883	$ 44	—	$ —	$ 212,921	$ (122,871)	$ 90,094

The accompanying notes are an integral part of these consolidated financial statements.

UROGEN PHARMA, LTD.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2018	2017	2016
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (75,657)	$ (20,000)	$ (1,941)
Adjustment to reconcile net loss to net cash from operating activities:			
Depreciation and amortization	417	207	213
Stock-based compensation	30,642	6,300	1,967
Fair value adjustment of warrants for preferred shares	—	168	2,740
Realized loss on sale of short-term investment	100	—	—
Changes in operating assets and liabilities:			
Decrease (increase) in inventory	316	(211)	(105)
Decrease (increase) in accounts receivable	—	83	(83)
Decrease (increase) in prepaid expenses and other current assets	318	(562)	739
Increase in accounts payable and accrued expenses	4,205	2,534	481
(Decrease) increase in deferred revenues	(650)	650	—
Increase in employee related accrued expenses	2,975	1,263	178
Net cash (used in) provided by operating activities	(37,334)	(9,568)	4,189
CASH FLOWS FROM INVESTING ACTIVITIES:			
Short-term investments	35,901	(36,001)	—
Change in restricted deposit	(54)	(5)	(24)
Purchase of property and equipment	(560)	(271)	(695)
Net cash provided by (used in) investing activities	35,287	(36,277)	(719)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from exercise of options into ordinary shares	2,401	404	—
Proceeds from exercise of warrants for preferred shares	—	382	570
Payment of deferred equity offering cost	—	—	(579)
Issuance of ordinary shares, net of issuance expenses	64,235	60,841	—
Issuance cost for secondary offering	(215)	(42)	—
Net cash provided by (used in) financing activities	66,421	61,585	(9)
INCREASE IN CASH AND CASH EQUIVALENTS	64,374	15,740	3,461
CASH, CASH EQUIVALENTS AND RESTRICED CASH AT BEGINNING OF THE YEAR	37,197	21,457	17,996
CASH, CASH EQUIVALENTS AND RESTRICTED CASH AT END OF THE YEAR	$ 101,571	$ 37,197	$ 21,457
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING ACTIVITIES:			
Non-cash issuance cost	$ 102	$ 202	$ 181
Exercise of warrants to preferred shares	$ —	$ 4,732	$ —

The accompanying notes are an integral part of these consolidated financial statements.

NOTE 1-BUSINESS AND NATURE OF OPERATIONS

Nature of Operations

UroGen Pharma Ltd. is an Israeli company incorporated in April 2004 ("UPL").

UroGen Pharma Inc., a subsidiary of UPL, was incorporated in Delaware in October 2015 and began operating in February 2016 ("UPI").

UPL and UPI (together the "Company") is a clinical stage biopharmaceutical company focused on developing novel therapies designed to change the standard of care for urological pathologies.

As of the date of issuance of the consolidated financial statements, the Company has the ability to fund its planned operations for at least the next 12 months. However, the Company's product candidates may never achieve commercialization and it will continue to incur losses for the foreseeable future. Therefore, in order to fund the Company's research and development expenses, general and administrative expenses and capital expenditures until such time that the Company can generate substantial revenues, the Company may need to raise additional funds.

NOTE 2-BASIS OF PRESENTATION AND MANAGEMENT PLANS

The Company has not generated any revenue from the sale of products since its inception. The Company has experienced net losses since its inception and has an accumulated deficit of $122.9 million and $47.2 million as of December 31, 2018 and 2017, respectively. The Company expects to incur losses and have negative net cash flows from operating activities as it expands its portfolio and engages in further research and development activities, particularly conducting preclinical studies and clinical trials.

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States.

The success of the Company depends on its ability to develop its technologies to the point of U.S. Food and Drug Administration ("FDA") approval and subsequent revenue generation or through the sale, merger, or other transfer of all or substantially all of the Company's assets and, accordingly, to raise enough capital to finance these developmental efforts. In the future, management will need to raise additional capital to finance the continued operating and capital requirements of the Company. Any amounts raised will be used to further develop the Company's technologies, acquire additional product licenses and for other working capital purposes. There can be no assurances that the Company will be able to secure such additional financing, or if available, that it will be sufficient to meet its needs. If the Company cannot obtain adequate working capital, it will be forced to reevaluate its planned business operations.

NOTE 3-SIGNIFICANT ACCOUNTING POLICIES AND SUPPLEMENTAL FINANCIAL INFORMATION

Principles of Consolidation

The Company's consolidated financial statements include the accounts of its subsidiary, UPI. Intercompany balances and transactions have been eliminated during consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results may differ from those estimates. As applicable to these consolidated financial statements, the most significant estimates and assumptions relate to the fair value of share-based compensation, the fair value of the warrants for preferred shares and timing of revenue recognition.

Functional Currency

The U.S. dollar ("Dollar") is the currency of the primary economic environment in which the operations of the Company and subsidiary are conducted. Therefore, the functional currency of the Company is the Dollar.

Accordingly, transactions in currencies other than the Dollar are measured and recorded in the functional currency using the exchange rate in effect at the date of the transaction. At the balance sheet date, monetary assets and liabilities that are denominated in currencies other than the Dollar are measured using the official exchange rate at the balance sheet date. The effects of foreign currency re-measurements are recorded in the consolidated statements of operations as "financial (income) expenses."

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less when purchased to be cash equivalents. Cash and cash equivalents consist primarily of money market funds and bank money market accounts and are stated at cost, which approximates fair value.

Short-Term Investments

The Company from time to time invests in short-term investments that consist of mutual and bond funds. While these investments are considered highly liquid and available to fund current operations, there is more than an insignificant risk of change in value due to interest rate, quoted price, or penalty on withdrawal and are therefore classified as short-term investments.

We classify our short-term investments as available-for-sale in accordance with FASB ASC Topic 320, "Investments — Debt and Equity Securities". Available-for-sale securities are carried at fair value with unrealized gains and losses reported in other comprehensive income/loss within shareholders' equity. The change in value for the year ended December 31, 2018 was $0.1 million.

Short-term investments are valued using models or other valuation methodologies that use Level 2 inputs. These models are primarily industry-standard models that consider various assumptions, including time value, yield curve, volatility factors, default rates, current market and contractual prices for the underlying financial instruments, as well as other relevant economic measures. Substantially all of these assumptions are observable in the marketplace, can be derived from observable data or are supported by observable levels at which transactions are executed in the marketplace.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to significant concentrations of credit risk, consist primarily of cash and cash equivalents and marketable securities. The primary objectives for the Company's investment portfolio are the preservation of capital and the maintenance of liquidity. The Company does not enter into any investment transaction for trading or speculative purposes.

The Company's investment policy limits investments to certain types of instruments such as certificates of deposit, money market instruments, obligations issued by the U.S. government and U.S. government agencies as well as corporate debt securities, and places restrictions on maturities and concentration by type and issuer. The Company maintains cash balances in excess of amounts insured by the FDIC and concentrated within a limited number of financial institutions. The accounts are monitored by management to mitigate the risk.

Financial instruments that potentially subject the Company to concentration of credit risk consist principally of cash and cash equivalents and short-term investments. The Company deposits cash and cash equivalents with highly rated financial institutions, and, as a matter of policy, limits the amounts of credit exposure to any single financial institution. The Company has not experienced any credit losses in these accounts and does not believe it is exposed to significant credit risk on these instruments.

Income Taxes

The Company provides for income taxes based on pretax income, if any, and applicable tax rates available in the various jurisdictions in which we operate. Deferred taxes are computed using the asset and liability method. Under the asset and liability method, deferred income tax assets and liabilities are determined based on the differences between the financial reporting and tax bases of assets and liabilities and are measured using the currently enacted tax rates and laws. A valuation allowance is recognized to the extent that it is more likely than not that the deferred taxes will not be realized in the foreseeable future.

The Company follows a two-step approach in recognizing and measuring uncertain tax positions. The first step is to evaluate the tax position for recognition by determining if the available evidence indicates that it is more likely than not that the position will be sustained upon examination by the taxing authorities based on the technical merits of the position. If this threshold is met, the second step is to measure the tax benefit as the largest amount that is more likely than not of being realized upon ultimate settlement. As of December 31, 2018 and 2017, the Company had not accrued a provision for uncertain tax positions. See Note 10 for further discussion related to income taxes.

Property and Equipment

Property and equipment is recorded at historical cost, net of accumulated depreciation, amortization and, if applicable, impairment charges. We review our property and equipment assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable.

Annual rates of depreciation are as follows:

	%
Computers and software	33
Laboratory equipment	15-30
Furniture	6-15
Manufacturing equipment	50

Leasehold improvements are amortized on a straight-line basis over the shorter of their estimated useful lives or lease terms. See Note 5 for further discussion regarding property and equipment.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following as of December 31, 2018 and 2017, respectively (in thousands):

	December 31, 2018	December 31, 2017
Accounts payable	$ 4,272	$ 2,839
Accrued clinical expenses	673	384
Accrued research and development costs	780	233
Accrued general and administrative expenses	1,029	239
Accrued other expense	1,786	740
Total accrued expenses and other current liabilities	$ 8,540	$ 4,435

Revenues

The Company derives virtually all of its revenues from its license and supply agreement with Allergan. Under the agreement, the Company grants Allergan an exclusive license to develop, commercialize, and otherwise exploit products that contain RTGel and agrees to supply Allergan with pre-clinical and clinical quantities of the RTGel product, also referred to as the RTGel vials. The license agreement contains up-front license fees, future supply fees, development, regulatory, and sales-based milestone payments, and sales-based royalty payments.

The Company determined that Allergan is its customer and the license and supply agreements are in scope of ASC 606, which was adopted as of January 1, 2018. The Company adopted ASC 606 under the modified retrospective method, which did not have a material impact on the Consolidated Statements of Operations. Previously, we analyzed revenues under ASC 605, which states that revenue is recognized only when all of the following conditions have been met: (i) there is persuasive evidence of an arrangement; (ii) delivery has occurred: (iii) the fee is fixed or determinable: and (iv) collectability of the fee is reasonably assured. The adoption of ASC 606 did not have a material impact on the timing and manner of recognized revenues.

Under ASC 606,in determining the appropriate amount of revenue to be recognized as it fulfills its obligations under the agreements with Allergan, the Company performs the following steps:

1) Identification of the contract;
2) Determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract;
3) Measurement of the transaction price, including the constraint on variable consideration;
4) Allocation of the transaction price to the performance obligations;
5) Recognition of revenue when or as the Company satisfies each performance obligation.

The license agreement contains two performance obligations: (a) the license component and (b) Allergan's right to require supply services of RTGel vials from the Company. The license component has standalone value (and therefore is accounted for separately from the supply services) since Allergan can use the license for its intended purposes without the Company's supply services.

In an arrangement with multiple goods and services, a good or service that is promised to a customer shall be considered a separate performance obligation if all of the following criteria are met:

1) The customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct); and
2) The entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract).

Allocating the Consideration in the Arrangement

Since the license to the Company's intellectual property was determined to be functional and distinct from the other performance obligations identified in the arrangement, the Company recognized revenues from non-refundable, up-front fees allocated to the license when the license was transferred to Allergan and Allergan was able to use and benefit from the license. During the year ended December 31, 2016, the Company received consideration in an amount of $17.5 million for both the license of the intellectual property as well as Allergan's right to future supply services (which would be provided in consideration for future payments to the Company according to the pricing stipulated in the supply agreement). The Company determined that the pricing of the supply services represented their standalone selling price. Accordingly, the Company allocated the entire upfront fee of $17.5 million to the license performance obligation.

Development and Regulatory Milestone Payments

At the inception of an arrangement that includes development milestone payments, the Company evaluates whether the development milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated development milestone value is included in the transaction price. Development milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The milestones are allocated entirely to the license performance obligation, as (1) the terms of milestone and royalty payments relate specifically to the license and (2) allocating milestones and royalties to the license performance obligation is consistent with the overall allocation objective, because management's estimate of the supply fee approximates the standalone selling price for RTGel vials and management's estimate of milestones and royalties approximates the standalone selling price of the license. During the year ended December 31, 2017, the Company recognized revenue of $7.5 million related to a development milestone payment resulting from Allergan's submission of an IND application for the Company's RTGel in combination with Allergan's BOTOX for the treatment of overactive bladder to the U.S. FDA.

Royalties Based on Allergan's Revenue

We arealso entitled to royalties based on Allergan's revenue from its product, however, these amounts would only be recognized when the conditions are met.

Supply of RTGel to Allergan

The Company recognizes revenue related to supply of RTGel at a point in time, upon delivery to Allergan. During the years ended December 31, 2018 and 2017, the Company recognized $1.1 million and $0.7 million of revenue related to RTGel vials supplied to Allergan, respectively. There were no material RTGel vial sales during the year ended December 31, 2016.

Shipping and handling costs associated with supply of RTGel vials are accounted for as a fulfillment cost and are in included in cost of revenues.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in executive, finance, accounting, legal, investor relations, facilities, business development and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to corporate matters, insurance, public company expenses relating to maintaining compliance with Nasdaq listing rules and SEC requirements, insurance and investor relations costs, and fees for accounting and consulting services. General and administrative costs are expensed as incurred, and the Company accrues for services provided by third parties related to the above expenses by monitoring the status of services provided and receiving estimates from its service providers, and adjusting its accruals as actual costs become known.

Research and Development

Research and development costs are expensed as incurred and consist primarily of the cost of salaries, share-based compensation expenses, payroll taxes and other employee benefits, subcontractors and materials used for research and development activities, including preclinical studies, clinical trials, manufacturing costs and professional services. The costs of services performed by others in connection with the research and development activities of an entity, including research and development conducted by others on behalf of the entity, shall be included in research and development costs and expensed as the contracted work is performed. The Company accrues for costs incurred as the services are being provided by monitoring the status of the trial or project and the invoices received from its external service providers. The Company adjusts its accrual as actual costs become known. Where contingent milestone payments are due to third parties under research and development arrangements or license agreements, the milestone payment obligations are expensed when the milestone results are achieved.

Grants received from the Israel Innovation Authority, f/k/a the Office of the Chief Scientist of Israel's Ministry of Industry, Trade and Labor (the "IIA") are recognized when the grant becomes receivable, provided there is reasonable assurance that the Company will comply with the conditions attached to the grant and there is reasonable assurance the grant will be received. The grant is deducted from the research and development expenses as the applicable costs are incurred. In the year ended December 31, 2016, the Company had an increase of $0.2 million to its research and development expenses as a result of its decision not to pursue one of its research programs that had been approved as a result of other financing opportunities. For the year ended December 31, 2016 an amount of $0.1 million was received from Allergan, in connection with the pre-clinical collaboration agreement signed in August 2015 and deducted from the research and development expenses.

The costs of intangibles that are purchased from others for a particular research and development project and that have no alternative future uses (in other research and development projects or otherwise) and therefore no separate economic values are research and development costs at the time the costs are incurred.

Share-Based Compensation

Share-based compensation cost is measured at the grant date based on the fair value of the award and is recognized as expense over the required service period, which is equal to the vesting period. The fair value of stock options is determined using the Black-Scholes option-pricing model. The fair value of a restricted stock unit equaled the closing price of our ordinary shares on the grant date.

As of December 31, 2016, the Company has early adopted the policy to account for forfeitures as they occur according to the FASB's Accounting Standards Update (ASU) 2016-09, Improvements to Employee Share-Based Payment Accounting.

The Company elected to recognize compensation costs for awards conditioned only on continued service that have a graded vesting schedule using the straight-line method and to value the awards based on the single-option award approach.

Equity awards granted to non-employees are re-measured at each reporting period at fair value until the commitment date had been reached which is usually the date the service is completed. The fair value of equity awards is charged to the statement of operations over the service period using the straight-line method.

Finance (Income) Expense

	Year Ended December 31,		
	2018	2017	2016
Changes in fair value of warrants for preferred shares	$ —	$ 168	$ 2,740
Interest income on cash and cash equivalents	(1,872)	(125)	(1)
Realized loss on sale of short-term investment	100	—	—
Other finance expenses	124	(12)	—
Total finance (income) expense	$ (1,648)	$ 31	$ 2,739

Net Loss per Common Share

Basic net loss per share is computed by dividing the net loss attributable to common shareholders by the weighted-average number of common shares outstanding. Diluted net loss per share is computed similarly to basic net loss per share except that the denominator is increased to include the number of additional common shares that would have been outstanding if the potential common shares had been issued and if the additional common shares were dilutive. In addition, the net loss attributable to common shareholders is adjusted for Series A and A-1 Preferred Stock dividends for the periods in which Series A and A-1 Preferred Stock is outstanding.

For all periods presented, potentially dilutive securities are excluded from the computation of fully diluted loss per share as their effect is anti-dilutive.

The following table summarizes the calculation of basic and diluted loss per common share for the periods presented (in thousands, except share and per share amounts):

	Year Ended December 31,		
	2018	2017	2016
Basic and diluted:			
Loss attributable to equity holders of the Company	$ 75,657	$ 20,000	$ 1,941
Dividend accumulated for preferred shares during the period	$ —	$ 825	$ 2,467
Loss attributable to equity holders of the Company, after deducting dividend accumulated for preferred shares	$ 75,657	$ 20,825	$ 4,408
Weighted-average number of ordinary shares	15,754,193	9,716,790	2,305,503
Loss per ordinary share	$ 4.80	$ 2.14	$ 1.91

Recent Accounting Pronouncements

In June 2018, the FASB issued ASU 2018-07, "Compensation-Stock Compensation" (“Topic 718” or “ASU 2018-07”) to improve the usefulness of information provided to users of financial statements while reducing cost and complexity in financial reporting and provide guidance aligning the measurement and classification for share-based payments to nonemployees with the guidance for share-based payments to employees. Under the guidance, the measurement of equity-classified nonemployee awards will be fixed at the grant date. This standard is effective for fiscal years beginning after December 15, 2018, and interim periods within those annual periods. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. The adoption of ASU 2018-07 will not have an impact on the Company’s Consolidated Statements of Operations.

In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-02, "Leases" ("Topic 842"). Topic 842 supersedes existing guidance in Leases ("Topic 840"). Topic 842 was subsequently amended by ASU No. 2018-01, Land Easement Practical Expedient for Transition to Topic 842; ASU No. 2018-10, Codification Improvements to Topic 842, Leases; and ASU No. 2018-11, Targeted Improvements. Topic 842 requires lessees to recognize right-of-use ("ROU") assets and lease liabilities on the balance sheet for leases with lease terms greater than twelve months, including those classified as operating leases. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the income statement. The lease liability will be measured at the present value of the unpaid lease payments and the ROU asset will be derived from the calculation of the lease liability. Lease payments will include fixed and in-substance fixed payments, variable payments based on an index or rate, exercise price of purchase options that are reasonably certain to be exercised, termination penalties, and probable amounts the lessee will owe under a residual value guarantee. Topic 842 also requires lessees to disclose key information about leasing arrangements. Lessor accounting will remain largely unchanged. The guidance is effective for annual periods beginning after December 15, 2018, with early adoption permitted.

The Company will apply the modified retrospective transition method and elect the transition option to use the effective date of January 1, 2019 as the date of initial application ("Transition Date"). Consequently, financial information will not be updated, and the disclosures required under the Topic 842 will not be provided for dates and periods before January 1, 2019.

Topic 842 provides a number of optional practical expedients in transition. The Company expects to elect the 'package of practical expedients', which permits not to reassess under Topic 842 its prior conclusions about lease identification, lease classification, and initial direct costs. The Company does not expect to elect the use-of-hindsight or the practical expedient pertaining to land easements; the latter not being applicable to the Company. As a result, the Company will in effect, continue to account for existing leases – i.e. leases for which the commencement date is before January 1, 2019 – in accordance with Topic 840 throughout the entire lease term, including periods after the effective date, with the exception that the Company will apply the new balance sheet recognition guidance for operating leases and apply Topic 842 for remeasurements and modifications after the Transition Date.

While continuing to assess all the effects of adoption, the Company expects that Topic 842 will have a material effect on its financial statements. On adoption, the Company currently expects to recognize additional operating lease liabilities of approximately $3.5 million, with corresponding ROU asset for existing operating leases. The Company does not expect a material impact on its Consolidated Statements of Operations or its Consolidated Statements of Cash Flows.

NOTE 4-FAIR VALUE MEASUREMENTS AND INVESTMENTS IN MARKETABLE SECURITIES

The Company follows authoritative accounting guidance, which among other things, defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability.

As a basis for considering such assumptions, a three-tier fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices (unadjusted) in active markets for identical assets or liabilities;

Level 2: Inputs other than quoted prices that are observable for the asset or liability, either directly or indirectly. These include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active.

Level 3: Unobservable inputs that reflect the reporting entity's own assumptions.

The carrying amounts of the Company's other current assets, accounts payable and accrued liabilities are generally considered to be representative of their fair value because of the short-term nature of these instruments. No transfers between levels have occurred during the periods presented.

Assets and liabilities measured at fair value on a recurring basis based on Level 1, Level 2, and Level 3 fair value measurement criteria as of December 31, 2018 are as follows (in thousands):

		Fair Value Measurements Using		
	Balance as of December 31, 2018	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Money market funds[1]	$ 89,965	$ 89,965	$ —	$ —

(1) Included within cash and cash equivalents on the Company's consolidated balance sheets.

Assets and liabilities measured at fair value on a recurring basis based on Level 1, Level 2, and Level 3 fair value measurement criteria as of December 31, 2017 are as follows (in thousands):

		Fair Value Measurements Using		
	Balance as of December 31, 2017	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Money market funds[1]	$ 26,127	$ 26,127	$ —	$ —
Short-term investments	36,001	—	36,001	—

(1) Included within cash and cash equivalents on the Company's consolidated balance sheets.

The Company's investments in money market funds are valued based on publicly available quoted market prices for identical securities as of December 31, 2018 and 2017.

NOTE 5-PROPERTY AND EQUIPMENT

Property and equipment, consists of the following as of December 31, 2018 and 2017 (in thousands):

	December 31,	
	2018	2017
Laboratory equipment	$ 241	$ 223
Computer equipment and software	271	167
Furniture	395	234
Leasehold improvements	561	531
Manufacturing equipment	227	227
	1,695	1,382
Less: accumulated depreciation and amortization	(747)	(577)
Property and equipment, net	$ 948	$ 805

Depreciation and amortization expense was $0.4 million $0.2 million and $0.2 million for the years ended December 31, 2018, 2017 and 2016, respectively.

NOTE 6-ALLERGAN LICENSE AGREEMENT

In October 2016, the Company entered into the Allergan Agreement with Allergan and 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, referred to as the Licensed Products, which are approved for the treatment of adults with overactive bladder who cannot use or do not adequately respond to anticholinergics. Additionally, the Company granted Allergan a non-exclusive, worldwide license to use certain of our trademarks as required for Allergan to practice its exclusive license with respect to the Licensed Products.

Under the Allergan Agreement, Allergan is solely responsible, at its expense, for developing the Licensed Products and obtaining all regulatory approvals for Licensed Products worldwide. Allergan is also solely responsible, at its expense, for commercializing the Licensed Products worldwide after receiving the regulatory approval to do so. Allergan is required to use commercially reasonable efforts to develop and commercialize the Licensed Products for overactive bladder in certain major market countries.

The Company will supply Allergan with certain quantities of RTGel for development of Licensed Products through Phase 2 clinical trials using BOTOX together with RTGel in patients with overactive bladder, at Allergan's request and expense. Allergan has the right to reduce the next milestone payment to us if there is a material supply failure from us. Prior to completion of the first Phase 2 clinical trial, Allergan has the right to request that the Company transfers to Allergan our manufacturing process for RTGel and Allergan will assume the responsibility to manufacture RTGel and Licensed Product for its own development and commercialization activities.

Allergan paid the Company a nonrefundable upfront license fee of $17.5 million upon signing the agreement, and, in the third quarter of 2017, the Company received an additional $7.5 million milestone payment upon the submission by Allergan of an IND to the FDA for a Licensed Product. In October 2017, Allergan began a Phase 2 study of RTGel in combination with BOTOX for the treatment of overactive bladder. Additionally, during the years ended December 31, 2018 and 2017 the Company recognized revenue of $1.1 million and $0.7 million related to RTGel that was supplied to Allergan, respectively.

Further, the Company is eligible to receive additional material milestone payments of up to an aggregate of $200.0 million upon the successful completion of certain development, regulatory and commercial milestones, including $20.0 million upon initiation of a Phase 3 clinical trial for a Licensed Product for overactive bladder; $15.0 million upon initiation of a Phase 3 clinical trial for a Licensed Product for a specified second indication; $50.0 million and $25.0 million upon the first commercial sale of a Licensed Product for overactive bladder in the United States and the European Union, respectively; $25.0 million and $15.0 million upon the first commercial sale of a Licensed Product for a specified second indication in the United States and the European Union, respectively; and $50.0 million upon net sales of all Licensed Products of $500.0 million. Allergan will pay the Company a tiered royalty in the low single digits based on worldwide annual net sales of Licensed Products, subject to certain reductions for the market entry of competing products and/or loss of our patent coverage of Licensed Products. The Company is responsible for payments to any third party for certain RTGel-related third party intellectual properties.

Under the Allergan Agreement, Allergan granted the Company a non-exclusive, sublicensable, fully paid-up, perpetual, worldwide license under any improvements Allergan makes to the composition, formulation, or manufacture of RTGel for the research, development, manufacture and commercialization of any product containing RTGel and any active ingredient (other than a clostridial toxin) for all indications other than indications covered by the agreement and an exclusive, sublicensable, royalty-bearing (in low single digits), perpetual worldwide license under such improvements for use in the prevention or treatment of oncology indications.

The Company plans to continue to research, develop and commercialize other products combining RTGel with other active ingredients, except that there are certain restrictions with respect to the overactive bladder and neurogenic detrusor overactivity indications. Neurogenic detrusor overactivity is when a known neurologic abnormality impairs the signaling systems between the bladder and the central nervous system, and the brain is unable to inhibit the detrusor muscles controlling urination.

Either party may terminate the Allergan Agreement for uncured material breach by the other party and for the insolvency of the other party. The Company 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 the Company, its 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 an uncured material breach by the Company, 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 the Company, all rights and licenses to Allergan will terminate, and the license Allergan granted to us under their improvements to RTGel will continue.

NOTE 7-EMPLOYEE RIGHTS UPON RETIREMENT

The Company is required by law to make severance payments upon dismissal of an employee or upon termination of employment in certain other circumstances.

The Company operates a number of post-employment defined contribution plans. A defined contribution plan is a program that benefits an employee after termination of employment, under which the Company regularly makes fixed payments to a separate and independent entity so that the Company has no legal or constructive obligation to pay additional contributions if the fund does not hold sufficient assets to pay all employees the benefits relating to employee service in the current and prior periods. The fund assets are not included in the Company's financial position.

The Company operates pension and severance compensation plans subject to Section 14 of the Israeli Severance Pay Law, 5723-1963. The plans are funded through payments to insurance companies or pension funds administered by trustees. In accordance with its terms, the plans meet the definition of a defined contribution plan, as defined above.

NOTE 8-SHAREHOLDERS' EQUITY

Ordinary Shares

The Company had 100.0 million ordinary shares authorized for issuance as of December 31, 2018 and 2017, respectively. The Company had 16.2 million and 13.8 million ordinary shares issued and outstanding as of December 31, 2018 and 2017, respectively. Each ordinary share is entitled to one vote. The holders of ordinary shares are also entitled to receive dividends whenever funds are legally available, when and if declared by the Board of Directors. Since its inception, the Company has not declared any dividends.

In May 2017, the Company completed an IPO on the Nasdaq Global Market, in which it issued 5,144,378 ordinary shares, at a public offering price of $13.00 per share, in consideration for $60.8 million, net of underwriting discounts and commissions and issuance costs, including exercise of the underwriters' option to purchase additional 671,005 ordinary shares at the IPO price.

Upon completion of the IPO, the Company converted all outstanding warrants for Preferred A-1 shares into 364,036 Preferred A-1 shares of the Company (see below). Subsequently, the Company converted all outstanding Preferred A and Preferred A-1 shares into ordinary shares at a ratio of 1:1. As of December 31, 2017, the Company's share capital was composed entirely of ordinary shares.

In January 2018, the Company completed an underwritten public offering of 1,682,926 of its ordinary shares, including 219,512 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $41.00 per share. The net proceeds to the Company from the public offering were approximately $64.2 million, after deducting the underwriting discounts and commissions and payment of other offering expenses.

See Note 13 for further discussion regarding an underwritten public offering of ordinary shares that the Company completed in January 2019.

Warrants for Preferred A-1 Shares

In 2014, as part of a share purchase agreement, the Company issued warrants (the "A-1 warrants") for preferred shares. The warrants were exercisable for Series A-1 preferred shares, in consideration for cash representing the exercise price. The A-1 warrants were measured at fair value in every reporting period, and changes in their fair value were recognized in earnings within finance expenses, net.

In connection with the completion of the IPO, the Company converted all outstanding warrants into 364,036 Preferred A-1 shares of the Company and subsequently converted all of its preferred shares, including the Preferred A-1 shares, into ordinary shares.

The Company's warrants outstanding prior to the IPO were exercisable for Series A-1 preferred shares at an exercise price of $7.81 per share. Prior to the IPO, such warrants were exercisable for 728,312 Preferred A-1 shares.

Series A Preferred Shares

In October 2015 the Company entered into an asset purchase agreement with Telormedix SA ("TMX") pursuant to which the Company purchased all of the intellectual property assets of TMX (in process R&D) in consideration for 691,200 Series A preferred shares of the

Company at a price per share of $5.94, which were subsequently converted into ordinary shares on the date of the IPO. The Company will issue additional shares upon the occurrence of each of three milestones as set in the agreement. The Company has deemed the probability of achieving these milestones to be remote. The acquired intellectual property costs totaling $4.1 million were expensed as incurred to research and development costs in accordance with ASC 730, as the intellectual property is purchased from others for a particular research and development project and has no alternative future uses and therefore no separate economic value.

On April 19, 2017, the Company's board of directors and shareholders approved an aggregate 3.2 for-1 share split of the Company's ordinary, Preferred A and Preferred A-1 shares. The share split was effected on April 19, 2017 by the issuance of 2.2 ordinary shares for each outstanding ordinary, Preferred A and Preferred A-1 share held immediately prior to the share split.

Upon the completion of the IPO, all Series A preferred shares converted to ordinary shares on a 1:1 ratio. Prior to the IPO, the Series A preferred shares were classified within permanent equity as they were not subject to liability classification under the scope of ASC 480, and meet all the requirements of equity classification under ASC 480-10-S99.

NOTE 9-SHARE-BASED COMPENSATION

In October 2010, the Company's Board of Directors approved a share option plan (the "Plan") for grants to Company employees, consultants, directors, and other service providers.

The grant of options to Israeli employees under the Plan is subject to the terms stipulated by Section 102 of the Israeli Income Tax Ordinance ("Section 102"). The option grants are subject to the track chosen by the Company, either the "regular income" track or the "capital gains" track, as set out in Section 102. The Company registered the Plan under the capital gains track, which offers more favorable tax rates to the employees. As a result, and pursuant to the terms of Section 102, the Company is not allowed to claim as an expense for tax purposes the amounts credited to the employees in respect of options granted to them under the Plan, including amounts recorded as salary benefits in the Company's accounts, with the exception of the work-income benefit component, if any, determined on grant date. For non-employees and for non-Israeli employees, the Plan is subject to Section 3(i) of the Israeli Income Tax Ordinance.

Certain management and professional level employees typically receive stock options and RSU grants upon commencement of employment. Eligible employees may also receive a grant of stock options or RSUs annually. Non-employee members of our Board of Directors and any new, future directors may receive a grant of RSUs and/or stock options annually. The term of any stock option granted under the Plan cannot exceed 10 years. Options shall not have an exercise price less than 100% of the fair market value of the Company's ordinary shares on the grant date, and generally vest over a period of three years. If the individual possesses more than 10% of the combined voting power of all classes of stock of the Company, the exercise price shall not be less than 110% of the fair market value of a common share of stock on the date of grant.

The Company's RSU and stock option grants provide for accelerated or continued vesting in certain circumstances as defined in the plans and related grant agreements, including a termination in connection with a change in control. RSUs generally vest in a 33% increment upon the first anniversary of grant, and in equal quarterly amounts for the two years following the one-year anniversary of the grant date. Stock options generally vest in a 33% increment upon the first anniversary of the grant date, and in equal quarterly amounts for the three years following the one-year anniversary of the grant date.

The expected volatility is based on the historical volatility of comparable companies with similar attributes to the Company, including industry, stage of life cycle, size and financial leverage. The risk-free interest rate assumption is based on observed interest rates appropriate for the expected term of the options granted. The expected term is the length of time until the expected dates of exercising the options and is estimated for employees using the simplified method due to insufficient specific historical information of employees' exercise behavior, and for non-employees, and directors using the contractual term.

In March 2017, the Company's Board of Directors adopted the 2017 Equity Incentive Plan ("2017 Plan"), which was approved by the shareholders in April 2017. The 2017 Plan provides for the grant of incentive stock options to the Company's employees and for the grant of nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards, and other forms of stock awards to the Company's employees, directors and consultants.

The maximum number of ordinary shares that may initially be issued under the 2017 Plan is 1,400,000. In addition, the number of ordinary shares reserved for issuance under the 2017 Plan will automatically increase on January 1st of each calendar year, from January 1, 2018 through January 1, 2026, so that the number of such shares reserved for issuance will equal 12% of the total number of ordinary

shares outstanding on the last day of the calendar month prior to the date of each automatic increase, or a lesser number of shares determined by our board of directors. The maximum number of ordinary shares that may be issued upon the exercise of incentive stock options under the 2017 Plan is 5,600,000. On January 1, 2018, the share reserve increased by 250,167 to 1,650,167. On October 12, 2018, the Company filed a registration statement on Form S-8 increasing the amount of registered ordinary shares of the Company's 2017 Plan by 1,900,000 to 3,550,167.

In April 2017, the Company's board of directors approved modifications of performance conditions for 67,200 restricted stock units and contingent options for executive management. The Company recorded an expense of $0.5 million under general and administrative expenses with respect to these modifications.

During the year ended December 31, 2018, the Company recorded $7.2 million in general and administrative and research and development expenses in the Company's Statements of Operations for the year ended December 31, 2018 related to the stock option modifications related to the termination of certain senior executives, based on the executive's respective allocations.

On January 2, 2019, the Company announced the resignation of its CEO, and the Company's board of directors approved a severance package, which included a combination of cash and modifications to grants of his related option awards in the amount of $3.4 million. The cash element followed the termination section in the CEO employment agreement, and the options element included acceleration to certain grants of his related option awards. The fair value of the modifications to these option awards was estimated at $2.8 million. The entire severance package was recorded in general and administrative and research and development expenses, based on salary allocations respectively, in the Company's Statements of Operations for the year ended December 31, 2018.

In August 2018, in addition to the modifications, one senior executive was granted 10,466 RSUs in which no compensation expense was taken because the award vests upon a future performance condition that is not currently probable of occurring.

For the years ended December 31, 2018 and 2017, the Company granted options to certain employees and non-employees as follows:

Options granted to employees and directors:

Set forth below are grants made by the Company to employees and directors as of December 31, 2018. The majority of options vest over three years and expire on the tenth anniversary of the date of grant.

a) During 2018, the Company granted 1,155,000 options to employees and directors with exercise prices ranging from $38.64 to $59.23 per share.

b) During 2017, the Company granted 589,600 options to employees and directors with exercise prices ranging from $1.78 to $39.26 per share.

c) During 2016, the Company granted 404,813 options to employees and directors with exercise prices ranging from $5 to $5.94 per share.

The fair value of options granted to employees and directors during 2018, 2017 and 2016 was $39.3 million, $10.9 million and $0.9 million, respectively.

The total unrecognized compensation cost of employee and director options at December 31, 2018 is $26.5 million, which is expected to be recognized over a weighted average period of 2.2 years.

The fair value of options granted to employees and directors was computed using the Black-Scholes model. The underlying data used for computing the fair value of the options are as follows:

	2018	2017	2016
Value of ordinary shares	$38.64-59.23	$13.00-39.26	$2.98-5.54
Dividend yield	0%	0%	0%
Expected volatility	72.59%-79.37%	71.53%-76.32%	74.8%-80%
Risk-free interest rate	2.30%-3.07%	1.85%-2.47%	1.4%–2.13%
Expected term	5.4-10 years	5.5-10 years	7 years

Options granted to consultants and other service providers:

Set forth below are grants made by the Company to consultants and service providers as of December 31, 2018. The majority of the options vest over a period of three years and expire on the seventh anniversary of the date of grant.

a) During 2018, the Company granted 40,000 options to consultants and service providers with exercise prices ranging from $43.67 to $59.23 per share.

b) During 2017, there were no new grants issued to consultants and service providers.

c) During 2016, the Company granted 132,032 options to consultants and service providers with exercise prices ranging from $0 to $5.94 per share.

The fair value as of December 31, 2018, 2017 and 2016 of options granted to consultants and service providers during 2018, 2017 and 2016 was $1.0 million, $0 and $0.7 million, respectively.

The fair value of options granted to consultants and other service providers was computed using the Black-Scholes model. The underlying data used for computing the fair value of the options are as follows:

	2018	2017	2016
Value of ordinary shares	$43.06-49.69	$1.58-37.21	$1.58-7.96
Dividend yield	0%	0%	0%
Expected volatility	72.00%-82.04%	68.45%-74.50%	72.72%-80%
Risk-free interest rate	1.72%-2.98%	1.38%-2.26%	1.56%-2.27%
Expected term	0.2-9.5 years	3.9-5.9 years	5.8-8.5 years

The following table summarizes the number of options outstanding under the Plan for the years ended December 31, 2018, 2017 and 2016, and related information:

	Employees and Directors		Consultants and Service providers	
	Number of options	Weighted Average price per share	Number of options	Weighted Average price per share
Outstanding as of January 1, 2016	1,411,400	$ 4.70	513,238	$ 3.48
Granted	404,813	$ 5.50	132,032	$ 7.15
Canceled/Forfeited	(60,800)	$ 5.94	(6,000)	$ 1.58
Exercised	—	$ —	(4,784)	$ 2.45
Outstanding as of December 31, 2016	1,755,413	$ 4.84	634,486	$ 4.27
Granted	589,600 *	$ 23.95	—	$ —
Canceled/Forfeited	(39,500)	$ 5.77	(5,686)	$ 2.93
Exercised	(560,243)	$ 4.39	(130,038)	$ 2.92
Outstanding as of December 31, 2017	1,745,270	$ 11.42	498,762	$ 4.64
Granted	1,155,000	$ 47.18	40,000	$ 47.56
Canceled/Forfeited	(153,313)	$ 35.19	(13,836)	$ 37.38
Exercised	(659,434)	$ 9.37	(89,468)	$ 6.20
Outstanding as of December 31, 2018	2,087,523	$ 30.11	435,458	$ 7.22

* Including 9,600 ordinary shares issuable upon the vesting of options granted in 2016, which were contingent upon the closing of the IPO

The intrinsic value of stock options exercised by employees and directors was $27.5 million, $17.9 million, and $0 for the years ended December 31, 2018, 2017, and 2016, respectively. The intrinsic value of stock options exercised by consultants and service providers was $4.1 million, $3.5 million, and $0.01 million for the years ended December 31, 2018, 2017, and 2016, respectively.

The following table summarizes the outstanding and exercisable options as of December 31, 2018:

	Options outstanding		Options exercisable	
Exercise price per share	Number of options outstanding at end of year	Weighted average remaining contractual life	Number of options exercisable at end of year	Weighted average remaining contractual life
$0.00 - 10.00	1,023,791	3.38	814,479	3.20
$10.01 - 20.00	215,079	6.71	140,078	5.79
$20.01 - 30.00	100,000	8.82	33,334	8.82
$30.01 - 40.00	225,000	6.18	114,998	3.40
$40.01 - 50.00	742,111	8.80	157,720	6.90
$50.01 - 59.23	217,000	9.37	36,499	9.43
	2,522,981		1,297,108	

The aggregate intrinsic value of the total vested and exercisable options and vested and not released restricted stock units as of December 31, 2018 is $38.9 million.

The following table summarizes information about RSU activity as of December 31, 2018:

	Outstanding Restricted Stock Units
Outstanding as of January 1, 2016	275,200
Granted	—
Vested and released	—
Forfeited	—
Outstanding as of December 31, 2016	275,200
Granted	123,300 *
Vested and released	(121,940)
Forfeited	—
Outstanding as of December 31, 2017	276,560
Granted	116,493
Vested and released	(118,447)
Forfeited	(10,907)
Outstanding as of December 31, 2018	263,699

* Including 28,800 ordinary shares issuable upon the vesting of options granted in 2016, which were contingent upon the closing of the IPO

The Company has not previously separately disclosed the table information shown above. The fair value of RSUs granted during 2018, 2017 and 2016 was $5.7 million, $3.3 million, and $0, respectively. The total unrecognized compensation cost of RSUs at December 31, 2018 is $5.2 million with a weighted average recognition period of 2.1 years.

The following table illustrates the effect of share-based compensation on the statements of operations:

	Year ended December 31,		
	2018	2017	2016
Research and development expenses	$ 12,038	$ 3,923	$ 1,167
General and administrative expenses	18,604	2,377	800
	$ 30,642	$ 6,300	$ 1,967

NOTE 10-INCOME TAXES

The Company is taxed under Israeli tax laws:

Corporate tax rate

Presented hereunder are the tax rates relevant to the Company in the years 2016-2018:

2016 – 25%

2017 – 24%

2018 – 23%

On January 4, 2016 the Knesset plenum passed the Law for the Amendment of the Income Tax Ordinance (Amendment 216) - 2016, by which, inter alia, the corporate tax rate would be reduced by 1.5% to a rate of 25% as from January 1, 2016.

Furthermore, on December 22, 2016 the Knesset plenum passed the Economic Efficiency Law (Legislative Amendments for Achieving Budget Objectives in the Years 2017 and 2018) – 2016, by which, inter alia, the corporate tax rate would be reduced from 25% to 23% in two steps. The first step will be to a rate of 24% as from January 2017 and the second step will be to a rate of 23% as from January 2018.

As a result of the reduction in the tax rate to 23% in two steps, the deferred tax balances as at December 31, 2018 were calculated according to the new tax rate specified in the Economic Efficiency Law (Legislative Amendments for Achieving Budget Objectives in the Years 2017 and 2018), at the tax rate expected to apply on the date of reversal.

Current taxes for the reported periods are calculated according to the tax rates presented above.

Income Tax Regulations (Rules on Bookkeeping by Foreign Invested Companies and Certain Partnerships and Determination of their Taxable Income), 1986:

As a "Controller Foreign Cooperation" (as defined in the Israeli Law for the Encouragement of Capital Investments-1959), the Company's management has elected to apply Income Tax Regulations (Rules for Maintaining Accounting Records of Foreign Invested Companies and Certain Partnerships and Determining Their Taxable Income) – 1986, from January 2018. Accordingly, its taxable income or loss is calculated in US Dollars.

Law for the Encouragement of Industry (Taxation), 1969:

The Company is an “Industrial Company” under the Law for the Encouragement of Industry (Taxation), 1969 and, therefore, is entitled to certain tax benefits, mainly are as follows:

- Amortization in three equal annual portions of issuance expenses when registering shares for trading as from the date the shares of the company were registered.
- An 8-year period of amortization for acquired patents and know-how used in the process of development performed by the enterprise.

Deferred income taxes:

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company and its subsidiary deferred tax assets are as follows:

	December 31,		
	2018	2017	2016
In respect of:			
Net operating loss carry forward	$ 16,943	$ 5,844	$ 3,280
Deferred rent	61	46	—
Research and development expenses	3,891	2,887	—
Stock-based compensation	4,769	897	—
Issuance costs	1,367	1,261	—
In-process research and development	629	761	806
Accrued expenses	598	5	—
Depreciation of fixed assets	(93)		
Other	84	24	72
Less—valuation allowance	(28,249)	(11,725)	(4,158)
Net deferred tax assets	$ —	$ —	$ —

The change in valuation allowance for the years ended December 31, 2018 and 2017 were as follows:

	2018	2017	2016
Balance at the beginning of the year	$ (11,725)	$ (4,158)	$ (4,499)
Changes during the year	(16,524)	(7,567)	341
Balance at the end of the year	$ (28,249)	$ (11,725)	$ (4,158)

The main reconciling item between the statutory tax rates of the Company and the effective rate is the share-based compensation and provision for full valuation allowance in respect of tax benefits from carryforward tax losses due to the uncertainty of the realization of such tax benefits.

Regarding the Company's US operations, as of December 31, 2018, UPI had federal tax net operating losses of $1.5 million and state tax net operating losses of $1.7 million in several jurisdictions available to carry forward and reduce future income tax liabilities. The federal and state net operating losses begin to expire after 2036.

The Internal Revenue Code contains provisions that may limit the use of the net operating tax loss carryforward available if significant changes occur in the stock ownership of UPI. In the event UPI has had a change in ownership, utilization of the carry-forwards could be restricted due to the "change in ownership provisions" under Section 382 of the Internal Revenue Code and similar state provisions. Such limitations could result in the expiration of the net operating carry-forwards before their utilization.

Losses for tax purposes carried forward to future years

As of December 31, 2018, the Company had approximately $72.1 million of net carry forward tax losses available to reduce future taxable income without limitation of use.

Tax assessments

UPL has received final tax assessments up to and including 2013 tax year.

NOTE 11-RELATED PARTIES

UPI entered into a lease agreement, dated as of November 2015 and commencing as of May 2016, for office space in New York. UPI shared the office space equitably with Kite Pharma, Inc., a Delaware corporation, which was a cosignatory to such lease agreement. Arie Belldegrun, M.D., UPL's chairman, served as the Chairman and Chief Executive Officer of Kite Pharma, Inc. until his resignation effective as of October 3, 2017, in connection with the acquisition of Kite Pharma, Inc. by Gilead Sciences, Inc.

In April 2018, UPI terminated its lease for offices at 689 Fifth Avenue in New York, and on December 1, 2018, UPI and Kite Pharma, Inc., completed a full assignment and assumption of the lease to Allogene Therapeutics, Inc. of which Arie Belldegrun, M.D., serves as the Chairman of the Board of Directors.

UPI recorded a loss on disposal of fixed assets of $0.2 million for the year ended December 31, 2018, regarding accelerated depreciation on the leasehold improvements associated with the lease, and there is no further liability as of December 31, 2018.

NOTE 12-COMMITMENTS AND CONTINGENCIES

In the normal course of business, the Company enters into contracts that contain a variety of indemnifications with its employees, licensors, suppliers and service providers. Further, the Company indemnifies its directors and officers who are, or were, serving at the Company's request in such capacities. The Company's maximum exposure under these arrangements is unknown as of December 31, 2018 and 2017. The Company does not anticipate recognizing any significant losses relating to these arrangements.

Leases

In April 2016, UPL signed an addendum to its November 2014 lease agreement for the Company's principal executive offices located in Israel, in order to increase the office space rented and to extend the rent period until 2019.

UPI entered into a lease agreement for its office for a period of seven years commencing on May 1, 2016. As part of the agreement UPI provided the lessor with a letter of credit which renews on an annual basis. On December 1, 2018 UPI completed a full assignment and assumption of the lease to Allogene Therapeutics, Inc. The letter of credit was returned and there is no further liability to UPI as of December 31, 2018.

In September 2017, UPI entered into a new lease agreement for its New York headquarters. The lease agreement commenced in October 2017 and shall terminate in February 2021. The remaining contractual obligation is approximately $1.5 million.

In April 2018, UPI entered into a new lease agreement for an office in Los Angeles, CA. The lease commencement date was July 10, 2018 and terminates in March 2024. The contractual obligation for the remainder of the lease is $1.4 million. The landlord provided a tenant allowance for leasehold improvements of $0.2 million that is accounted for as a lease incentive and is being amortized to rent expense ratably over the life of the lease.

Rent expense charged to operations was $1.2 million, $0.6 million, and $0.3 million for the years ended December 31, 2018, 2017 and 2016, respectively.

The following table summarizes our lease obligations at December 31, 2018 (in thousands):

YEARS ENDED DECEMBER 31,	Operating Lease
2019	$ 1,136
2020	1,251
2021	676
2022	567
2023	301
2024 and thereafter	58
Total minimum lease payments	$ 3,989

Grants from the IIA

The Company has received grants from the IIA for research and development funding. Up until 2007, the IIA participation in the funding of the Company's operations was as part of the Director General Directive 8.2 of Israel by grants provided to Granot Ventures. Since 2008, the funding was provided directly to Company.

The Company is committed to pay royalties to the Government of Israel on proceeds from sales of products in the research and development of which the IIA participates by way of grants. At the time the grants were received, successful development of the related projects was not assured. In the case of failure of a project that was partly financed as above, the Company is not obligated to pay any such royalties. Under the terms of the funding from the IIA, royalties of 3% to 5% are payable on sales of products developed from a project so funded, up to 100% of the amount of the grant received by the Company (dollar linked); with the addition of annual interest at a rate based on 12-month LIBOR. The Company is subject to several conditions, including restrictions on its intellectual property.

As of December 31, 2018, the maximum royalty amount payable by the Company under these funding arrangements is $2.1 million (excluding interest, and inclusive of the $0.8 million in royalties that the Company has accrued as of December 31, 2018). 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. 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. As of December 31, 2018, the Company has 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 year ended December 31, 2018.

NOTE 13-SUBSEQUENT EVENTS

In January 2019, the Company completed an underwritten public offering of 4,207,317 ordinary shares, including 548,780 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $41.00 per share. The net proceeds to the Company from the offering were approximately $161.8 million, after deducting the underwriting discounts and commissions and payment of other offering expenses.

On January 3, 2019, we appointed Elizabeth Barrett as our President and Chief Executive Officer, replacing Ron Bentsur in those capacities. Concurrently, Ms. Barrett was appointed as a member of our board of directors (the "Board") and Mr. Bentsur resigned from the Board. In connection with Ms. Barrett's employment, she was granted 277,432 options to purchase the Company's ordinary shares, as well as 317,065 RSUs, with a combined fair value of $24.1 million.

NOTE 14-SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for 2018 and 2017 are as follows (in thousands, except per share data):

	2018				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Total revenues	$ 481	$ 364	$ 283	$ —	$ 1,128
Total operating expenses	$ 13,691	$ 18,480	$ 20,317	$ 24,017	$ 76,505
Loss from operations	$ (13,640)	$ (18,434)	$ (21,089)	$ (24,017)	$ (77,180)
Net loss attributable to common shareholders	$ (13,382)	$ (18,026)	$ (20,533)	$ (23,716)	$ (75,657)
Net loss per share attributable to common shareholders - basic and diluted	$ (0.88)	$ (1.14)	$ (1.28)	$ (1.46)	$ (4.80)

	2017				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Total revenues	$ 19	$ —	$ 7,812	$ 327	$ 8,158
Total operating expenses	$ 3,539	$ 5,951	$ 7,820	$ 10,198	$ 27,508
Loss from operations	$ (3,538)	$ (5,951)	$ (303)	$ (10,158)	$ (19,950)
Net loss attributable to common shareholders	$ (3,417)	$ (6,199)	$ (298)	$ (10,086)	$ (20,000)
Net loss per share attributable to common shareholders - basic and diluted	$ (1.74)	$ (0.70)	$ (0.02)	$ (0.74)	$ (2.14)

Net loss per share is computed independently for each of the quarters presented in the tables above. Therefore, the sum of the quarterly per-share calculations will not equal the annual per share calculation.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive and financial officers (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosures controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of December 31, 2018. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure.

Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective at a reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management has assessed the effectiveness of our internal control over financial reporting based on the framework set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013 framework). Based on our evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2018.

The effectiveness of our internal control over financial reporting has been audited by Kesselman & Kesselman (a member firm of PricewaterhouseCoopers International Limited, or PwC), an independent registered public accounting firm, as stated in their attestation report herein, which is included under "Item 8—Financial Statements."

Inherent Limitations of Internal Controls

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Internal Control over Financial Reporting

We regularly review our system of internal control over financial reporting and make changes to our processes and systems to improve controls and increase efficiency, while ensuring that we maintain an effective internal control environment. Changes may include such activities as implementing new, more efficient systems, consolidating activities, and migrating processes. During the quarter ended December 31, 2018, there were no changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance

The information required by this Item and not set forth below will be set forth in the section headed "—Election of Directors" and "Information Regarding the Board of Directors and Corporate Governance" in our definitive Proxy Statement for our 2019 Annual Meeting of Shareholders to be filed with the SEC by April 30, 2019 (our "Proxy Statement") and is incorporated in this Annual Report by reference.

We have adopted a code of ethics for directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees, known as the Corporate Code of Ethics and Conduct. The Corporate Code of Ethics and Conduct is available on our website at *http://www.urogen.com* under the Corporate Governance section of our Investors page. We will promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals, the name of such person who is granted the waiver and the date of the waiver. Shareholders may request a free copy of the Corporate Code of Ethics and Conduct from c/o UroGen Pharma Ltd., 499 Park Avenue, Suite 1200, New York, NY 10022.

Item 11. Executive Compensation

The information required by this Item will be set forth in the section headed "Executive Compensation" in our Proxy Statement and is incorporated in this Annual Report by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item will be set forth in the section headed "Security Ownership of Certain Beneficial Owners and Management" in our Proxy Statement and is incorporated in this Annual Report by reference.

Information regarding our equity compensation plans will be set forth in the section headed "Executive Compensation" in our Proxy Statement and is incorporated in this Annual Report by reference.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required by this Item will be set forth in the section headed "Transactions With Related Persons" in our Proxy Statement and is incorporated in this Annual Report by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item will be set forth in the section headed "—Ratification of Selection of Independent Registered Public Accounting Firm" in our Proxy Statement and is incorporated in this Annual Report by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a)(1) Financial Statements.

The response to this portion of Item 15 is set forth under Part II, Item 8 above.

(a)(2) Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the Financial Statements or Notes thereto set forth under Item 8 above.

(a)(3) Exhibits.

Exhibit Number	Exhibit Description
3.1	Articles of Association of the Registrant (incorporated by reference to Exhibit 3.1 to the Form 6-K filed on May 18, 2017).
10.1*	Form of Officer Indemnity and Exculpation Agreement (incorporated by reference to Exhibit 99.2 to the Form 6-K filed on July 13, 2018).
10.2*	Amended and Restated 2010 Israeli Share Option Plan (incorporated by reference to Exhibit 4.2 to the Form 20-F filed on March 15, 2018).
10.3	Investors' Rights Agreement, dated September 18, 2014, as amended on October 1, 2015 and April 12, 2016, among the Registrant and the Registrant's shareholders (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form F-1 (File No. 333-217201)).
10.4	Asset Purchase Agreement, dated October 1, 2015, between the Registrant and Telormedix SA (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form F-1 (File No. 333-217201)).
10.5†	License Agreement, dated as of October 7, 2016, by and between the Registrant and Allergan Pharmaceuticals International Limited (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form F-1 (File No. 333-217201)).
10.6*	2017 Equity Incentive Plan, as amended.
10.7*	2017 Israeli Equity Incentive Sub Plan to the 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form F-1 (File No. 333-217201)).
10.8	Open Market Sales Agreement, dated October 12, 2018, by and between the Registrant and Jefferies LLC (incorporated by reference to Exhibit 1.2 to the Form F-3 filed on October 12, 2019 (File No. 333-227811).
10.9*	Employment Agreement by and between the Registrant and Elizabeth Barrett, dated as of January 3, 2019.
10.10*	Employment Agreement by and between the Registrant and Peter Pfreundschuh, dated as of July 31, 2018.
10.11*	Employment Agreement by and between the Registrant and Stephen Mullennix, dated as of January 17, 2018.
10.12*	Employment Agreement by and between the Registrant and Mark Schoenberg, dated as of December 5, 2017.
10.13*	Separation and Release Agreement between the Registrant and Ron Bentsur, dated as of January 3, 2019.
10.14*	Separation and Agreement between the Company and Gary Titus, dated as of July 11, 2018.
21.1	Subsidiary of the Registrant (incorporated by reference to Exhibit 21.1 to the Registrant's Registration Statement on Form F-1 (File No. 333-217201)).
23.1	Consent of Kesselman & Kesselman, a member firm of PricewaterhouseCoopers International Limited, an independent registered public accounting firm.
31.1	Certification of Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

31.2	Certification of Chief Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certifications of Chief Executive Officer and Chief Financial Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial information from the Annual Report on Form 10-K of UroGen Pharma Ltd. for the year ended December 31, 2018, formatted in XBRL (extensible Business Reporting Language): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Changes in Shareholders Equity, (iv) Consolidated Statements of Cash Flows, and (v) the Notes to Consolidated Financial Statements.

* Management contract or compensatory plan.

† Registrant has been granted confidential treatment for certain portions of this exhibit. This exhibit omits the information subject to this confidentiality treatment. Omitted portions have been filed separately with the SEC.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

UROGEN PHARMA, LTD.

February 28, 2019

By: /s/ Elizabeth Barrett
Elizabeth Barrett
Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned directors and officers of UroGen Pharma, Ltd. (the "Company"), hereby severally constitute and appoint Elizabeth Barrett and Peter Pfreundschuh, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Elizabeth Barrett Elizabeth Barrett	Chief Executive Officer, Director *(Principal Executive Officer)*	February 28, 2019
/s/ Peter Pfreundschuh Peter Pfreundschuh	Chief Financial Officer *(Principal Financial and Accounting Officer)*	February 28, 2019
/s/ Arie Belldegrun Arie Belldegrun, M.D.	Chairman	February 28, 2019
/s/ Cynthia Butitta Cynthia Butitta	Director	February 28, 2019
/s/ Fred E. Cohen Fred E. Cohen	Director	February 28, 2019
/s/ Kathryn Falberg Kathryn Falberg	Director	February 28, 2019
/s/ Stuart Holden Stuart Holden, M.D.	Director	February 28, 2019
/s/ Ran Nussbaum Ran Nussbaum	Director	February 28, 2019
/s/ Shawn C. Tomasello Shawn C. Tomasello	Director	February 28, 2019