UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)
☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended September 30, 2022

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	**98-1460746**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
400 Alexander Park Drive, Princeton, New Jersey	**08540**
(Address of principal executive offices)	**(Zip Code)**

(646) 768-9780

Registrant's telephone number, including area code

N/A

(Former name, former address and former fiscal year, if changed since last report)

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

Title of each class	Trading Symbol	Name of exchange on which registered
Ordinary Shares, par value NIS 0.01 per share	URGN	The Nasdaq Stock Market LLC

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

Large accelerated filer	☐	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 Exchange Act). Yes ☐ No ☒

As of November 7, 2022, the registrant had 23,090,039 ordinary shares, par value NIS 0.01 per share, outstanding.

UroGen Pharma Ltd.
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Trademarks and Trade Names

Unless the context requires otherwise, references in this Quarterly Report to the "Company," "UroGen," "we," "us" and "our" refer to UroGen Pharma Ltd. and its subsidiary, UroGen Pharma, Inc.

UroGen, RTGel and *Jelmyto* are trademarks of ours that we use in this Quarterly Report. This Quarterly 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 Quarterly 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.

Part I—Financial Information

Item 1. Financial Statements.

UroGen Pharma Ltd.
Condensed Consolidated Balance Sheets
(unaudited; in thousands, except share amounts and par value)

	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 28,686	$ 44,360
Marketable securities	67,225	44,779
Restricted cash	812	1,226
Accounts receivable	9,429	11,717
Inventories	4,862	4,832
Prepaid expenses and other current assets	10,580	7,476
Total current assets	121,594	114,390
Non-current assets:		
Property and equipment, net	1,519	1,967
Restricted deposit	223	223
Right of use assets	2,666	1,180
Marketable securities	—	675
Other non-current assets	2,471	1,311
Total Assets	$ 128,473	$ 119,746
Liabilities and Shareholders' Equity (Deficit)		
Current liabilities:		
Accounts payable and accrued expenses	$ 9,356	$ 12,102
Employee related accrued expenses	6,625	6,948
Other current liabilities	3,018	3,330
Total current liabilities:	18,999	22,380
Non-current liabilities:		
Prepaid forward obligation	96,192	85,713
Long-term debt	71,870	—
Long-term lease liabilities	1,856	398
Uncertain tax positions liability	2,842	2,842
Total Liabilities	191,759	111,333
Commitments and Contingencies (Note 18)		
Shareholders' Equity (Deficit):		
Ordinary shares, NIS 0.01 par value, 100,000,000 shares authorized at September 30, 2022 and December 31, 2021; 23,011,324 and 22,462,995 shares issued and outstanding as of September 30, 2022 and December 31, 2021, respectively	63	61
Additional paid-in capital	485,041	475,698
Accumulated deficit	(548,235)	(467,321)
Accumulated other comprehensive loss	(155)	(25)
Total Shareholders' Equity (Deficit)	(63,286)	8,413
Total Liabilities and Shareholders' Equity (Deficit)	$ 128,473	$ 119,746

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

UroGen Pharma Ltd.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(unaudited; in thousands, except share and per share amounts)

	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2022	2021	2022	2021
Revenue	$ 16,097	$ 11,351	$ 46,265	$ 31,868
Cost of revenue	2,020	1,244	5,391	3,568
Gross profit	14,077	10,107	40,874	28,300
Operating expenses:				
Research and development expenses	13,093	11,923	38,429	34,560
Selling, general and administrative expenses	19,071	21,624	61,204	66,117
Operating loss	(18,087)	(23,440)	(58,759)	(72,377)
Financing on prepaid forward obligation	(4,819)	(6,828)	(16,478)	(9,948)
Interest expense on long-term debt	(2,694)	—	(5,215)	—
Interest and other income, net	478	57	604	269
Loss before income taxes	(25,122)	(30,211)	(79,848)	(82,056)
Income tax expense	(709)	—	(1,066)	(312)
Net Loss	$ (25,831)	$ (30,211)	$ (80,914)	$ (82,368)
Statements of Comprehensive Loss				
Net loss	$ (25,831)	$ (30,211)	$ (80,914)	$ (82,368)
Other comprehensive (loss)				
Unrealized (loss) on investments	(99)	(41)	(130)	(267)
Comprehensive Loss	$ (25,930)	$ (30,252)	$ (81,044)	$ (82,635)
Net loss per ordinary share - basic and diluted	$ (1.13)	(1.35)	$ (3.56)	$ (3.69)
Weighted average number of shares outstanding used in computation of basic and diluted loss per ordinary share	22,798,263	22,380,598	22,711,686	22,318,589

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

UroGen Pharma Ltd.
Condensed Consolidated Statements of Shareholders' Equity (Deficit)
(unaudited; in thousands, except share amounts)

	Ordinary Shares		Additional paid-in capital	Accumulated Deficit	Other comprehensive income (loss)	Total
	Number of Shares	Amount				
Balance as of July 1, 2022	22,727,891	$ 62	$ 481,485	$ (522,404)	$ (56)	$ (40,913)
Changes During the Three Months Ended September 30, 2022						
Exercise of options into ordinary shares	283,433	1	1,116			1,117
Share-based compensation			2,440			2,440
Other comprehensive income					(99)	(99)
Net loss				(25,831)		(25,831)
Balance as of September 30, 2022	23,011,324	$ 63	$ 485,041	$ (548,235)	$ (155)	$ (63,286)
Balance as of July 1, 2021	22,354,533	$ 61	$ 464,823	$ (408,658)	$ 45	$ 56,271
Changes During the Three Months Ended September 30, 2021						
Exercise of options into ordinary shares	50,312	—	3			3
Share-based compensation			5,515			5,515
Other comprehensive loss					(41)	(41)
Net loss				(30,211)		(30,211)
Balance as of September 30, 2021	22,404,845	$ 61	$ 470,341	$ (438,869)	$ 4	$ 31,537

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

UroGen Pharma Ltd.
Condensed Consolidated Statements of Shareholders' Equity (Deficit)
(unaudited; in thousands, except share amounts)

	Ordinary Shares					
	Number of Shares	Amount	Additional paid-in capital	Accumulated Deficit	Other comprehensive income (loss)	Total
Balance as of January 1, 2022	22,462,995	$ 61	$ 475,698	$ (467,321)	$ (25)	$ 8,413
Changes During the Nine Months Ended September 30, 2022						
Exercise of options into ordinary shares	548,329	2	1,131			1,133
Share-based compensation			8,212			8,212
Other comprehensive loss					(130)	(130)
Net loss				(80,914)		(80,914)
Balance as of September 30, 2022	23,011,324	$ 63	$ 485,041	(548,235)	$ (155)	$ (63,286)
Balance as of January 1, 2021	22,167,791	$ 60	$ 452,525	$ (356,501)	271	$ 96,355
Changes During the Nine Months Ended September 30, 2021						
Exercise of options into ordinary shares	237,054	1	60			61
Share-based compensation			17,756			17,756
Other comprehensive loss					(267)	(267)
Net loss				(82,368)		(82,368)
Balance as of September 30, 2021	22,404,845	$ 61	$ 470,341	$ (438,869)	$ 4	$ 31,537

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

UroGen Pharma Ltd.
Condensed Consolidated Statements of Cash Flow
(unaudited; in thousands)

	Nine Months Ended September 30,	
	2022	**2021**
Cash Flows From Operating Activities		
Net loss	$ (80,914)	$ (82,368)
Adjustment to reconcile net loss to net cash from operating activities:		
Depreciation and amortization	688	618
Inventory Obsolescence	615	—
Accrued financing on prepaid forward obligation	11,019	8,583
Amortization (accretion) on marketable securities	(93)	343
Share-based compensation	8,212	17,756
Amortization of discount on long-term debt	1,077	—
Amortization of right of use assets	679	704
Changes in operating assets and liabilities:		
Inventory	(645)	(1,844)
Accounts receivable	2,288	(737)
Prepaid expenses and other current assets	(3,104)	(2,749)
Other non-current assets	(1,000)	(1,573)
Accounts payable and accrued expenses	(2,746)	1,032
Employee related accrued expenses	(323)	(3,078)
Other current liabilities	(704)	(595)
Lease liabilities	(856)	(914)
Net cash used in operating activities	(65,807)	(64,822)
Cash Flows From Investing Activities		
Purchases of marketable securities	(63,009)	(51,594)
Sales of marketable securities	—	2,463
Maturities of marketable securities	41,202	44,625
Purchases of property and equipment	(241)	(550)
Net cash (used in) provided by investing activities	(22,048)	(5,056)
Cash Flows From Financing Activities		
Proceeds from prepaid forward arrangement	—	72,417
Proceeds from exercise of options into ordinary shares	1,133	61
Proceeds from issuance of long-term debt	70,793	—
Issuance cost related to at-the-market issuances	(160)	(127)
Net cash provided by financing activities	71,766	72,351
Increase (Decrease) in Cash and Cash Equivalents	(16,089)	2,473
Cash, Cash Equivalents and Restricted Cash at Beginning of Period	45,587	54,090
Cash, Cash Equivalents and Restricted Cash at End of Period	$ 29,498	$ 56,563
Supplemental Disclosures of Non-Cash Activities		
Right of use assets obtained in exchange for new operating lease liabilities	$ 2,165	$ (36)
Non-cash issuance cost	$ —	$ 7

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

UroGen Pharma Ltd.
Notes to the Unaudited Condensed 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 wholly owned 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 biotechnology company dedicated to developing and commercializing innovative solutions that treat urothelial and specialty cancers. Since commencing operations, the Company has devoted substantially all of its efforts to securing intellectual property rights, performing research and development activities, including conducting clinical trials and manufacturing activities, hiring personnel, launching the Company's first commercial product, *Jelmyto* (mitomycin) for pyelocalyceal solution, formerly known as UGN-101, clinical development of UGN-102, and raising capital to support and expand these activities.

On April 15, 2020, the U.S. Food and Drug Administration ("FDA") granted expedited approval for *Jelmyto*, a first-in-class treatment indicated for adults with low-grade upper tract urothelial cancer ("low-grade UTUC"). *Jelmyto* consists of mitomycin, an established chemotherapy, and sterile hydrogel, using our proprietary sustained release RTGel technology. It has been designed to enable longer exposure of urinary tract tissue to mitomycin, thereby enabling the treatment of tumors by non-surgical means.

Note 2 – Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP") for interim financial information and in accordance with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all the information and footnotes required by GAAP for complete financial statements. In the opinion of the Company's management, the accompanying condensed consolidated financial statements contain all adjustments (consisting of normal recurring accruals and adjustments) necessary for fair statement of its financial position, results of operations and cash flows of the Company at the dates and for the periods indicated. Interim results are not necessarily indicative of results for the full fiscal year. The year-end condensed consolidated balance sheet data was derived from audited financial statements but does not include all disclosures required by accounting principles generally accepted in the United States. The unaudited condensed consolidated financial statements should be read in conjunction with the consolidated financial statements and the notes thereto contained in the Company's Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission ("SEC") on March 21, 2022.

The Company has experienced net losses since its inception and has an accumulated deficit of $548.2 million and $467.3 million as of September 30, 2022 and December 31, 2021, respectively. The Company expects to incur losses and have negative net cash flows from operating activities as it executes on its strategy including engaging in further research and development activities, particularly conducting non-clinical studies and clinical trials.

The success of the Company depends on the ability to successfully commercialize its technologies to support its operations and strategic plan. Based on management's cash flow projections the Company believes that its cash and cash equivalents and marketable securities are sufficient to fund the Company's planned operations for at least the next 12 months. The Company anticipates that it will need to raise additional capital in the future. There can be no assurances that the Company will be able to secure such additional financing if at all, or on terms that are satisfactory to the Company, and that it will be sufficient to meet its needs. In the event the Company is not successful in obtaining sufficient funding, this could force us to delay, limit, or reduce our product development, commercialization efforts or other operations.

Note 3 – Significant Accounting Policies

Principles of Consolidation

The condensed consolidated financial statements include the accounts of UPL and 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 revenue and expense during the reporting period. Actual results may differ from those estimates. As applicable to the unaudited condensed consolidated financial statements, the critical accounting estimates relate to the fair value of share-based compensation, measurement of revenue, estimate of uncertain tax positions, and measurement of liabilities accounted for under the interest method.

Functional Currency

The U.S. dollar ("Dollar") is the currency of the primary economic environment in which the operations of the Company 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 condensed consolidated statements of operations as "Interest and other income, net."

Cash and Cash Equivalents; Marketable Securities

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

Cash and cash equivalents and marketable securities totaled $95.9 million as of September 30, 2022. The Company accounts for its investments, which include cash equivalents and marketable securities, as available-for-sale in accordance with the Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 320, "Investments — Debt and Equity Securities". Available-for-sale debt securities are carried at fair value with unrealized gains and losses reported in other comprehensive income/loss within shareholders' equity. Realized gains and losses are recorded as a component of interest and other income, net. The cost of securities sold is based on the specific-identification method.

Certain 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. The majority 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.

For individual debt securities classified as available-for-sale securities where there has been a decline in fair value below amortized cost, the Company determines whether the decline resulted from a credit loss or other factors. The Company records impairment relating to credit losses through an allowance for credit losses, limited by the amount that the fair value is less than the amortized cost basis. Impairment that has not been recorded through an allowance for credit losses is recorded through other comprehensive income, net of applicable taxes.

Restricted cash is related primarily to cash held to secure corporate credit cards; restricted deposits are related to cash held to secure leases.

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 Federal Deposit Insurance Corporation and concentrated within a limited number of financial institutions. The accounts are monitored by management to mitigate the risk.

The Company's product sales are recognized through the Company's arrangement with a single customer, a third-party national specialty distributor. The Company assesses the need for an allowance for doubtful accounts primarily based on creditworthiness, historical payment experience and general economic conditions. The Company has not experienced any credit losses related to this customer and has not currently recognized any allowance for doubtful accounts.

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 it operates, including Israel and the United States. 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. After concluding that a particular filing position can be recognized (i.e., has a more-likely-than-not chance of being sustained), ASC 740-10-30-7 requires that the amount of benefit recognized be measured using a methodology based on the concept of cumulative probability. Under this methodology, the amount of benefit recorded represents the largest amount of tax benefit that is greater than 50% likely to be realized upon settlement with a taxing authority that has full knowledge of all relevant information. See Note 16 for further discussion related to income taxes.

Inventory

The Company capitalizes inventory costs related to products to be sold in the ordinary course of business. The Company makes a determination of capitalizing inventory costs for a product based on, among other factors, status of regulatory approval, information regarding safety, efficacy and expectations relating to commercial sales and recoverability of costs. For *Jelmyto*, the Company commenced capitalization of inventory at the receipt of FDA approval.

The Company values its inventory at the lower of cost or net realizable value. The Company measures inventory approximating actual cost under a first-in, first-out basis. The Company assesses recoverability of inventory each reporting period to determine any write down to net realizable value resulting from excess or obsolete inventories.

Property and Equipment

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

Property and equipment are depreciated over the following useful lives (in years):

	Useful Lives
Computers and software	3
Laboratory equipment	3 - 6.5
Furniture	5 - 16.5
Manufacturing equipment	2 - 10

Leasehold improvements are amortized on a straight-line basis over the shorter of their estimated useful lives or lease terms. See Note 8 for further discussion regarding property and equipment.

Prepaid Forward Obligation

The Company is party to a transaction with RTW Investments (the “RTW Transaction”) in which the Company received funds to support the continued launch of *Jelmyto* and the development of UGN-102 in return for tiered, future cash payments based on net sales of *Jelmyto* and UGN-102, if approved by the FDA. The net proceeds received under the RTW Transaction were recognized as a long-term liability. The subsequent measurement for the liability follows the accounting principles defined in ASC Topic 835-30, “Imputation of Interest”. See Note 9 for further discussion related to the prepaid forward obligation.

Long-Term Debt

The Company is party to a loan agreement with funds managed by Pharmakon Advisors, L.P. (“Pharmakon”). The Company recognizes interest expense in current earnings, and accrued interest within other current liabilities on the condensed consolidated balance sheets. The Company recognizes capitalized financing expenses as a direct offset to the long-term debt on the Company's condensed consolidated balance sheets, and amortizes them over the term of the debt using the effective interest method. See Note 10 for further discussion related to long-term debt.

Leases

The Company is a lessee in several noncancelable operating leases, primarily for office space, office equipment and vehicles. The Company currently has no finance leases.

The Company accounts for leases in accordance with ASC Topic 842, “Leases”. The Company determines if an arrangement is a lease at inception. Right-of-use (“ROU”) assets and operating lease liabilities are recognized based on the present value of lease payments over the lease term as of the commencement date. Operating lease ROU assets are presented as operating lease right-of-use assets on the condensed consolidated balance sheets. The current portion of operating lease liabilities is included in other current liabilities and the long-term portion is presented separately as operating lease liabilities on the condensed consolidated balance sheets.

Lease expense is recognized on a straight-line basis for operating leases. Variable lease payments associated with the Company’s leases are recognized when the event, activity, or circumstance in the lease agreement on which those payments are assessed occurs. Variable lease payments are presented as operating expense on the condensed consolidated statements of operations in the same line item as expense arising from fixed lease payments.

The Company’s lease terms may include options to extend the lease. The lease extensions are included in the measurement of the right-of-use asset and lease liability when it is reasonably certain that it will exercise that option.

Because most of the Company’s leases do not provide an implicit rate of return, an incremental borrowing rate is used based on the information available at the commencement date in determining the present value of lease payments on an individual lease basis. The Company’s incremental borrowing rate for a lease is the rate of interest it would have to pay on a collateralized basis to borrow an amount equal to the lease payments under similar terms.

ROU assets for operating leases are periodically reviewed for impairment losses under ASC 360-10, “Property, Plant, and Equipment”, to determine whether an ROU asset is impaired, and if so, the amount of the impairment loss to recognize.

Revenue

Product sales from *Jelmyto* are recognized as revenue under ASC 606 at the point in time that control of the product has been transferred to the customer, generally at the point the product has been delivered to the treating physician. All product sales of *Jelmyto* are recognized through the Company's arrangement with a single customer, a third-party national specialty distributor. Net revenue recognized include management’s estimate of returns, consideration paid to the customer, chargebacks relating to differences between the wholesale acquisition cost and the contracted price offered to the end consumer, chargebacks relating to 340b drug pricing programs, Medicaid drug rebate programs, and the Company’s copay assistance program, which are estimated based on industry benchmarking studies as well as the Company’s historical experience.

Research and Development Expenses

Research and development costs are expensed as incurred and consist primarily of the cost of salaries, share-based compensation expense, payroll taxes and other employee benefits, subcontractors and materials used for research and development activities, including nonclinical studies, clinical trials, manufacturing costs and professional services. The costs of services performed by others in connection with the research and development activities of the Company, including research and development conducted by others on behalf of the Company, 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 such development milestone results are achieved.

Selling General and Administrative Expenses

Selling, general and administrative expenses consist primarily of personnel costs (including share-based compensation related to directors, employees and consultants). Other significant costs include commercial, medical affairs, external professional service costs, facility costs, accounting and audit services, legal services, and other consulting fees. Selling, 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.

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 options is determined using the Black-Scholes option-pricing model. The fair value of a restricted stock unit (“RSU”) equaled the closing price of the Company’s ordinary shares on the grant date. The Company accounts for forfeitures as they occur in accordance with ASC Topic 718, “Compensation—Stock Compensation”.

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.

Net Loss per Ordinary Share

Basic net loss per share is computed by dividing the net loss attributable to ordinary shareholders by the weighted-average number of ordinary 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 ordinary shares that would have been outstanding if the potential ordinary shares had been issued and if the additional ordinary shares were dilutive.

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

Recently Issued Accounting Pronouncements

The Company has reviewed the Accounting Standards Updates recently issued by the Financial Accounting Standards Board, and determined that they are not applicable to the Company.

Note 4 – Other Financial Information

Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consisted of the following as of September 30, 2022 and December 31, 2021 (in thousands):

	September 30, 2022	December 31, 2021
Accounts payable	$ 2,545	$ 5,786
Accrued sales reserves	687	497
Accrued clinical expenses	2,285	1,377
Accrued research and development expenses	1,118	1,748
Accrued selling, general and administrative expenses	2,139	1,965
Accrued other expenses	582	729
Total accounts payable and accrued expenses	$ 9,356	$ 12,102

Interest and Other Income, Net

Interest and other income, net consisted of the following as of September 30, 2022 and 2021 (in thousands):

	Nine Months Ended September 30,	
	2022	2021
Interest income	$ 469	$ 345
Other income (expense), net	135	(76)
Interest and other income, net	$ 604	$ 269

Note 5 – Inventories

Inventories consisted of the following as of September 30, 2022 and December 31, 2021 (in thousands):

	September 30, 2022	December 31, 2021
Raw materials (1)	$ 5,100	$ 3,894
Finished goods	1,863	1,958
Total inventories	$ 6,963	$ 5,852

(1) $2.1 million and $1.0 million of raw materials are included within other non-current assets on the condensed consolidated balance sheets at September 30, 2022 and December 31, 2021, respectively.

Note 6 – Fair Value Measurements

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 cash, restricted cash, 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 assets and liabilities.

The carrying value of the prepaid forward obligation (See Note 9 - Prepaid Forward Obligation) approximates its fair value. The Company estimated the fair value of the prepaid forward obligation using Level 3 inputs, including internally developed financial forecasts and management's estimate of probability of success related to product candidates, and determined that the effective interest rate in the obligation approximates market rates for loans with similar terms and risk characteristics.

The Company estimated the fair value of long-term debt (see Note 10 - Long-Term Debt) using the income approach with Level 3 inputs. The Company estimated future floating rate interest payments using a forward curve of a three-month benchmark rate, and estimated fair value based on publicly available data reported in the financial statements of publicly traded venture lending companies. Based on a reasonable range of yields for debt instruments of similar tenor in a similar industry, the Company determined that the carrying value of the long-term debt on the Company's balance sheet approximates its fair value.

No transfers between levels have occurred during the periods presented.

Assets measured at fair value on a recurring basis based on Level 1 and Level 2 fair value measurement criteria as of September 30, 2022 are as follows (in thousands):

		Fair Value Measurements Using	
	Balance as of September 30, 2022	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)
Marketable securities			
US government	46,452	46,452	—
Corporate bonds	4,406	—	4,406
Commercial paper	12,312	—	12,312
Certificates of deposit	4,055	—	4,055
Total marketable securities	67,225	46,452	20,773

Assets measured at fair value on a recurring basis based on Level 1 and Level 2 fair value measurement criteria as of December 31, 2021 are as follows (in thousands):

		Fair Value Measurements Using	
	Balance as of December 31, 2021	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)
Assets:			
Cash equivalents			
Money market funds	$ 21,402	$ 21,402	$ —
Marketable securities			
US government	19,307	19,307	—
Corporate bonds	8,652	—	8,652
Commercial paper	14,492	—	14,492
Certificates of deposit	3,003	—	3,003
Total marketable securities	45,454	19,307	26,147
Total assets at fair value	$ 66,856	$ 40,709	$ 26,147

Note 7 – Investments

The following table summarizes the Company's investments as of September 30, 2022 (in thousands):

	Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
Marketable securities:				
US government	$ 46,554	$ —	$ (102)	$ 46,452
Corporate bonds	4,416	—	(10)	4,406
Commercial paper	12,336	—	(24)	12,312
Certificates of deposit	4,074	—	(19)	4,055
Total marketable securities	$ 67,380	$ —	$ (155)	$ 67,225

The Company classifies its investments as available-for-sale and they consist entirely of debt securities. As of September 30, 2022, the amortized cost of investments included an immaterial amount of accrued interest. As of September 30, 2022, marketable securities were in a net unrealized loss position. Unrealized gains and losses on available-for-sale debt securities are included as a component of comprehensive loss.

As of September 30, 2022, the aggregate fair value of investments held by the Company in an unrealized loss position was $64.9 million which consisted of 28 securities. The unrealized loss was primarily driven by rising interest rates. The Company does not expect to settle the debentures at a price less than the amortized cost basis of the investment; the Company expects to recover the entire amortized cost basis of the security. In accordance with the Company's general investment strategy, the Company does not intend to sell the investments before maturity. As of September 30, 2022, the Company believes the cost basis for its marketable securities were recoverable in all material aspects and no credit losses were recognized in the period.

The Company's investments as of September 30, 2022 mature at various dates through August 2023. The fair values of investments by contractual maturity consist of the following (in thousands):

	September 30, 2022	December 31, 2021
Maturities within one year	$ 67,225	$ 44,779
Maturities after one year through three years	—	675
Total investments	$ 67,225	$ 45,454

Note 8 – Property and Equipment

Property and equipment, consists of the following as of September 30, 2022 and December 31, 2021 (in thousands):

	September 30, 2022	December 31, 2021
Laboratory equipment	$ 444	$ 360
Computer equipment and software	2,168	2,064
Furniture	597	597
Leasehold improvements	617	617
Manufacturing equipment	607	555
	4,433	4,193
Less: accumulated depreciation and amortization	(2,914)	(2,226)
Property and equipment, net	$ 1,519	$ 1,967

Depreciation and amortization expense was $0.2 million and $0.7 million for the three and nine months ended September 30, 2022 and $0.2 million and $0.6 million for the three and nine months ended September 30, 2021.

Note 9 – Prepaid Forward Obligation

In March 2021, the Company entered into a prepaid forward agreement with RTW Investments ("RTW"). Under the terms of the RTW Transaction, the Company received $75.0 million ($72.4 million net of transaction costs) to support the continued launch of *Jelmyto* and the development of UGN-102. In return for the transferred funds, RTW is entitled to receive tiered, future cash payments based on aggregate worldwide annual net product sales of *Jelmyto* in an amount equal to: (i) 9.5% of annual net sales up to $200 million, (ii) 3.0% of annual net sales for annual net sales between $200 million and $300 million, and (iii) 1.0% of annual net sales for annual net sales above $300 million. If certain revenue thresholds for *Jelmyto* aggregate worldwide annual net sales are not met, the future cash payments to RTW with respect to *Jelmyto* annual net sales up to $200 million will increase by 3.5%, and may decrease back to 9.5% dependent on the Company meeting certain subsequent *Jelmyto* aggregate worldwide annual net sales thresholds. The rate in effect for the nine months ended September 30, 2022 for annual sales up to $200 million was 13.0%.

In addition, subject to FDA approval of UGN-102, RTW is entitled to receive tiered, future cash payments based on aggregate worldwide annual net product sales of UGN-102 in an amount equal to: (i) 2.5% of annual net sales up to $200 million, (ii) 1.0% of annual net sales for annual net sales between $200 million and $300 million, and (iii) 0.5% of annual net sales for annual net sales above $300 million. If the Company does not receive FDA approval for UGN-102 by a specified date, the future cash payments to RTW with respect to aggregate worldwide annual net sales of *Jelmyto* across all *Jelmyto* annual net sales tiers will increase by 1.5%.

In accordance with the prepaid forward agreement, the Company will be required to make payments of amounts owed to RTW each calendar quarter, through and until the quarter in which the aggregate cash payments received by RTW are equal to or greater than $300 million. As security for the payment and fulfilment of these amounts throughout the arrangement, the Company has granted RTW a first priority security interest in *Jelmyto* and UGN-102, including the regulatory approvals, intellectual property, material agreements, proceeds and accounts receivable related to these products.

In May 2021, following the receipt of necessary regulatory approvals, the Company received the $75.0 million prepaid forward payment ($72.4 million net of transaction costs) from RTW and recognized an associated prepaid forward obligation liability. Each period the Company makes a payment to RTW, an expense is recognized related to financing on the prepaid forward obligation based on an imputed rate derived from the expected future payments. Management reassesses the effective rate each period based on the current carrying value of the obligation and the revised estimated future payments. Changes in future payments from previous estimates are included in future financing expense. The Company does not expect to make any principal payments in the next 12 months.

The following table shows the activity with respect to the carrying value of the prepaid forward liability, in thousands:

Prepaid forward obligation at closing of RTW Transaction	$ 75,000
Capitalized closing costs	(2,599)
Financing on prepaid forward obligation	17,291
Amounts paid and payable	(3,979)
Carrying value of prepaid forward obligation as of December 31, 2021	85,713
Financing on prepaid forward obligation	16,478
Amounts paid and payable	(5,999)
Carrying value of prepaid forward obligation as of September 30, 2022	$ 96,192

Note 10 – Long-Term Debt

On March 7, 2022, the Company entered into a loan agreement with Pharmakon for a senior secured term loan of up to $100 million in two tranches. The first tranche of $75 million was funded in March 2022. At its option, the Company may draw up to an additional $25 million before December 31, 2022, subject to customary bring down conditions and deliverables. The facility will mature five years from initial funding and can be prepaid in whole at the Company's discretion, at any time, subject to prepayment premiums and make-whole amounts. The loan will require interest-only payments for the first 48 months followed by principal and interest payments with interest accruing using 3-month London Inter-Bank Offered Rate ("LIBOR") (with a 1.25% floor) plus 8.25%. In the event of the cessation of LIBOR, the benchmark governing the interest rate will be replaced with a rate based on the secured overnight financing rate published by the Federal Reserve Bank of New York. The Company is not required to maintain any financial covenants.

The Company incurred financing expenses of $4.2 million which are recognized as a direct offset to the long-term debt on the Company's condensed consolidated balance sheet. These debt issuance costs are amortized over the term of the debt using the effective interest method, and are recorded in the condensed consolidated statements of operations as "Interest expense".

The following table shows the activity with respect to the carrying value of the long-term debt, in thousands:

Long-term debt at closing of Pharmakon loan	$	75,000
Capitalized costs and discounts		(4,207)
Interest expense		5,215
Amounts paid and payable		(4,138)
Carrying value of Pharmakon loan as of September 30, 2022	$	71,870

Note 11 – Leases

Operating Leases

The Company had the following office and laboratory facility leases as of September 30, 2022:

- In April 2016, UPL signed an addendum to its November 2014 lease agreement for the Company's offices located in Israel, in order to increase the office space rented and to extend the rent period until 2019. In March 2019, UPL utilized the agreement extension option and extended the rent period for an additional three years until August 2022. In July 2022, the Company signed a lease extension agreement for the Company's offices located in Israel, extending the term of the lease through September 2025. The Company's remaining contractual obligation under this lease is approximately $0.9 million as of September 30, 2022.

- In September 2017, UPI entered into a new lease agreement for its office space in New York, which the Company previously used as its headquarters. The lease agreement commenced in October 2017 and terminated in February 2021.

- In April 2018, UPI entered into a new lease agreement for an office in Los Angeles, California. The lease commencement date was July 10, 2018 and terminates in March 2024. The landlord provided a tenant allowance for leasehold improvements of $0.2 million that was accounted for as a lease incentive. The Company's remaining contractual obligation under this lease is approximately $0.4 million as of September 30, 2022. In November 2019, UPI entered into a sublease for this office space, with a lease commencement date of January 1, 2020 and continuing until the end of the lease term in March 2024. The subtenants exercised their early access clause and moved into the premises at the end of November 2019. The remaining rental payments to be received over the lease term is approximately $0.4 million as of September 30, 2022. The Company accounts for the sublease as an operating lease in accordance with ASC 842-10-25-2 and ASC 842-10-25-3. The main lease was considered for impairment and the amount was determined to be immaterial.

- In November 2019, UPI entered into a new lease agreement for an office in Princeton, New Jersey, which the Company now uses as its headquarters. The lease commencement date was November 29, 2019, with an original lease term of 38 months, expiring January 31, 2023. In June 2022, the Company signed a lease extension for the Princeton office, extending the term of the lease through January 31, 2026. The Company's remaining contractual obligation under this lease is approximately $1.9 million as of September 30, 2022.

In addition, the Company has other operating office equipment and vehicle leases. The Company's operating leases may require minimum rent payments, contingent rent payments adjusted periodically for inflation, or rent payments equal to the greater of a minimum rent or contingent rent. The Company's leases do not contain any residual value guarantees or material restrictive covenants. The Company's leases expire at various dates from 2022 through 2026, with varying renewal and termination options.

The components of lease cost for the three and nine months ended September 30, 2022 and 2021 were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating lease cost	$ 219	$ 259	$ 735	$ 786
Sublease income	(56)	(56)	(168)	(168)
Variable lease cost	16	15	52	51
	$ 179	$ 218	$ 619	$ 669

The amounts recognized as of September 30, 2022 and December 31, 2021 were as follows (in thousands):

	September 30, 2022	December 31, 2021
Right of use assets	$ 2,666	$ 1,180
Long-term lease liabilities	1,856	398
Other current liabilities	940	1,089

As of September 30, 2022, no impairment losses have been recognized to date.

Supplemental information related to leases for the nine months ended September 30, 2022 and 2021 is as follows (in thousands):

	Nine Months Ended September 30,	
	2022	2021
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows from operating leases	3,926	2,734
Right-of-use assets obtained in exchange for new operating lease liabilities	2,606	135
Weighted-average remaining lease term of operating leases (in years)	2.95	1.68
Weighted-average discount rate of operating leases	10.21%	5.51%

As of September 30, 2022, maturities of lease liabilities were as follows (in thousands):

	Operating Leases
Years ending December 31,	
Remainder of 2022	$ 300
2023	1,161
2024	918
2025	799
2026 and thereafter	49
Total future minimum lease payments	$ 3,227
Less: Interest	(431)
Present value of lease liabilities	$ 2,796

Subleases

As of September 30, 2022, undiscounted cash flows to be received under the Company's operating sublease on an annual basis were as follows (in thousands):

	Operating Leases
Years ending December 31,	
Remainder of 2022	$ 61
2023	251
2024	49
2025	—
2026 and thereafter	—
	$ 361

Sublease income is recognized net within operating expenses. Sublease income for the three and nine months ended September 30, 2022 and 2021 was as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Sublease income from fixed lease payments	$ 56	$ 56	$ 168	$ 168

Note 12 – Revenue From Product Sales

Net product sales consist of the following for the three and nine months ended September 30, 2022 and 2021 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Jelmyto	$ 16,097	$ 11,351	$ 46,265	$ 31,868

Net revenue recognized includes management's estimate of returns, consideration paid to the customer, chargebacks relating to differences between the wholesale acquisition cost and the contracted price offered to the end consumer, chargebacks relating to 340b drug pricing programs, Medicaid drug rebate programs, and the Company's copay assistance program, which are estimated based on industry benchmarking studies as well as the Company's historical experience. Reserves related to items that are contractually able to be net settled are recognized as contra accounts receivables. The following table shows the activity with respect to sales reserves for period ended of September 30, 2022 (in thousands):

	Reserves related to government sponsored programs	Other reserves	Total accrued sales reserves
Balance as of December 31, 2021	$ 373	$ 1,335	$ 1,708
Accruals	4,410	4,432	8,842
Utilizations	(4,226)	(3,999)	(8,225)
Balance as of September 30, 2022	$ 557	$ 1,768	$ 2,325

Note 13 – License and Collaboration Agreements

Agenus Agreement

In November 2019, the Company entered into a license agreement with Agenus Inc., pursuant to which Agenus granted to the Company an exclusive, worldwide (not including Argentina, Brazil, Chile, Colombia, Peru, Venezuela and their respective territories and possessions), royalty-bearing, sublicensable license under Agenus's intellectual property rights to develop, make, use, sell, import, and otherwise commercialize products incorporating a proprietary monoclonal antibody of Agenus known as AGEN1884 (zalifrelimab), an anti-CTLA-4 antagonist, for the treatment of cancers of the urinary tract via intravesical delivery. Initially, the Company plans to develop AGEN1884 in combination with UGN-201 for the treatment of high-grade NMIBC.

Pursuant to the license agreement, the Company paid Agenus an upfront fee of $10.0 million and has agreed to pay Agenus up to $115.0 million upon achieving certain clinical development and regulatory milestones, up to $85.0 million upon achieving certain commercial milestones, and royalties on net sales of licensed products in the 14%-20% range. The Company will be responsible for all development and commercialization activities. Under the terms of the license agreement, Agenus has agreed to use commercially reasonable efforts to supply AGEN1884 to the Company for use in preclinical studies or clinical trials.

Unless earlier terminated in accordance with the terms of the license agreement, the license agreement will expire on a product-by-product and country-by-country basis at the later of (a) the expiration of the last to expire valid claim of a licensed patent right that covers the licensed product in such country or (b) 15 years after the first commercial sale of the licensed product in such country. The Company may terminate the license agreement for convenience upon 180 days' written notice to Agenus. Either party may terminate the license agreement upon 60 days' notice to the other party if, prior to the first commercial sale of a licensed product, the Company substantially ceases to conduct development activities of the licensed products for nine consecutive months (and during such period, Agenus has complied with its obligations under the license agreement) other than in response to a requirement of an applicable regulatory authority or an event outside of the Company's control. In addition, either party may terminate the license agreement in the event of an uncured material breach of the other party.

MD Anderson Agreement

In January 2021, the Company announced that it entered into a three-year strategic research collaboration agreement with MD Anderson focusing on the sequential use of UGN-201 and UGN-301 as an investigational treatment for high-grade NMIBC. Under the terms of the agreement, MD Anderson and the Company will collaborate on the design and conduct of non-clinical and clinical studies with oversight from a joint steering committee. The Company will provide funding, developmental candidates, and other support. Pursuant to the agreement, the Company makes bi-annual payments to MD Anderson to fund the collaboration. As of September 30, 2022, the Company has made payments to MD Anderson totaling $2.0 million recognized evenly over the associated period through research and development expenses. In July 2022, the Company determined that it had achieved the objectives that it established when the agreement was initiated, and notified MD Anderson that it was exercising its right to conclude the collaboration in 2022 as the Company did not foresee initiating further development activities as part of the collaboration, although the Company will continue to collaborate on existing joint projects. As a result of this notification, the Company is not responsible for any further fixed bi-annual funding payments, although the Company will be responsible for costs related to existing joint projects that exceed the payments already made to MD Anderson.

Note 14 – Shareholders' Equity

The Company had 100.0 million ordinary shares authorized for issuance as of September 30, 2022 and December 31, 2021. The Company had 23.0 million and 22.5 million ordinary shares issued and outstanding as of September 30, 2022 and December 31, 2021, 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 (the "Board"). Since its inception, the Board has not declared any dividends.

Note 15 – Share-Based Compensation

In October 2010, the Board approved a share option plan (the "2010 Plan") for grants to Company employees, consultants, directors, and other service providers. Subsequently, in March 2017, the Board adopted the 2017 Equity Incentive Plan (the "2017 Plan" and, together with the 2010 Plan, the "Plans"), which was approved by the shareholders in April 2017. The 2017 Plan provides for the grant of stock options, stock appreciation rights, restricted stock awards, RSU awards, performance share awards, performance cash awards, and other forms of share awards to the Company's employees, directors and consultants.

The grant of options to Israeli employees under the Plans 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 Plans 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 Plans, 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 Plans are subject to Section 3(i) of the Israeli Income Tax Ordinance.

Employees are typically granted stock options and/or restricted stock units ("RSUs"), upon commencement of employment. Also, eligible employees may receive an annual grant of options or RSUs. Non-employee members of the Board typically receive a grant of stock options upon initial appointment to the Board, and stock options annually. The term of any option granted under the Plans 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 equity of the Company, the exercise price shall not be less than 110% of the fair market value of an ordinary share on the date of grant.

The Company's RSU and 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 either equal quarterly or annual amounts for the two years following the one-year anniversary of the grant date. Options generally vest in a 33% increment upon the first anniversary of the grant date, and in either equal quarterly or annual amounts for the two years following the one-year anniversary of the grant date.

The expected volatility is based on a mix of the Company's historical volatility, and 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.

The maximum number of ordinary shares that was initially authorized for issuance under the 2017 Plan was 1,400,000. On January 1, 2018, the share reserve increased by 250,167 to 1,650,167 shares. On October 12, 2018, the Company increased the amount of ordinary shares authorized for issuance under the 2017 Plan by 1,900,000 to 3,550,167 shares. On June 8, 2020 the Company's shareholders approved an increase to the amount of ordinary shares authorized for issuance under the 2017 Plan by 400,000 to 3,950,167 shares. On June 7, 2021, the Company's shareholders approved an increase to the amount of ordinary shares authorized for issuance under the 2017 Plan by 400,000 to 4,350,167 shares. On June 8, 2022, the Company's shareholders approved an increase to the amount of ordinary shares authorized for issuance under the 2017 Plan by 400,000 to 4,750,167 shares.

In May 2019, the Company adopted the UroGen Pharma Ltd. 2019 Inducement Plan (the "Inducement Plan"). Under the Inducement Plan, the Company is authorized to issue up to 900,000 ordinary shares pursuant to inducement awards. The only persons eligible to receive grants under the Inducement Plan are individuals who satisfy the standards for inducement grants under Nasdaq Marketplace Rule 5635(c)(4) and the related guidance under Nasdaq IM 5635-1, including individuals who were not previously an employee or director of the Company or are following a bona fide period of non-employment, in each case as an inducement material to such individual's agreement to enter into employment with the Company. In December 2021, the Board approved a 300,000 increase in the share reserve of the Inducement Plan.

As of September 30, 2022, 3,442,209 ordinary shares are subject to outstanding awards under the Company's share-based compensation plans and 1,601,242 ordinary shares remain available for future awards.

The following table illustrates the effect of share-based compensation on the condensed consolidated statements of operations (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Research and development expenses	$ 642	$ 971	$ 2,040	$ 3,119
Selling, general and administrative expenses	1,798	4,544	6,172	14,637
	$ 2,440	$ 5,515	$ 8,212	$ 17,756

The total unrecognized compensation cost of options and RSUs at September 30, 2022 is $12.2 million with a weighted average recognition period of 1.67 years.

Note 16 – **Income Taxes**

UroGen Pharma Ltd. is taxed under Israeli tax laws. As of September 30, 2022, the Company continues to maintain a full valuation allowance against deferred tax assets for all jurisdictions. In evaluating the need for a valuation allowance, the Company considers all sources of taxable income available to realize the deferred tax asset, including the future reversal of existing temporary differences, forecasts of future taxable income, and tax planning strategies. The Company has cumulative global pretax losses for the years ended 2021, 2020 and 2019, and for the nine months ended September 30, 2022. The Company will continue to assess the extent to which its deferred tax assets may be realized in the future and will adjust the valuation allowance as needed.

The Company has a liability for uncertain tax positions of $2.8 million as of September 30, 2022, for tax positions relating to transfer pricing between affiliated entities. The Company recognizes interest accrued and penalties related to uncertain tax positions as a component of income tax expense. As of September 30, 2022, the Company's liability for uncertain tax positions includes $0.9 million of accrued interest and penalties.

The Company operates on a global basis and is subject to tax laws and regulations in the United States and Israel. The estimate of the Company's tax liabilities relating to uncertain tax positions requires management to assess uncertainties and to make judgments about the application of complex tax laws and regulations, expectations regarding the outcome of tax authority examinations, as well as the ultimate measurement of potential liabilities.

The uncertain tax positions are reviewed quarterly and adjusted as events occur that could affect potential liabilities for additional taxes, including lapsing of applicable statutes of limitations, correspondence with tax authorities, proposed assessments by tax authorities, identification of new issues, and issuance of new legislation or regulations. The Company believes that adequate amounts of tax have been provided in income tax expense for any adjustments that may result from its uncertain tax positions. Based upon the information currently available, the Company does not reasonably expect changes in its existing uncertain tax positions in the next 12 months and has recorded the gross uncertain tax positions as a long-term liability.

Note 17 – **Related Parties**

There were no related party transactions for the nine months ended September 30, 2022 or 2021.

Note 18 – **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 September 30, 2022 and December 31, 2021. The Company does not anticipate recognizing any significant losses relating to these arrangements.

Leases

See Note 11 for further discussion regarding lease commitments.

Note 19 – **Subsequent Events**

On October 21, 2022, the Company requested the advance of the second tranche (the "Tranche B Loan") under the Pharmakon loan agreement in the amount of $25.0 million. The funding of the Tranche B Loan is expected to occur on December 16, 2022, subject to customary bring down conditions and deliverables. The proceeds of the Tranche B Loan will be used to fund the Company's general corporate and working capital requirements.

The Company has evaluated and determined there were no further subsequent events.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited condensed consolidated financial statements and related notes included in this Quarterly Report and the audited financial statements and notes thereto as of and for the year ended December 31, 2021 and the related Management's Discussion and Analysis of Financial Condition and Results of Operations, both of which are contained in our Annual Report on Form 10-K for the year ended December 31, 2021 ("Annual Report"), which was filed with the SEC on March 21, 2022. The information in this discussion contains forward-looking statements and information within the meaning of Section 27A of the Securities Act of 1933, as amended ("Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended ("Exchange Act"), which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to, statements concerning our strategy, future operations, future financial position, future revenues, trends, seasonality, projected costs, prospects and plans and objectives of management. The words "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation, the risks set forth in Part II, Item 1A, "Risk Factors" in this Quarterly Report. 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 Quarterly 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. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements.

Overview

We are a biotechnology company dedicated to developing and commercializing innovative solutions that treat urothelial and specialty cancers. We have developed *RTGel*® reverse-thermal hydrogel, a proprietary sustained release, hydrogel-based technology that has the potential to improve therapeutic profiles of existing drugs. Our technology is designed to enable longer exposure of the urinary tract tissue to medications, making local therapy a potentially more effective treatment option. Our approved product *Jelmyto*® (mitomycin) for pyelocalyceal solution, and our investigational candidate, UGN-102 (mitomycin) for intravesical solution, are designed to ablate tumors by non-surgical means and to treat several forms of non-muscle invasive urothelial cancer, including low-grade upper tract urothelial cancer ("low-grade UTUC") and low-grade intermediate risk non-muscle invasive bladder cancer ("low-grade intermediate risk NMIBC"), respectively. In addition, our immuno-uro-oncology pipeline includes UGN-301 (zalifrelimab), an anti-CTLA-4 antibody, which we intend to study as a combination therapy with multiple potential agents.

We estimate that the annual treatable patient population of low-grade UTUC in the United States is approximately 6,000 to 7,000; the estimated annual treatable population of low-grade intermediate risk NMIBC is approximately 80,000.

RTGel is 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 warmed to body temperature. 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, forming a transient reservoir of drug that disintegrates over time while preventing rapid excretion, providing for increased dwell time. *RTGel* leverages the physiologic flow of urine to provide a natural exit from the body.

We believe that *RTGel*, when formulated with an active drug, may allow for the improved efficacy of treatment of various types of urothelial and specialty cancers and urologic diseases without compromising the safety of the patient or interfering with the natural flow of fluids in the urinary tract. *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 up to 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 *Jelmyto* and UGN-102. 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.

Jelmyto

On April 15, 2020, the FDA approved our new drug application ("NDA") for *Jelmyto* (mitomycin) for pyelocalyceal solution, formerly known as UGN-101, for the treatment of adult patients with low-grade UTUC. *Jelmyto* consists of mitomycin, an established chemotherapy, and sterile hydrogel, using our proprietary sustained release *RTGel* technology. It has been designed to prolong exposure of urinary tract tissue to mitomycin, thereby enabling the treatment of tumors by non-surgical means. New product exclusivity for *Jelmyto* exists through April 15, 2023, Orphan Drug exclusivity through April 15, 2027, as well as a composition of matter patent set to expire in early 2031. The main patents that protect *Jelmyto* in the United States are set to expire on January 20, 2031. These patents were listed in the FDA's Orange Book (Approved Drug Products with Therapeutic Equivalence Evaluations).

Low-grade UTUC is a rare cancer that develops in the lining of the upper urinary tract, ureters and kidneys. In the United States, there are approximately 6,000 - 7,000 new or recurrent low-grade UTUC patients annually. It is a challenging condition to treat due to the complex anatomy of the urinary tract system. Prior to *Jelmyto*, the current standard of care included endoscopic resection(s) and radical nephroureterectomy, which involves the removal of the renal pelvis, kidney, ureter and bladder cuff. Treatment is further complicated by the fact that low-grade UTUC is most commonly diagnosed in patients over 70 years of age, who may already have compromised kidney function and may suffer further complications as a result of a major surgery. We are focused on changing the way urothelial cancers are treated, an area in which there has been no significant advancements in recent years. *Jelmyto* is the first drug therapy of its kind, providing an alternative to endoscopic resection(s) and/or radical nephroureterectomy.

The FDA approval is based on results from our Phase 3 OLYMPUS trial showing *Jelmyto* achieved clinically significant disease eradication in adults with low-grade UTUC. Findings from the final study results include:

- Complete response ("CR") (primary endpoint) of 58% (41/71) in the intent-to-treat population and in the sub-population of patients who were deemed not capable of surgical removal at diagnosis.
- At the 12-month time point for assessment of durability, 23 patients remained in CR of a total of 41 patients, eight had experienced recurrence of disease and ten patients were unable to be evaluated.
- Durability of response was estimated to be 81.8% at 12 months by Kaplan-Meier analysis. The median duration of response was not reached.
- The most commonly reported adverse events (≥ 20%) were ureteric obstruction, flank pain, urinary tract infection, hematuria, abdominal pain, fatigue, renal dysfunction, nausea, dysuria and vomiting. Most adverse events were mild to moderate and manageable using well established treatments. No treatment-related deaths occurred.

In June 2020, we initiated our commercial launch of *Jelmyto* in the United States. We have staffed, trained and prepared a customer-facing team that includes territory business managers with deep experience in both urology and oncology. These territory business managers are led by seven regional business directors. Each region is additionally supported by one to two clinical nurse educators to provide education and training around instillation, as well as a field reimbursement manager to help ensure access and reimbursement for appropriate patients. In addition, our organization currently includes several medical science liaisons who appropriately engage with physicians interested in learning more about UroGen, *Jelmyto* and our technology, both in person and virtually. In total, our customer-facing team comprises approximately 80 colleagues.

We are committed to helping patients access *Jelmyto*. Our market access teams have laid the foundation for coverage and reimbursement, meeting multiple times with payors. All Medicare patients are covered and the vast majority of commercial plans have policies in place, in whole covering over 150 million lives. In addition to reimbursement and access, we have also been focused on ensuring seamless integration into physician practices. We have implemented processes to help make *Jelmyto* preparation and administration safe and seamless for practitioners and patients, including entering into an agreement with a major national specialty pharmacy under which the pharmacy, following receipt of a patient prescription, prepares the *Jelmyto* admixture on our behalf. In September 2022, the FDA authorized an extension of the in-use period for Jelmyto admixture from eight hours to 96 hours (four days) following reconstitution of the product, adding convenience and flexibility in managing patient care. In October 2020, a Medicare C-Code was issued for *Jelmyto*. The Centers for Medicare & Medicaid Services established a permanent and product-specific J-code for *Jelmyto* that took effect on January 1, 2021, and replaced the C-Code. We have also launched a registry to capture data and evaluate real world outcomes in patients with low-grade UTUC that have been or will be treated with *Jelmyto*. The purpose of the registry is to study the use of *Jelmyto* in clinical practice in the United States and address specific clinical questions.

In the first two full fiscal years following the initiation of our commercial launch of *Jelmyto* in June 2020, we have experienced a moderate decline in revenue during the third quarter from the preceding quarter. We believe this result is primarily attributable to the nature of low-grade disease, which does not require immediate treatment and therefore we believe there is an impact in the summer months. However, it is too early to say with confidence whether this seasonality trend will continue in future periods. Moreover, our future *Jelmyto* revenue will be impacted by various factors and we expect our *Jelmyto* revenue to fluctuate quarter-to-quarter for the foreseeable future.

UGN-102 (mitomycin) for intravesical solution

UGN-102 is our sustained-release formulation of mitomycin that we are developing for the treatment of low-grade intermediate risk NMIBC.

In October 2021, we reported final data from the Phase 2b OPTIMA II trial. The single-arm, open label trial completed enrollment of 63 patients at clinical sites across the United States and Israel in September 2019. Patients were treated with six weekly instillations of UGN-102 and underwent assessment of CR (the primary endpoint) four to six weeks following the last instillation. Consistent with our previous reports showing that 65%, or 41 out of 63 patients, treated with UGN-102 achieved a complete response three months after the start of therapy. In this subset of patients, 39 (95%), 30 (73%), and 25 (61%) remained disease-free at six, nine, and 12 months after treatment initiation, respectively. The probability of durable response nine months after CR (12 months after treatment initiation) was estimated to be 72.5% by Kaplan-Meier analysis. Thirteen patients had documented recurrences. Fifty-seven of 63 (90%) patients completed all six instillations of UGN-102 according to study protocol. Median duration of response was not reached. The most common adverse events, greater than 10%, were most often reported as mild to moderate in severity and include dysuria, hematuria, urinary frequency, fatigue, urgency and urinary tract infection. The final data was published online in The Journal of Urology in October 2021 and was included in the January 2022 print edition.

Urothelial cancer, which is comprised of bladder cancer and UTUC, affects a large, and what we believe to be, an underserved patient population. Annual expenditures for Medicare alone in the United States for the treatment of urothelial cancer were estimated to be at least $5.0 billion in 2020. The majority of the expenditures are spent on tumor resection surgeries such as transurethral resection of bladder tumor ("TURBT"). The prevalence of bladder cancer in the United States based on most recently published data was approximately 724,000 and estimated 2021 annual incidence of bladder cancer was approximately 85,000. We estimate based upon a review of peer-reviewed literature and publicly available data that there are approximately 80,000 low-grade intermediate risk NMIBC patients in the United States annually. We believe that UGN-102 has the potential to be a new therapeutic option for the treatment of low-grade intermediate risk NMIBC patients.

UGN-102 is administered locally using the standard practice of intravesical instillation directly into the bladder via a catheter. The instillation into the bladder is expected to take place in a physician’s office as a non-operative same-day treatment, in comparison with TURBT or similar surgical procedures, which are operations conducted under general anesthesia and may require 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.

We initiated the Phase 3 ATLAS trial in December 2020 and until November 2021, were enrolling patients in this trial comparing UGN-102 with or without TURBT to standard of care, TURBT. In parallel, we continued to engage in discussions with the FDA and, based on this dialogue, we designed a trial in order to demonstrate the efficacy and safety of UGN-102. This new Phase 3 ENVISION trial is a single-arm, multinational, multicenter study evaluating the efficacy and safety of UGN-102 as primary chemoablative therapy in patients with low-grade intermediate risk NMIBC. The design for the Phase 3 ENVISION trial is similar to our Phase 2 OPTIMA II trial in that the patient population will have similar clinical characteristics, receive the same treatment regimen and undergo the same efficacy and safety assessments and qualitative follow-up. Study participants will receive six once-weekly intravesical instillations of UGN-102. The planned primary endpoint will evaluate the complete response rate at three months after the first instillation, and the key secondary endpoint will evaluate durability over time in patients who achieve complete response at the three-month assessment.

In February 2022, we announced the initiation of the Phase 3 ENVISION trial, which is expected to enroll approximately 220 patients across 90 sites, with completion of enrollment expected by the end of 2022. Assuming positive findings, we anticipate submitting an NDA for UGN-102 in 2024. In November 2021, as a result of the FDA's acceptance of a single arm approach (the ENVISION Trial), we stopped enrollment of the Phase 3 ATLAS study. However, at the time enrollment was stopped, any patients who had signed an informed consent were able to complete screening, and if eligible were randomized into the trial. Patients continue to be followed in the Phase 3 ATLAS study, and clinical results from these patients are expected to generate additional safety data and other insights in our evaluation of UGN-102 as a primary therapy in the treatment of low-grade intermediate risk NMIBC.

We have also initiated a Phase 3b study with the objective of demonstrating whether UGN-102 can be administered at home by a qualified home health professional, avoiding the need for repeated visits to a healthcare setting for instillation. Patients in the ongoing Phase 3b study will receive six once-weekly intravesical instillations of UGN-102. The Phase 3b study aims to enroll up to 10 patients across four centers, with completion of enrollment anticipated by the end of 2022. The initial treatment visit will occur at the investigative site and instillation will be performed by a qualified physician. Treatment visits two to six will take place at the patient's home and instillation will be performed by a properly trained and qualified home health professional. The primary endpoint of the study is the incidence of treatment-emergent adverse events ("TEAEs"), serious TEAEs, TEAEs of special interest, discontinuations from at home study treatment, and clinically significant abnormalities in laboratory tests (hematology, serum chemistry, and urinalysis). We believe establishing a precedent for a convenient at home solution may facilitate access-to-care and address quality of life issues that certain patients may face with the current standard of care.

UGN-301 (zalifrelimab) intravesical solution

Our immuno-uro-oncology pipeline includes UGN-301, an anti-CTLA-4 monoclonal antibody, which we intend to study as a combination therapy with multiple potential agents. Non-human primate toxicity studies supported the initiation of a multi-arm Phase 1 study of UGN-301 in combination with other agents. We believe that this approach leverages our unique drug delivery technology and provides an opportunity to evaluate intravesical delivery of UGN-301 in combination with other immuno-modulators, chemotherapies, gene therapy and innate immune stimulators.

High-grade NMIBC is a highly aggressive form of bladder cancer. TURBT followed by adjuvant intravesical immunotherapy with Bacillus of Calmette and Guerin ("BCG") is the current standard of care therapy for high-grade NMIBC. However, the high rates of recurrence and significant risk of progression to muscle-invasive tumors are particularly dangerous. Radical cystectomy, or bladder removal is strongly advocated in patients with BCG-unresponsive NMIBC (i.e., patients with BCG-refractory and BCG-relapsing tumors in whom further BCG therapy is not recommended) or for patients who cannot tolerate BCG.

The first combination we are seeking to investigate clinically involves the sequential use of UGN-201 (imiquimod), a toll-like receptor-7 ("TLR 7") agonist, and UGN-301 in high-grade NMIBC ("high-grade NMIBC"). UGN-201 is a liquid formulation of imiquimod for intravesical administration that has been optimized for delivery in the urinary tract. We believe that UGN-201 may elicit an innate immune response in the presence of released bladder cancer antigens, which may translate into a long lasting acquired immune response. We believe the combination of UGN-301 and UGN-201 could elicit an innate as well as adaptive immune response and potentially represent a valid post-

TURBT adjuvant treatment of high-grade NMIBC. UGN-301 is delivered using our proprietary *RTGel* technology, which has been designed to significantly improve the effectiveness of certain intravesical therapy. In November 2019, we entered into a worldwide license agreement with Agenus Inc. to develop and commercialize zalifrelimab via intravesical delivery for the treatment of urinary tract cancers, initially in high-grade NMIBC. We believe that the combination of UGN-301 and UGN-201 makes local therapy a potentially more effective treatment option while minimizing systemic exposure and potential side effects.

In March 2022, we announced FDA clearance of our Investigational New Drug application ("IND") to begin a novel Phase 1 clinical study of UGN-301 in patients with recurrent NMIBC. The novel study design will utilize a Master Protocol that we believe is a more efficient and streamlined approach to development. It will provide more flexibility to add study arms as the trial progresses and is expected to increase efficiency and potentially reduce costs. We expect the Master Protocol will allow the Company to more quickly evaluate safety, tolerability and dosing of UGN-301 in combination with additional immunomodulators and chemotherapies, with the goal of developing optimized treatment regimens for patients. The multi-arm Phase 1 study, which is expected to support the development of UGN-301 in high-grade NMIBC, was initiated in April 2022 and is actively enrolling.

Our Research and Development and License Agreements

Agenus Agreement

In November 2019, we entered into a license agreement with Agenus Inc., pursuant to which Agenus granted us an exclusive, worldwide (not including Argentina, Brazil, Chile, Colombia, Peru, Venezuela and their respective territories and possessions), royalty-bearing, sublicensable license under Agenus's intellectual property rights to develop, make, use, sell, import, and otherwise commercialize products incorporating a proprietary monoclonal antibody of Agenus known as AGEN1884 (zalifrelimab), an anti-CTLA-4 antagonist, for the treatment of cancers of the urinary tract via intravesical delivery. UGN-301 is a formulation of zalifrelimab administered using *RTGel* technology that is in Phase 1 clinical development for high-grade NMIBC.

MD Anderson Agreement

In January 2021, we announced that we had entered into a three-year strategic research collaboration agreement with MD Anderson focusing on the sequential use of UGN-201 and UGN-301 as an investigational treatment for high-grade NMIBC. Under the terms of the agreement, we and MD Anderson agreed to collaborate on the design and conduct of non-clinical and clinical studies with oversight from a joint steering committee. We agreed to provide funding, developmental candidates, and other support. Pursuant to the agreement, we have made bi-annual payments to MD Anderson to fund the collaboration, totaling $2.0 million and recognized evenly over the associated period through research and development expenses. In July 2022, we determined that we had achieved the objectives that we established when the agreement was initiated, and notified MD Anderson that we were exercising our right to conclude the collaboration in 2022 as we did not foresee initiating further development activities as part of the collaboration, although we will continue to collaborate on existing joint projects. As a result of this notification, we are not responsible for any further fixed bi-annual funding payments, although we will be responsible for costs related to existing join projects that exceed the payments already made to MD Anderson.

For additional information regarding our research and development and license agreements, see Note 13 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report.

Impact of COVID-19 Pandemic

COVID-19 could have a detrimental impact on our ongoing and future clinical trials, our ongoing commercial launch and future commercialization activities for *Jelmyto*, and our ability to access capital markets.

According to the Centers for Disease Control and Prevention, as of October 2022, over 68% of the U.S. population has completed their primary series of vaccination. However, as circumstances evolve, in particular related to the emergence of variants and subvariants, it will be important to understand potential impacts to patients and the hospital system, and the ability for patients to access *Jelmyto.* While it is difficult to predict the ultimate impact of the ongoing COVID-19 pandemic on our business and the healthcare industry, we continue to monitor the evolving COVID-19 situation, and the potential further impacts that the pandemic and the related government response may have on our business.

Components of Operating Results

Revenue

During the three and nine months ended September 30, 2022 we recognized $16.1 million and $46.3 million of revenue, respectively from sales of our product, *Jelmyto*.

Cost of Revenue

Cost of revenue consists primarily of inventory and related costs associated with the manufacturing, distribution, warehousing and preparation of *Jelmyto,* including inventory impairment. In periods prior to receiving FDA approval for *Jelmyto*, we recognized inventory and related costs associated with the manufacture of *Jelmyto* as research and development expenses.

Research and Development Expenses

Research and development expenses, net consist primarily of:

- salaries and related costs, including share-based compensation expense, for our personnel in research and development functions;
- expense incurred under agreements with third parties, including clinical research organizations (“CROs”), subcontractors, suppliers and consultants, nonclinical studies and clinical trials;
- expense incurred to acquire, develop and manufacture nonclinical study and clinical trial materials;
- expense incurred to purchase active pharmaceutical ingredient (“API”) in support of R&D activities and other related manufacturing costs; 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. We estimate nonclinical study and clinical trial expense based on the services performed pursuant to contracts with research institutions and contract research organizations that conduct and manage nonclinical studies and clinical trials on our behalf based on actual time and expense 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 such development milestone results are achieved.

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 nonclinical 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 expense required for us to reach commercialization of our product candidates. Due to the inherently unpredictable nature of nonclinical 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 nonclinical 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;
- delays or operational challenges resulting from the ongoing COVID-19 pandemic;
- 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.

Other than *Jelmyto*, which was approved by the FDA in April 2020, we have not received approval of any of our product candidates. UGN-102 and UGN-301 are still in clinical development, and the outcome of these efforts is uncertain. As such, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our 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.

License fees and development milestone payments related to in-licensed products and technology are expensed as incurred or when achieved, in the case of milestones, if it is determined at that point that they have no established alternative future use.

Selling and Marketing Expenses

To date, selling and marketing expenses consist primarily of commercial personnel costs (including share-based compensation) along with pre-commercialization and commercialization activities related to *Jelmyto*. We anticipate that our selling and marketing expenses will remain relatively consistent for the remainder of 2022.

General and Administrative Expenses

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

We anticipate that our general and administrative expenses will remain relatively consistent for the remainder of 2022, and may increase in the future to support the potential approval and commercialization of our product candidates and our continued research and development programs.

Financing on prepaid forward obligation

Financing on prepaid forward obligation is comprised of financing expense related to the RTW Transaction (see Note 9 to our condensed consolidated financial statements included in this Quarterly Report).

Interest expense

Interest expense is comprised of interest related to our long-term debt with Pharmakon (see Note 10 to our condensed consolidated financial statements included in this Quarterly Report).

Interest and Other Income, Net

Interest and other income, net, consisted primarily of interest income.

Income Taxes

We have yet to generate net taxable income in Israel. We have historically incurred operating losses resulting in carry forward tax losses totaling approximately $335.8 million as of December 31, 2021. 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. Income tax expense also consists of our estimate of uncertain tax positions, and related interest and penalties. See Note 16 to the condensed consolidated financial statements for further information.

Critical Accounting Policies and Estimates

The preparation of our unaudited condensed consolidated 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, and the revenue and expense incurred during the reported periods. In accordance with GAAP, we base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances at the time such estimates are made. Actual results may differ from these estimates under different assumptions or conditions. We discussed the critical accounting policies used in the preparation of our financial statements in *Management's Discussion and Analysis of Financial Condition and Results of Operations* included in our Annual Report as well as in the Note 3 to the condensed consolidated financial statements included in this Quarterly Report.

Results of Operations

Comparison of the three months ended September 30, 2022 and 2021

The following table sets forth our results of operations for the three months ended September 30, 2022 and 2021.

	Three Months Ended September 30,		
	2022	2021	Change
	(in thousands)		
Revenue	$ 16,097	$ 11,351	$ 4,746
Cost of revenue	2,020	1,244	776
Gross profit	14,077	10,107	3,970
Operating expenses:			
Research and development	13,093	11,923	1,170
Selling and marketing	11,882	12,473	(591)
General and administrative	7,189	9,151	(1,962)
Total operating expenses	32,164	33,547	(1,383)
Operating loss	(18,087)	(23,440)	5,353
Financing on prepaid forward obligation	(4,819)	(6,828)	2,009
Interest expense on long-term debt	(2,694)	—	(2,694)
Interest and other income, net	478	57	421
Loss before income taxes	(25,122)	(30,211)	5,089
Income tax expense	(709)	—	(709)
Net loss	$ (25,831)	$ (30,211)	$ 4,380

Revenue

Revenue was $16.1 million and $11.4 million for the three months ended September 30, 2022 and 2021, respectively. The increase in revenue of $4.7 million reflects the increased volume of sales of our product *Jelmyto*.

Cost of Revenue

Cost of revenue was $2.0 million and $1.2 million for the three months ended September 30, 2022 and 2021, respectively. In periods prior to receiving FDA approval for *Jelmyto*, we recognized inventory and related costs associated with the manufacture of *Jelmyto* as research and development expenses. We expect this to continue to impact cost of revenue through approximately the second quarter of 2023 as we produce *Jelmyto* at costs reflecting the full cost of manufacturing and as we deplete inventories that we had expensed prior to receiving FDA approval. Gross margin would have been approximately 86.9% versus 87.5% for the three months ended September 30, 2022, if we had not sold *Jelmyto* units that were expensed prior to regulatory approval.

Research and Development Expenses

Research and development expenses were $13.1 million and $11.9 million for the three months ended September 30, 2022 and 2021, respectively. The overall increase of $1.2 million is primarily attributable to the Phase 3 ENVISION study for UGN-102, research into ingredient scale-up and production efficiency for *Jelmyto*, partially offset by lower stock-based compensation expenses in 2022.

Selling and Marketing Expenses

Selling and marketing expenses were $11.9 million and $12.5 million for the three months ended September 30, 2022 and 2021, respectively. The decrease in selling and marketing expenses of $0.6 million is primarily attributable to lower stock-based compensation expenses in 2022.

General and Administrative Expenses

General and administrative expenses were $7.2 million and $9.2 million for the three months ended September 30, 2022 and 2021, respectively. The decrease in general and administrative expenses of $2.0 million resulted primarily from a decrease in stock-based compensation expenses in 2022.

Financing on Prepaid Forward Obligation

Financing on prepaid forward obligation was $4.8 million and $6.8 million for the three months ended September 30, 2022 and 2021, respectively. The measurement of financing on prepaid forward obligation is an accounting estimate under the "imputed interest method" of accounting (see Note 3 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report) which is affected by estimated future payments to RTW, which are based on a percentage of revenues. The decrease in financing on prepaid forward obligation of $2.0 million was driven primarily by changes in underlying assumptions for remeasuring the effective rate.

Interest Expense on Long-term Debt

Interest expense was $2.7 million and zero for the three months ended September 30, 2022 and 2021, respectively. The cost in 2022 relates to the Pharmakon loan which closed in March 2022.

Interest and Other Income, Net

Interest and other income, net was $0.5 million and $0.1 million for the three months ended September 30, 2022 and 2021, respectively. The increase in interest and other income, net was primarily due to minor fluctuations in interest earned on investments and foreign exchange.

Comparison of the nine months ended September 30, 2022 and 2021

The following table sets forth our results of operations for the nine months ended September 30, 2022 and 2021.

	Nine Months Ended September 30,		
	2022	2021	Change
		(in thousands)	
Revenue	$ 46,265	$ 31,868	$ 14,397
Cost of revenue	5,391	3,568	1,823
Gross profit	40,874	28,300	12,574
Operating expenses:			
Research and development	38,429	34,560	3,869
Selling and marketing	38,075	35,418	2,657
General and administrative	23,129	30,699	(7,570)
Total operating expenses	99,633	100,677	(1,044)
Operating loss	(58,759)	(72,377)	13,618
Financing on prepaid forward obligation	(16,478)	(9,948)	(6,530)
Interest expense on long-term debt	(5,215)	—	(5,215)
Interest and other income, net	604	269	335
Loss before income taxes	(79,848)	(82,056)	2,208
Income tax expense	(1,066)	(312)	(754)
Net loss	$ (80,914)	$ (82,368)	$ 1,454

Revenue

Revenue was $46.3 million and $31.9 million for the nine months ended September 30, 2022 and 2021, respectively. The increase in revenue of $14.4 million reflects the increased volume of sales of our product *Jelmyto*.

Cost of Revenue

Cost of revenue was $5.4 million and $3.6 million for the nine months ended September 30, 2022 and 2021, respectively. In periods prior to receiving FDA approval for *Jelmyto*, we recognized inventory and related costs associated with the manufacture of *Jelmyto* as research and development expenses. We expect this to continue to impact cost of revenue through approximately the second quarter of 2023 as we produce *Jelmyto* at costs reflecting the full cost of manufacturing and as we deplete inventories that we had expensed prior to receiving FDA approval. Gross margin would have been approximately 87.8% versus 88.3% for the nine months ended September 30, 2022, if we had not sold *Jelmyto* units that were expensed prior to regulatory approval.

Research and Development Expenses

Research and development expenses were $38.4 million and $34.6 million for the nine months ended September 30, 2022 and 2021, respectively. The overall increase of $3.8 million is primarily attributable to the Phase 3 ENVISION study for UGN-102, research into ingredient scale-up and production efficiency for *Jelmyto*, partially offset by lower stock-based compensation expenses in 2022.

Selling and Marketing Expenses

Selling and marketing expenses were $38.1 million and $35.4 million for the nine months ended September 30, 2022 and 2021, respectively. The increase in selling and marketing expenses of $2.7 million is primarily attributable to increased market access and brand marketing expenditures, and other expenses related to our participation in the American Urological Association's annual meeting, as well as our annual sales meeting, which did not occur in 2021, partially offset by lower stock-based compensation expenses in 2022.

General and Administrative Expense

General and administrative expense was $23.1 million and $30.7 million for the nine months ended September 30, 2022 and 2021, respectively. The decrease in general and administrative expense of $7.6 million resulted primarily from a decrease in stock-based compensation expenses in 2022.

Financing on Prepaid Forward Obligation

Financing on prepaid forward obligation was $16.5 million and $9.9 million for the nine months ended September 30, 2022 and 2021, respectively. The measurement of financing on prepaid forward obligation is an accounting estimate under the "imputed interest method" of accounting (see Note 3 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report) which is affected by estimated future payments to RTW, which are based on a percentage of revenues. The increase in financing on prepaid forward obligation of $6.6 million was driven primarily from a full nine months of financing cost in 2022 for the RTW Transaction, which closed in May 2021, partially offset by changes in underlying assumptions for remeasuring the effective rate.

Interest Expense

Interest expense was $5.2 million and zero for the nine months ended September 30, 2022 and 2021, respectively. The cost in 2022 relates to the Pharmakon loan which closed in March 2022.

Interest and Other Income, Net

Interest and other income, net was $0.6 million and $0.3 million for the nine months ended September 30, 2022 and 2021, respectively. The increase in interest and other income, net of $0.3 million was primarily due to higher interest earned on cash, cash equivalents and marketable securities.

Liquidity and Capital Resources

As of September 30, 2022, we had $95.9 million in cash and 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. Based on our cash flow projections, we believe that our current cash and cash equivalents and marketable securities are sufficient to fund our planned operations beyond the next 12 months.

Through September 30, 2022, we funded our operations primarily through public equity offerings, private placements of equity securities and our funding arrangements with RTW and Pharmakon.

In December 2019, we entered into a sales agreement (the “ATM Sales Agreement”) with Cowen and Company, LLC (“Cowen”) pursuant to which we may from time to time offer and sell our ordinary shares having an aggregate offering price of up to $100.0 million. The shares are offered and will be sold pursuant to a shelf registration statement on Form S-3 which was declared effective by the SEC on January 2, 2020.

During the second quarter of 2020, we sold 700,000 ordinary shares under the ATM Sales Agreement, for gross proceeds of approximately $16.6 million. The net proceeds to us after deducting sales commissions to Cowen and other issuance expenses were approximately $15.8 million. The remaining capacity under the ATM Sales Agreement is approximately $83.4 million.

In March 2021, we entered into a prepaid forward agreement with RTW, pursuant to which RTW agreed to provide us with an upfront cash payment of $75.0 million to support the launch of *Jelmyto* and the development of UGN-102, and we agreed to provide RTW with tiered future payments based on global annual net product sales of *Jelmyto* and UGN-102, if approved. In May 2021, following the receipt of necessary regulatory approvals, we received the $75.0 million prepaid forward payment ($72.4 million net of transaction costs) from RTW.

On March 7, 2022, we entered into a loan agreement ("Loan Agreement") with Pharmakon for a senior secured term loan of up to $100.0 million in two tranches. The first tranche of $75.0 million ($72.6 million of proceeds were received, $70.8 million net of additional transaction costs) was funded in March 2022. At our option, we may draw up to an additional $25.0 million before December 31, 2022, subject to customary bring down conditions and deliverables. The Pharmakon loan will mature five years from initial funding and can be prepaid in whole at our discretion, at any time, subject to prepayment premiums and make-whole amounts. The Pharmakon loan will require interest-only payments for the first 48 months followed by principal and interest payments with interest accruing using 3-month LIBOR (with a 1.25% floor) plus 8.25%. In the event of the cessation of LIBOR, the benchmark governing the interest rate will be replaced with a rate based on the secured overnight financing rate published by the Federal Reserve Bank of New York. On October 21, 2022, we requested the advance of the second tranche (the "Tranche B Loan") under the Loan Agreement in the amount of $25.0 million. The funding of the Tranche B Loan is expected to occur on December 16, 2022, subject to customary bring down conditions and deliverables.

We have incurred losses since our inception and negative cash flows from our operations, and as of September 30, 2022 we had an accumulated deficit of $548.2 million. We anticipate that we will continue to incur losses for the reasonably foreseeable future. Our primary uses of capital are, and we expect will continue to be, commercialization activities, 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 expense and general and administrative costs, partially offset by proceeds from sales of *Jelmyto*.

We cannot estimate the actual amounts necessary to successfully commercialize any approved products, including *Jelmyto*, 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. There can be no assurances that we will be able to secure such additional financing if at all, or on terms that are satisfactory to us, and that it will be sufficient to meet its needs. In the event we are not successful in obtaining sufficient funding, this could force us to delay, limit, or reduce our product development, commercialization efforts or other operations.

Funding and Material Cash Requirements

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

- the progress, timing and completion of clinical trials for UGN-102 and UGN-301;
- nonclinical studies and clinical trials for any of our other product candidates;
- the costs related to obtaining regulatory approval UGN-102 and UGN-301 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 *Jelmyto* and UGN-102 and any of our other product candidates, and costs involved in the continued 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;
- revenues we may derive either directly or in the form of royalty payments from future sales of *Jelmyto*, UGN-102, UGN-301, RTGel reverse thermal hydrogel and any other product candidates; and
- the repayment of outstanding debt.

Accordingly, we will need to obtain 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.

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 that further limit or restrict our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, the terms of the Pre-Paid Forward Contract with RTW and the Loan Agreement limit our ability to take certain actions, including incurring additional indebtedness.

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 Part II, Item 1A – Risk Factors. We will require 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

In April 2016, we signed an addendum to our November 2014 lease agreement for our executive offices located in Israel, in order to increase the office space rented and to extend the rent period until 2019. In March 2019, we utilized the agreement extension option and extended the rent period for an additional three years until August 2022. In July 2022, we signed a lease extension agreement extending the term of the lease through September 2025.

In April 2018, we 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. In November 2019, we subleased our offices in Los Angeles, CA. The lease commencement date was January 1, 2020 and terminates in March 2024. The subtenants exercised their early access clause and moved into the premises at the end of November 2019.

Also, in November 2019, we entered into a new lease agreement, dated effective October 31, 2019, for an office in Princeton, NJ. The lease commencement date was November 29, 2019 and the lease term is 38 months. In June 2022, the Company signed an amendment to its November 2019 lease agreement to extend the term for an additional three years through January 31, 2026.

The total obligation for future minimum lease payments under our operating leases is $2.8 million as of September 30, 2022. See Note 11 to the condensed consolidated financial statements appearing elsewhere in this Quarterly Report for further information.

In March 2022, UroGen Pharma Ltd., Urogen Pharma, Inc., as the borrower ("Borrower"), and certain direct and indirect subsidiaries of the Company party thereto from time to time, as guarantors ("Guarantors" and, collectively with UroGen Pharma Ltd. and Borrower, "Credit Parties"), entered into the Loan Agreement with funds managed by Pharmakon Advisors, L.P., including BPCR Limited Partnership (as a "Lender"), BioPharma Credit Investments V (Master) LP (as a "Lender"), and BioPharma Credit PLC, as collateral agent for the Lenders (in such capacity, "Collateral Agent"), pursuant to which the Lenders agreed to make the Term Loans to the Borrower in an aggregate principal amount of up to $100.0 million to be funded in two tranches: (i) the Tranche A Loan of $75.0 million was advanced in March, 2022 and (ii) the Tranche B Loan of $25.0 million will be advanced at Borrowers election, subject to certain conditions, subject to the customary bring down conditions and deliverables, and in no event later than December 31, 2022. On October 21, 2022, we requested the advance of the Tranche B Loan under the Loan Agreement in the amount of $25.0 million. The funding of the Tranche B Loan is expected to occur on December 16, 2022, subject to customary bring down conditions and deliverables. The Term Loans will mature on the fifth-year anniversary of the Tranche A Closing Date (the “Maturity Date”). The Term Loans bear interest at 8.25% plus three-month LIBOR per annum with a LIBOR floor of 1.25%. In the event of the cessation of LIBOR, the benchmark governing the interest rate will be replaced with a rate based on the secured overnight financing rate published by the Federal Reserve Bank of New York as described in the Loan Agreement. Interest is payable quarterly in arrears. Repayment of outstanding principal of the Term Loans will be made in four equal quarterly payments of principal commencing after the 17th-quarter anniversary of the Tranche A Closing Date. The obligations of the Borrower under the Loan Agreement are guaranteed on a full and unconditional basis by UroGen Pharma Ltd. and the other Guarantor and are secured by substantially all of the respective Credit Parties’ tangible and intangible assets and property, including intellectual property, subject to certain exceptions.

Cash Flows

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

	Nine Months Ended September 30,	
	2022	2021
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$ (65,807)	$ (64,822)
Investing activities	(22,048)	(5,056)
Financing activities	71,766	72,351
Net change in cash and cash equivalents	$ (16,089)	$ 2,473

Operating Activities

Net cash used in operating activities was $65.8 million during the nine months ended September 30, 2022, compared to $64.8 million during the nine months ended September 30, 2021. The $1.0 million increase was attributable primarily to financing costs related to the prepaid forward obligation and Pharmakon loan, as well as timing of certain accruals.

Investing Activities

Net cash used in investing activities was $22.0 million during the nine months ended September 30, 2022, compared to $5.0 million during the nine months ended September 30, 2021. The net change of $17.0 million is primarily related to reinvestment in securities.

Financing Activities

Net cash provided by financing activities was $71.8 million during the nine months ended September 30, 2022, compared to $72.4 million during the nine months ended September 30, 2021. The decrease of $0.6 million is related to proceeds from the Pharmakon loan in the current year as compared to proceeds from the prepaid forward arrangement with RTW in the prior year.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

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 and marketable securities. As of September 30, 2022, we had $95.9 million of cash and cash equivalents and marketable securities. We invest our cash primarily in money market accounts, but also 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 September 30, 2022, this change would not have had a material effect on the fair value of our cash and cash equivalents and marketable securities 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 three and nine months ended September 30, 2022.

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 the New Israeli Shekel ("NIS"). As a result, we are exposed to the risk that 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 dollar depreciated against the NIS during 2021 by a total of 3.2%. 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. If a 10% change in NIS-to-Dollar exchange rates were to have occurred during the three months ended September 30, 2022, this change would not have had a material effect on our operating expenses.

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 4. 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 September 30, 2022. 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 September 30, 2022, 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.

Changes in Internal Control over Financial Reporting

Changes in our internal control over financial reporting may include such activities as implementing new, more efficient systems, consolidating activities, and migrating processes. There were no changes in our internal control over financial reporting during the quarter ended September 30, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Part II—Other Information

Item 1. 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 1A. Risk Factors.

Risk Factor Summary

Below is a summary of the principal factors that make an investment in our ordinary shares speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors," and should be carefully considered, together with other information in this Quarterly Report and our other filings with the SEC before making investment decisions regarding our ordinary shares.

- We are highly dependent on the successful commercialization of our only approved product, *Jelmyto*.
- We have limited experience as an organization in marketing and distributing products and are therefore subject to certain risks in relation to the commercialization of *Jelmyto* and any of our product candidates that receive regulatory approval.
- The market opportunities for *Jelmyto* and our product candidates may be smaller than we anticipate or limited to those patients who are ineligible for established therapies or for whom prior therapies have failed and may be small.
- *Jelmyto* and any of our product candidates that receive regulatory approval may fail to achieve the broad degree of physician adoption and use and market acceptance necessary for commercial success.
- *Jelmyto* and 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.
- In addition to *Jelmyto*, we are dependent on the success of our lead product candidate, UGN-102, and our other product candidates, including obtaining regulatory approval to market our product candidates in the United States.
- 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.

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

- We currently contract with third-party subcontractors and single-source suppliers for certain raw materials, compounds and components necessary to produce *Jelmyto* for commercial use, and to produce UGN-102, UGN-201 and UGN-301 for nonclinical studies and clinical trials, and expect to continue to do so to support commercial scale production of UGN-102 and UGN-201, if approved, as well as UGN-301 if approved as a monotherapy or for any approved product that includes UGN-301. There are significant risks associated with the manufacture of pharmaceutical products and contracting with contract manufacturers, including 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 commercialization efforts. This increases the risk that we will not have sufficient quantities of *Jelmyto*, UGN-102, UGN-201 or UGN-301 or be able to obtain such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

- 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.

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

- Our business could be adversely affected by the effects of health pandemics or epidemics, including the ongoing COVID-19 pandemic.

- 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.

- Our indebtedness resulting from our Loan Agreement could adversely affect our financial condition or restrict our future operations.

- We will require 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.

- 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.

- If the FDA does not conclude that UGN-102 satisfies the requirements under 505(b)(2) or if the requirements for our 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.

- *Jelmyto* and any of our product candidates that receive regulatory approval 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.

- 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.

- 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.

Risk Factors

You should carefully consider the following risk factors, as well as the other information in this Quarterly Report, before deciding whether to purchase, hold or sell shares of our ordinary shares. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this Quarterly Report and those we may make from time to time. When evaluating our business, you should consider all of the factors described as well as the other information in our Annual Report, including our financial statements and the related notes, "Management's Discussion and Analysis of Financial Condition and Results of Operation" and Item 1A, "Risk Factors." We have marked with an asterisk (*) those risk factors that did not appear as risk factors in, or contain changes to the similarly titled risk factors included in, Item 1A of our Annual Report. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our ordinary shares would likely decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Business and Strategy

We are highly dependent on the successful commercialization of our only approved product, Jelmyto.*

Jelmyto is our first product, which we commercially launched in the United States in June 2020. We have not commercialized any other product candidates. We have invested significant efforts and financial resources in the research and development of *Jelmyto*, our first and only product approved for commercial sale. We are focusing a significant portion of our activities and resources on *Jelmyto*, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize *Jelmyto* in the United States.

Successful commercialization of *Jelmyto* is subject to many risks. We initiated our commercial launch of *Jelmyto* in June 2020, and prior to that, we had never, as an organization, launched or commercialized any product. There is no guarantee that our ongoing commercial launch of *Jelmyto* or our future commercialization efforts will be successful, or that we will be able to successfully launch and commercialize any other product candidates that receive regulatory approval. There are numerous examples of unsuccessful product launches and failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us. While we have established our commercial team and have hired our U.S. sales force, we will need to maintain, further train and develop our team in order to be prepared to successfully coordinate the ongoing launch and commercialization of *Jelmyto*. Even if we are successful in maintaining and further developing our commercial team, there are many factors that could cause the ongoing launch and commercialization of *Jelmyto* to be unsuccessful, including a number of factors that are outside our control. We must also properly educate physicians and nurses on the skillful preparation and administration of *Jelmyto*, and 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.

Because no drug has previously been approved by the FDA for the treatment of low-grade UTUC, it is especially difficult to estimate *Jelmyto*'s market potential. The commercial success of *Jelmyto* depends on the extent to which patients and physicians accept and adopt *Jelmyto* as a treatment for low-grade UTUC, and we do not know whether our or others' estimates in this regard will be accurate. For example, if the patient population suffering from low-grade UTUC is smaller than we estimate or if physicians are unwilling to prescribe or patients are unwilling to be treated with *Jelmyto* due to label warnings, adverse events associated with product administration or other reasons, the commercial potential of *Jelmyto* will be limited. Physicians may not prescribe *Jelmyto* and patients may be unwilling to be treated with *Jelmyto* if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for *Jelmyto* in our post-marketing commitments, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of *Jelmyto*. Thus, significant uncertainty remains regarding the commercial potential of *Jelmyto*.

In addition, our ongoing commercial launch of *Jelmyto* and subsequent commercialization efforts could be hindered by the COVID-19 pandemic, although we are currently not able to predict or quantify any such potential impact with any degree of certainty.

If the launch or commercialization of *Jelmyto* is unsuccessful or perceived as disappointing, our share price could decline significantly and the long-term success of the product and our company could be harmed.

Jelmyto has only been studied in a limited number of patients and in limited populations. Following the initiation of our commercial launch in June 2020, Jelmyto is now available to a much larger number of patients and in broader populations, and we do not know whether the results of Jelmyto use in such larger number of patients and broader populations will be consistent with the results from our clinical studies.

Jelmyto has been administered only to a limited number of patients and in limited populations in clinical studies, including our successful pivotal Phase 3 OLYMPUS clinical trial for the treatment of adult patients with low-grade UTUC. While the FDA granted approval of *Jelmyto* based on the data included in the NDA, including data from the Phase 3 OLYMPUS clinical trial, we do not know whether the results when a large number of patients and broader populations are exposed to *Jelmyto*, including results related to safety and efficacy, will be consistent with the results from earlier clinical studies of *Jelmyto* that served as the basis for the approval of *Jelmyto*. New data relating to *Jelmyto*, including from spontaneous adverse event reports and post-marketing studies in the United States, and from other ongoing clinical studies, may result in changes to the product label and may adversely affect sales, or result in withdrawal of *Jelmyto* from the market. The FDA and regulatory authorities in other jurisdictions may also consider the new data in reviewing potential marketing applications in other jurisdictions, or imposing post-approval requirements. If any of these actions were to occur, it could result in significant expense and delay or limit our ability to generate sales revenues.

We have limited experience as an organization in marketing and distributing products and are therefore subject to certain risks in relation to the commercialization of Jelmyto and any of our product candidates that receive regulatory approval.

Our strategy is to build and maintain a fully integrated biotechnology company to successfully execute the commercialization of *Jelmyto* in the United States. *Jelmyto* is our only product that has been approved for sale by any regulatory body, and it became available in the United States in June 2020. While we have established a commercial management team and have also established a field-based organization comprised of approximately 80 individuals, including a sales team, reimbursement support team, clinical nurse educators, national account managers and medical science liaisons, we currently have very limited experience commercializing pharmaceutical products as an organization. In order to successfully commercialize *Jelmyto*, we must continue to develop our sales, marketing, managerial, compliance and related capabilities or make arrangements with third parties to perform these services. 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. These efforts will continue to be expensive and time-consuming, and we cannot be certain that we will be able to successfully further develop these capabilities. Additionally, we will need to maintain and further develop our sales force, and we will be competing with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. In the event we are unable to effectively develop and maintain our commercial team, including our sales force, our ability to effectively commercialize *Jelmyto* would be limited, and we would not be able to generate product revenues successfully. If we fail to establish and maintain an effective sales and marketing infrastructure, 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.

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize Jelmyto will be harmed.*

None of the members of our sales force had ever promoted *Jelmyto* prior to its launch in June 2020. In addition, *Jelmyto* is the first drug approved by the FDA for the treatment of low-grade UTUC. As a result, we are and will continue to be required to expend significant time and resources to train our sales force to be credible, persuasive, and compliant with applicable laws in marketing *Jelmyto* for the treatment of low-grade UTUC to physicians and nurses. In addition, we must train our sales force to ensure that a consistent and appropriate message about *Jelmyto* is being delivered to our customers. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate customers about the benefits and risks of *Jelmyto* and its proper administration, our efforts to successfully commercialize *Jelmyto* could be put in jeopardy, which would negatively impact our ability to generate product revenues.

Additionally, in light of the COVID-19 pandemic, we have developed digital materials and programs for our sales force to use in order to engage virtually with their target physicians when in-person engagement is not safe or feasible. Beginning in the second quarter of 2021, our territory business managers have been able to engage in higher levels of in-person physician interaction than they were previously during the pandemic. However, there can be no assurance that our territory business managers will continue to have in-person access to physicians as a result of the ongoing evolution of the COVID-19 pandemic (including the emergence of variants), or that digital materials and virtual engagement will be effective at growing and sustaining prescription levels of *Jelmyto*. Disruptions in the prescription volume of *Jelmyto* could also occur:

- if patients are physically quarantined or are unable or unwilling to visit healthcare providers;
- if physicians restrict access to their facilities for a material period of time;
- if healthcare providers prioritize treatment of acute or communicable illnesses over treatment of low-grade UTUC;
- if pharmacies are closed or suffering staff shortages or supply chain disruptions;
- if patients lose access to employer-sponsored health insurance due to periods of high unemployment; or
- as a result of general disruptions in the operations of payors, distributors, logistics providers and other third parties that are necessary for *Jelmyto* to be prescribed, reconstituted, instilled and reimbursed.

The market opportunities for Jelmyto and our product candidates may be smaller than we anticipate or 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 candidate UGN-102 as an alternative to surgery as the standard of care for certain urothelial cancers. However, there is no guarantee that this product candidate will be approved or that we will not have to conduct additional clinical trials. Even if approved, the market opportunity for UGN-102 may be smaller than we anticipate or limited to those patients who are ineligible for established therapies or for whom prior therapies have failed. Our other or future product candidates may face similar risks.

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 pivotal Phase 3 OLYMPUS clinical trial for *Jelmyto* was designed to evaluate the use of *Jelmyto* for the treatment of tumors in the renal pelvis (the funnel-like dilated part of the ureter in the kidney) and was not designed to evaluate the use of *Jelmyto* for the treatment of tumors in the ureter (the tube that connects the kidneys to the bladder). Even though *Jelmyto* is approved for the treatment of low-grade 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 *Jelmyto*. Even if we 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, low-grade 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 low-grade UTUC. If our estimates of the incidence and prevalence of low-grade UTUC are incorrect, *Jelmyto*'s commercial viability may prove to be limited, which may negatively affect our financial results.

Jelmyto and any of our product candidates that receive regulatory approval may fail to achieve the broad degree of physician adoption and use and market acceptance necessary for commercial success.

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

- the clinical indications for which the product is approved;
- the safety and efficacy data from the clinical trial(s) supporting the approved clinical indications;
- the approved labeling and packaging for our products, including the degree of product preparation and administration convenience and ease of use that is afforded to physicians by the approved labeling and product packaging;
- the prevalence and severity of adverse side effects and the level of benefit/risk observed in our clinical trials;
- sufficient patient satisfaction with the results and administration of our products 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 *Jelmyto*, and our lead product candidate UGN-102 as locally-administered drug replacements to current surgical standards of care;
- the cost of treatment, safety and efficacy of our products in relation to alternative treatments, including the recurrence rate of our treatments;
- the extent to which the costs of our products 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 products, including the treatment of low-grade UTUC with *Jelmyto* and the treatment of low-grade intermediate risk NMIBC with UGN-102, if approved, 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 education of physicians or nurses for the skillful administration of our approved product, *Jelmyto*, and UGN-102, if approved, 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; 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 *Jelmyto*, UGN-102 or any of our other product candidates are 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.

Jelmyto and 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 biotechnology 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.

We are aware of several pharmaceutical companies that are developing drugs in the fields of urology and uro-oncology, such as AADi, LLC, Biocancell Ltd., Celgene, CG Oncology Inc., FKD Therapies Oy, GSK, ImmunityBio, Janssen, Merck Sharp & Dohme Corp, Roche, Samyang Biopharma, Seagen Inc., Steba Biotech Ltd., Viralytics Limited and Vyriad. We are aware of a company called Steba Biotech with an IND granted in December 2020 which has initiated a Phase 3 study of padeliporfin ImPACT for the treatment of adult patients with low-grade and unifocal high-grade UTUC in the first quarter of 2021. We are also aware that other companies, such as Janssen and Lipac are conducting, or have recently conducted clinical trials for product candidates for the treatment of low-grade intermediate risk NMIBC. 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 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, surgical tumor resection procedures. 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. Generic mitomycin injectable drug products, while approved by FDA for gastric and pancreatic cancers, are neither approved for low-grade UTUC nor reconstituted with hydrogel as *Jelmyto* is, although they may be used off-label by physicians for the treatment of low-grade UTUC, as they have been prior to the approval of *Jelmyto*.

Our ability to market Jelmyto and any of our product candidates that receive marketing approval is and 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.

Jelmyto is indicated for adult patients with low-grade UTUC. We are currently developing UGN-102, UGN-201 and UGN-301 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 we are found to have improperly promoted off-label uses of Jelmyto or any of our product candidates that receive regulatory approval, 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 and may not be promoted based on overstated efficacy or omission of important safety information. For example, we cannot promote the use of our product *Jelmyto* in a manner that is inconsistent with the approved label, but we are permitted to share truthful and non-misleading information that is otherwise consistent with the product's FDA approved labeling. However, physicians are able, in their independent medical judgment, to use *Jelmyto* 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. In addition, while we have established product liability insurance relating to our commercialization of *Jelmyto*, there can be no assurance that we will be able to maintain this insurance on commercially reasonable terms or that this insurance will be sufficient. 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.

In addition to Jelmyto, we are dependent on the success of our lead product candidate, UGN-102, and our other product candidates, including obtaining regulatory approval to market our product candidates in the United States.*

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. Other than *Jelmyto*, all of our product candidates, including our lead product candidate, UGN-102, remain in clinical development and have not yet received regulatory approval from the FDA or any other regulatory agency in the United States or any other country. Our business depends upon obtaining these regulatory approvals. There are no drugs that have been approved by the FDA for the primary treatment of low-grade intermediate risk NMIBC, and only a limited number of drugs have been approved by the FDA as adjuvant treatment for BCG unresponsive NMIBC. The FDA can delay, limit or deny approval of our product candidates for many reasons.

The success of our product candidates is subject to significant risks, including risks associated with successfully completing current and future clinical trials, such as:

- the FDA's acceptance of our parameters for regulatory approval relating to UGN-102 and our other product candidates, including our proposed indications, primary and secondary endpoint assessments and measurements, safety evaluations and regulatory pathways, and proposed labeling and packaging;
- our ability to successfully complete the FDA requirements related to chemistry, manufacturing and controls ("CMC"), for UGN-102 and our other product candidates, and if completed, their sufficiency to support an NDA;
- the FDA's timely acceptance of our INDs, for our product candidates and our inability to commence clinical trials in the United States without such IND acceptances;
- 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 nonclinical studies or clinical trials;
- the FDA's acceptance of the population studied in our clinical trials being sufficiently large, broad and representative to assess efficacy and safety in the patient population for which we seek approval;
- 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;
- our ability to demonstrate that clinical or other benefits of our product candidates outweigh any safety or other perceived risks;
- 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 NDA for UGN-102;
- if applicable, the recommendation of the FDA's advisory committee to approve our applications to market 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 FDA's determination that the Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act ("FDCA") regulatory pathway ("505(b)(2)") is available for our product candidates;
- the prevalence and severity of adverse events associated with our product candidates, including UGN-102, as there are no drugs and related drug administration procedures approved for the primary treatment of low-grade 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, risks, administration and use of our product candidates, if approved, particularly in light of the fact that there are no drugs that have been approved by the FDA for the primary treatment of low-grade NMIBC, and only a limited number of drugs have been approved by the FDA as adjuvant treatment for high-grade NMIBC;
- 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;
- the FDA's acceptance of the quality of our drug substance or drug product, formulation, labeling, packaging, or the specifications of our product candidates is sufficient for approval;
- our ability to develop, validate and maintain a commercially viable manufacturing process that is compliant with cGMP;

- the FDA's acceptance of the manufacturing processes or facilities of third-party manufacturers with which we contract;
- our ability to secure supply of the raw materials from TAPI (Teva Active Pharmaceutical Ingredients) or other suppliers for our product candidates to support clinical trials and commercial use;
- our ability to manufacture or secure finished product from third-party suppliers for product candidates, including UGN-102, if approved;
- our ability to obtain, maintain, protect and enforce our intellectual property rights with respect to our product candidates;
- the extent to which the costs of our products, once approved, 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; and
- our ability to properly train physicians or nurses for the skillful preparation and administration of any of our product candidates that receive approval, including 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. Further, these risks and uncertainties impact all of our clinical programs that we pursue and have been amplified by the ongoing COVID-19 pandemic, as described below. Accordingly, we cannot assure you that we will be able to advance any more of our product candidates through clinical development, or to obtain additional regulatory approval of any 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. Even if we receive approval of any of the product candidates in our pipeline or future product candidates, there is no assurance that we will be able to successfully commercialize any of them.

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

Positive results in nonclinical 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 nonclinical 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. We initiated the Phase 3 ATLAS trial in December 2020 and until November 2021, were enrolling patients in this trial assessing UGN-102 with or without TURBT compared to standard of care, TURBT. Following discussions with the FDA, we initiated our Phase 3 ENVISION trial, a new single-arm Phase 3 trial of UGN-102 in low-grade, intermediate-risk, NMIBC in the first quarter of 2022. The design for the Phase 3 ENVISION trial is similar to our Phase 2 OPTIMA II trial in that the patient population will have similar clinical characteristics, receive the same treatment regimen and undergo the same efficacy and safety assessments and qualitative follow-up. However, there can be no assurance that the Phase 3 ENVISION trial will have a higher probability of clinical or regulatory success notwithstanding similarities in its design to our Phase 2 OPTIMA II trial. If our clinical trials do not ultimately indicate that our product candidates are safe and effective for their intended use, the FDA may not approve any NDA that we may submit 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. Publications based on interim data may differ from FDA approved product labeling. 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. 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-102 or any other investigational 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 obtaining approval for product candidates and may be unable to do so successfully.

As a company, we have limited experience in conducting clinical trials and have progressed only one 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. 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 yet applied for regulatory approvals to market UGN-102 or the other product candidates in our pipeline, 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 nonclinical 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. After submission of an NDA, the FDA may raise additional questions on any data contained in the application. These questions may come in the form of information requests or in the NDA 74-day letter as review issues. We must address these questions during the review, but we do not know whether our responses will be acceptable to the FDA. 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, before approving, or as a condition of approving, NDAs for our product candidates.

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, nonclinical, 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, 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 nonclinical product candidates into clinical development and through regulatory approval and commercialization.*

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

- generating adequate and sufficient nonclinical 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.

These risks and uncertainties impact all of our nonclinical programs that we pursue and have been amplified by the recent COVID-19 pandemic, as described below. If we are unsuccessful in advancing our nonclinical product candidates into clinical trials in a timely fashion, our business may be harmed. Even if we are successful in advancing our nonclinical product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this Quarterly 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 nonclinical, 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 contract research organizations ("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 ("IRB") approval at each clinical trial site;
- identify, recruit, enroll and retain 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.

Jelmyto or any of our product candidates may produce undesirable side effects that we may not have detected in our previous nonclinical 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, *Jelmyto* and our product candidates may be associated with side effects or adverse events that can vary in severity and frequency. Side effects or adverse events associated with the use of *Jelmyto* or any of our product candidates, including 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 nonclinical testing, Compassionate Use Program for *Jelmyto,* clinical trials and post-marketing experience, we have observed several adverse events and serious adverse events ("SAEs"), including ureteric obstruction, ureteral stenosis, inhibition of urine flow, rash, flank pain, kidney swelling, kidney infection, renal dysfunction, hematuria, fatigue, nausea, abdominal pain, dysuria, vomiting, urinary tract infection, urgency in urination and pain during urination. In addition, we have observed transient perturbation of laboratory measures of renal and hematopoietic function. 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 adverse events or SAEs 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 *Jelmyto* or our product candidates could require us to perform additional studies or halt development or sale of *Jelmyto* or our product candidates or expose us to product liability lawsuits, which will harm our business.

Furthermore, our Phase 2b clinical trial for UGN-102 involved larger patient bases than in our prior studies of these candidates, and the commercial marketing of *Jelmyto* and, if approved, UGN-102, 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 products or 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 nonclinical 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 market acceptance or approval of the affected product or product candidate and could substantially increase development or commercialization costs, force us to withdraw from the market any approved product, 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.

We may face future developmental and regulatory difficulties related to Jelmyto and any of our product candidates that receive marketing approval. In addition, we are subject to government regulations and we may experience delays in obtaining required regulatory approvals to market our proposed product candidates.*

We are subject to certain post-marketing commitments related to *Jelmyto*, including a requirement for a period of five years to provide annual updates for the duration of response for all patients with ongoing complete responses enrolled in the Phase 3 OLYMPUS trial. With respect to our current and future 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.

If we are not successful in developing, receiving regulatory approval for and commercializing our nonclinical and clinical product candidates, our ability to expand our business and achieve our strategic objectives could be impaired.

Although we have received FDA approval of *Jelmyto* for pyelocalyceal solution, for the treatment of adult patients with low-grade UTUC, and we plan to devote a substantial portion of our resources to the continued clinical testing and potential approval of UGN-102 for the treatment of low-grade intermediate risk NMIBC, another key element of our strategy is to discover, develop and commercialize a portfolio of products 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-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. 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.

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

We may utilize a variety of types of licensing, 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 that we consider material. 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.

Any 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;
- 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.

Collaborations may not lead to development or commercialization of product candidates in the most efficient manner, or at all, and may otherwise experience challenges. For example, in August 2020, we announced that the Phase 2 APOLLO trial did not meet the primary endpoint. The data suggested that this result may have been due to BOTOX not effectively permeating the urothelium. In November 2021 the arrangement was terminated.

If any future material 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 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 perception of us in the business and financial communities could be harmed.

We currently contract with third-party subcontractors and single-source suppliers for certain raw materials, compounds and components necessary to produce Jelmyto for commercial use, and to produce UGN-102, UGN-201 and UGN-301 for nonclinical studies and clinical trials, and expect to continue to do so to support commercial scale production of UGN-102 and UGN-201, if approved, as well as UGN-301 if approved as a monotherapy or for any approved product that includes UGN-301. There are significant risks associated with the manufacture of pharmaceutical products and contracting with contract manufacturers, including 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 commercialization efforts. This increases the risk that we will not have sufficient quantities of Jelmyto, UGN-102, UGN-201 or UGN-301 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 *Jelmyto* for commercial use and UGN-102, UGN-201 and UGN-301 for our nonclinical studies and clinical trials, and expect to rely on third party subcontractors and suppliers for commercial use for any of our drug candidates that receive regulatory approval. We currently depend on Teva Pharmaceuticals Industries Ltd ("Teva"), as our single-source supplier of mitomycin active pharmaceutical ingredient ("API") for *Jelmyto* and UGN-102. We rely on Cenexi-Laboratoires Thissen s.a., and Isotopia Molecular Imaging Ltd. as our single contracted suppliers for the mitomycin and gel contained in *Jelmyto* and UGN-102, respectively. We also currently depend on a single source supplier for imiquimod for UGN-201 and zalifrelimab for UGN-301. 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 *Jelmyto* for commercial sale and our product candidates for our clinical trials and their subsequent commercial sale, if approved. Even if we are able to engage alternate suppliers on reasonable terms, we may face delays or increased costs in our supply chain that could jeopardize the commercialization of *Jelmyto* and the development of UGN-102. We do not have any control over the availability of raw materials. If we or our suppliers and 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 *Jelmyto* or any other approved products.

We expect to continue to rely on these or other subcontractors and suppliers to support our commercial requirements for *Jelmyto*, as well as UGN-102 or any of our other product candidates if approved for marketing by the FDA or foreign regulatory authorities. We also rely on a single third-party manufacturer to produce our proprietary drug product, or final mitomycin formulation, necessary for our clinical trial and commercial requirements. We plan to continue to rely on third parties for the production of mitomycin API, the gel contained in *Jelmyto,* UGN-102 and UGN-301, and for imiquimod for UGN-201, and for zalifrelimab for UGN-301, as well as for the raw materials, compounds and components necessary to produce our product candidates and for nonclinical studies and clinical trials.

Even though we are approved as a commercial supplier of *Jelmyto*, we have limited experience as a company in the commercial supply of drugs and may never be successful as a commercial supplier of drug products containing mitomycin. In addition, cost-overruns, unexpected delays, equipment failures, logistics breakdowns, 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, although we commercially supply *Jelmyto*, further build-out is required and establishing such commercial-scale supply capabilities requires additional investment, is 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 *Jelmyto* commercial supply capabilities may cost more than we currently anticipate, and delays or problems may adversely impact our ability to provide sufficient quantities of *Jelmyto* to support our ongoing commercial launch and commercialization of *Jelmyto* as well as our financial condition.

While we currently have over 12 months of mitomycin API and/or *Jelmyto* finished product on hand to continue our commercial and clinical operations as planned, depending on the duration of the COVID-19 pandemic and whether further disruptions occur, we may face such delays or costs in future years. Although we believe we have sufficient quantities of mitomycin API for planned manufacturing operations during 2022, a prolonged supply interruption of certain components could adversely affect our ability to conduct commercialization activities and planned clinical trials. If any third party in our supply or distribution chain for materials or finished product is adversely impacted by restrictions resulting from the ongoing COVID-19 pandemic, including staffing shortages, production slowdowns and disruptions in delivery systems, our supply chain may be disrupted, limiting our ability to manufacture and distribute *Jelmyto* for commercial sales and our product candidates for our clinical trials and research and development operations.

In addition, before we can begin to commercially manufacture any product candidates that receive regulatory approval in the future other than *Jelmyto*, whether in a third-party facility or in our own facility, once established, we must obtain regulatory approval from the FDA for our manufacturing process and facility in order to sell such products in the United States. A manufacturing authorization would also have to be obtained from the appropriate European Union regulatory authorities in order to sell such products in the European Union. In order to obtain approval, we will need to ensure that all of the processes, methods and equipment of such manufacturing facilities are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any vendors, contract laboratories or suppliers are 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 ("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 in-line or investigational 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 *Jelmyto*, 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 *Jelmyto*, UGN-102 or any other product candidates that we may develop could delay, prevent or impair our clinical development or commercialization efforts.

We currently use single source suppliers relative to production of the *RTGel* products, the ureteral catheter and injector which are required to be used with *Jelmyto*. Both the ureteral catheter and injector are used as part of the delivery of *Jelmyto*. We are assessing second source suppliers regarding certain components of *Jelmyto* and are advancing these conversations as a means to ensure both a second source and potential future reductions in cost of revenues. However, there can be no assurance that we will be able to secure any second-source suppliers for these key components on a timely basis, on favorable terms, or at all.

We rely on third party transportation to deliver materials to our facilities and ship products to our customers. Transport operators are exposed to various risks, such as extreme weather conditions, natural disasters, work stoppages, personnel shortages, and operating hazards, as well as interstate and international transportation requirements. In addition, transport operators have been affected by the impact of the COVID-19 pandemic and related shipping crisis and backlog, which has led to increased shipping costs and supply chain disruptions that may impact our operations in the future.

If we experience transportation problems, or if there are other significant changes in the cost of these services, we may not be able to arrange efficient alternatives and timely means to obtain materials or ship products to our customers. Our failure to obtain such materials, ship products or maintain sufficient buffer inventory could materially and adversely impact our business, financial condition and results of operations.

We may need to enter into agreements with additional distributors or suppliers, and there is no guarantee that we will be able to do so on commercially reasonable terms or at all. If we are unable to maintain and, if needed, expand, our network of specialty distributors or suppliers, this would expose us to substantial risk in our clinical development or commercialization efforts.

Failure to obtain marketing approval in international jurisdictions would prevent our approved product, Jelmyto, and 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 commercialized 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. For example, have entered into an exclusive license agreement with Neopharm Ltd. ("Neopharm"), pursuant to which Neopharm is leading the process for seeking regulatory approval of *Jelmyto* in Israel. Neopharm initiated the regulatory approval process in June 2021. Although the submission is supported by the results from our Phase 3 OLYMPUS trial, there can be no assurance that *Jelmyto* will be approved for marketing in Israel in the timeframe we expect. Even if *Jelmyto* is approved for marketing in Israel, there can be no assurance that it will achieve the broad degree of physician adoption and use and market acceptance necessary for commercial success.

We rely on third parties and consultants to assist us in conducting our clinical trials for our 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-102 or any of our other product candidates.*

We do not have the ability to independently conduct many of our nonclinical 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 UGN-102 or any of our other product candidates.

We and the third parties upon whom we rely are required to comply with Good Clinical Practice ("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 GMP 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; healthcare privacy and security laws; and bribery and anti-corruption 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, clinical investigators or other third parties 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.

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 nonclinical 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 economically manufacture 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 will need to continue to increase the size of our organization. If we fail to manage our growth effectively, our business could be disrupted.*

As of September 30, 2022, we had 195 employees, of whom 40 are based in Israel and 155 are based in the United States. We will need to continue to expand our development, quality, managerial, operational, finance, marketing, sales 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.

As we continue to grow as an organization, including by expanding our development efforts and building out and developing our commercial capabilities to support our ongoing commercial launch of *Jelmyto*, we will evaluate, and may implement, changes to our organization that may be appropriate in order to properly manage and direct our growth and transformation into a commercial-stage company. 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. In addition, the ongoing COVID-19 pandemic could make recruiting and training more difficult. 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 or other significant changes to our organization could delay the execution of our development, commercialization and strategic objectives or disrupt our operations; and if we are not successful in commercializing our approved product or any of our product candidates that may receive regulatory approval, 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 face or will face an even greater risk with the commercialization of *Jelmyto* and any investigational product candidates that receive marketing approval. 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 *Jelmyto* and our investigational product candidates 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. As a result of receiving marketing approval of *Jelmyto*, we have expanded our insurance coverage to include the commercialization of *Jelmyto*; however, we may be unable to continue to obtain this liability insurance on commercially reasonable terms and such insurance may be insufficient to cover our exposure. In addition, if and when we obtain approval for marketing UGN-102 or any other product candidate, we intend to further expand our insurance coverage to include the commercialization of UGN-102 or any other approved product; however, we may be unable to obtain this additional liability insurance on commercially reasonable terms.

If we fail to attract and keep senior management and key 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, scientific and other 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.

If our security measures are compromised, or our information technology systems or those of our vendors, and other relevant third parties fail or suffer security incidents, loss or leakage of data, and other disruptions, this could result in a material disruption of our drug development program, compromise sensitive information related to our business, harm our reputation, trigger our breach notification obligations, prevent us from accessing critical information, and expose us to liability or other adverse effects to our business.*

In the ordinary course of our business, we may collect, process and store proprietary, confidential and sensitive information, including personal data (including health information), intellectual property, trade secrets, and proprietary business information owned or controlled by ourselves or other parties (collectively, sensitive information). We face several risks relative to protecting the security, confidentiality, integrity and availability of this sensitive information, including loss of access risk, inappropriate use or disclosure, inappropriate modification, and the risk of being unable to adequately monitor, audit and modify our controls over our sensitive information. This risk extends to the third-party service providers who handle elements of our operations and data processing.

We, our CROs and other contractors, consultants, third-party vendors, and other third parties on which we rely, depend on information technology, telecommunication systems and data processing for significant elements of our operations, including, for example, systems handling human resources, financial reporting and controls, regulatory compliance and other infrastructure operations. Notwithstanding the implementation of security measures, these information technology systems are potentially vulnerable to breakdown, service interruptions, system malfunction, natural disasters, fire, terrorism, war and telecommunication and electrical failures, as well as security incidents from inadvertent or intentional actions by our personnel, third-party vendors, contractors, consultants, business partners, or third parties, or from cyber-attacks by malicious third parties (including the deployment of malware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information), which may compromise our information technology, telecommunication systems and data, or that of our third-party vendors and other contractors and consultants, or lead to data leakage. The risk of a security incident or disruption, particularly through accidental actions or omissions by trusted insiders, cyber-attacks or cyber intrusions has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. Additionally, some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities.

Ransomware attacks are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, disruption of clinical trials, loss of data (including data related to clinical trials), loss of income, significant extra expenses to restore data or systems, reputational loss and the diversion of funds. To alleviate the financial, operational and reputational impact of a ransomware attack, ransomware attack victims may prefer to make payment demands, but if we were to be a victim of such an attack, we may be unwilling or unable to do so (including, for example, if applicable laws or regulations prohibit such payments). Similarly, supply chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach or disruption of our systems and networks or the systems or networks of third parties that support us. The COVID-19 pandemic and our remote workforce also poses increased risks to our information technology systems and data, as more of our employees work from home, utilizing network connections outside our premises. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies.

While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after a security incident has occurred. Despite our efforts to identify and address vulnerabilities, if any, in our information technology systems, our efforts may not be successful. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities.

Additionally, applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences. These consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. For example, failures or significant downtime of our information technology or telecommunication systems or those used by our third-party service providers could cause significant interruptions in our operations and adversely impact the confidentiality, integrity and availability of sensitive information, including preventing us from conducting clinical trials, tests or research and development activities and preventing us from managing the administrative aspects of our business. 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 incident 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. If the information technology systems of our third-party vendors and other contractors become subject to disruptions or security incidents, we may have insufficient recourse against such third parties and may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

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; buying or selling of our ordinary shares while in possession of material non-public information; 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 and a Compliance Program, 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 significant 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.

Most states also have statutes or regulations similar to these federal laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. We and/or our future partners may be subject to administrative, civil and criminal sanctions for violations of any of these federal and state laws. Pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free goods, improper consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations, which could have a significant impact on the conduct of our business.

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, transportation 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 ("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. For example, the dollar depreciated against the NIS during 2021 by a total of 3.2%. 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. If the dollar cost of our operations in Israel increases, our dollar-measured results of operations will be adversely affected.

Our business could be adversely affected by the effects of health pandemics or epidemics, including the ongoing COVID-19 pandemic.*

A pandemic, including the ongoing COVID-19 pandemic or other public health epidemics, poses the risk that we or our employees, contractors, suppliers, customers, and other partners may be prevented from conducting certain business activities for an indefinite period of time, including due to spread of the disease within these groups or due to shutdowns that may be requested or mandated by governmental authorities. While it is not possible at this time to estimate the impact that COVID-19 could have on our business, the COVID-19 pandemic and mitigation measures have had and may in the future have an adverse impact on global economic conditions which could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed. The measures taken or that may be taken by various governments, in response to COVID-19 could disrupt the supply chain of material needed for our product candidates and our approved product, *Jelmyto*, interrupt healthcare services, delay coverage decisions from Medicare and third party payors, delay ongoing and planned clinical trials involving our product candidates and have a material adverse effect on our business, financial condition and results of operations. In addition, we and many of our potential customers and partners worldwide have in the past and may in

the future be subject to stay-at-home orders as a result of the COVID-19 pandemic. In addition, our ongoing commercial launch of *Jelmyto* and subsequent commercialization activities could be hindered by the COVID-19 pandemic, although we are currently not able to predict or quantify any such potential impact with any degree of certainty. However, the worldwide spread of the COVID-19 virus has previously resulted and may in the future result in a varying degree of interruption or slowdown of economic activity, thereby impacting demand for a broad variety of goods and services, including potentially for *Jelmyto*, while also disrupting sales channels and marketing activities for an unknown period of time.

The timelines and conduct of our ongoing clinical trials may be affected by the COVID-19 pandemic. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic and patients' ability or willingness to participate in clinical trials. For those patients who are enrolled and desire to continue in the clinical trials, some patients may not be able or willing to comply with clinical trial protocols if quarantines or governmental orders impede patient movement or interrupt healthcare services. Similarly, we may face increased challenges with the ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, which could adversely impact our clinical trial operations, timelines and outcomes. While we remain in close contact with our clinical sites and suppliers to attempt to assess the impacts that COVID-19 may have on our clinical trials and projected timelines and we have reviewed and acknowledged recent FDA guidance in our protocols, and follow such guidance where possible, with in an effort to ensure the ongoing safety of the patients in our clinical trials and the continued collection of high quality data, there is no guarantee that such efforts will be successful. As challenging as conducting clinical trials is during normal times, the risks, operational challenges and costs of conducting clinical trials have increased substantially during the pandemic.

Additionally, during most of the COVID-19 pandemic, our sales force has had physical access to hospitals, surgery centers, clinics, healthcare providers and pharmacies curtailed, which we believe has affected our sales to date and may in the future have a material adverse effect on our future sales. Beginning in the second quarter of 2021, our territory business managers have been able to engage in higher levels of in-person physician interaction than they were previously during the pandemic. However, there can be no assurance that our territory business managers will continue to have in-person access to physicians as a result of the ongoing evolution of the COVID-19 pandemic (including the emergence of variants). In addition, while we have developed digital materials and programs for our sales force to use in order to engage virtually with their target physicians when in-person engagement is not safe or feasible, digital materials and virtual engagement may not be effective at growing and maintaining prescription levels of *Jelmyto*. Additionally, patients who are currently using *Jelmyto* or who are eligible to use *Jelmyto*, may be unable to meet with their healthcare providers in person, which may reduce the number of new patient starts and hinder the ability of healthcare providers to complete the recommended number of *Jelmyto* instillations, affecting our revenues both in our currently approved indication and potentially impacting our anticipated launches in other indications, if approved.

Moreover, the COVID-19 pandemic continues to evolve, including as a result of the emergence of SARS-CoV-2 variants, and the extent to which the COVID-19 pandemic may impact our business, results of operations and financial position will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the number of cases and the severity of those cases, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, and the effectiveness of actions taken in the United States and other countries to contain, prevent and treat the disease.

To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in the "Risk Factors" section of this report.

Certain of our clinical trials and other significant operations (including our Israeli corporate offices and contract manufacturers) are located outside of the United States and, therefore, our results may be adversely affected by geopolitical, economic and military instability.*

Certain of our clinical trials, such as the Phase 3 ATLAS trial, are operated outside of the United States, including in the Ukraine and Russia. We continue to follow patients in ATLAS, in the region. However, due to the ongoing war, we have experienced difficulty in following up with patients in the region, and we may not have the ability to continue follow up of these patients. The failure to identify and operationalize any alternative clinical sites may have an adverse effect on patient enrollment, and could result in delays in enrolling, carrying out, and/or completing our clinical trials. If we experience delays in achieving our development objectives within a timeframe that meets our prospective customers' expectations, our business, prospects, financial results and reputation could be harmed.

Geopolitical, economic and military conditions around the world may directly affect our business. Any hostilities involving any of the countries in which we operate, including terrorist activities, political instability or violence in the region or the interruption or curtailment of trade or transport between such country and its trading partners could adversely affect our operations and results of operations and adversely affect the market price of our ordinary shares.

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

We currently dedicate certain resources to comply with numerous laws and regulations in each jurisdiction in which we operate outside of the United States. Our business activities in these foreign countries may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate.

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

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

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 biotechnology 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 $110.8 million and $128.5 million for the years ended December 31, 2021 and 2020, respectively. As of September 30, 2022, we had an accumulated deficit of $548.2 million. We expect to continue to incur significant expenses and 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 nonclinical 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 nonclinical 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 for *Jelmyto* and any other products approved for sale, including marketing, sales and distribution costs;
- our degree of success in commercializing *Jelmyto*;
- the cost of third-party manufacturing of our products candidates and any approved 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;
  the repayment of outstanding debt;
- any product liability or other lawsuits related to our products or business arrangements;
- scientific breakthroughs in the field of urothelial cancer treatment and diagnosis that could significantly diminish the demand for our product candidates or make them obsolete; and
- changes in reimbursement or other laws, regulations or 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 biotechnology industry. Drug development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have not obtained regulatory approval for or commercialized any product except *Jelmyto* and we have not commercialized any of our products or generated any revenue from product sales.

Our indebtedness resulting from our Loan Agreement could adversely affect our financial condition or restrict our future operations.*

On March 7, 2022, UroGen Pharma Ltd., UroGen Pharma, Inc., as the borrower (“Borrower”), and certain direct and indirect subsidiaries of the Company party thereto from time to time, as guarantors (“Guarantors” and, collectively with UroGen Pharma Ltd. and Borrower, “Credit Parties”) entered into a loan agreement (“Loan Agreement”) with funds managed by Pharmakon Advisors, L.P., including BPCR Limited Partnership (as a “Lender”), BioPharma Credit Investments V (Master) LP (as a “Lender”), and BioPharma Credit PLC, as collateral agent for the Lenders (in such capacity, “Collateral Agent), pursuant to which the Lenders agreed to make term loans to the Borrower in an aggregate principal amount of up to $100 million ("Term Loans"), to be funded in two tranches: (i) the first tranche (“Tranche A Loan”) was advanced in the amount of $75 million, in March 2022 (“Tranche A Closing Date”) and (ii) the second tranche (“Tranche B Loan”) of $25 million will be advanced at the Borrower’s election, subject to the customary bring down conditions and deliverables, and in no event later than December 31, 2022. On October 21, 2022, we requested the advance of the Tranche B Loan under the Loan Agreement in the amount of $25.0 million. The funding of the Tranche B Loan is expected to occur on December 16, 2022, subject to customary bring down conditions and deliverables. There is no assurance that the Tranche B Loan will be funded as expected or at all.

The obligations of the Borrower under the Loan Agreement are guaranteed on a full and unconditional basis by UroGen Pharma Ltd. and the other Guarantor and are secured by substantially all of the respective Credit Parties’ tangible and intangible assets and property, including intellectual property, subject to certain exceptions.

The Loan Agreement contains negative covenants that, among other things and subject to certain exceptions, restrict our ability to:

- sell or dispose of assets, including certain intellectual property;
- amend, modify or waive certain agreements or organizational documents;
- consummate certain change in control transactions;
- incur certain additional indebtedness;
- incur any non-permitted lien or other encumbrance on the Credit Parties’ assets;
- pay dividends or make any distribution or payment on or redeem, retire or purchase any equity interests; and
- make payments of certain subordinated indebtedness.

In addition, we are required under the Loan Agreement to comply with various operating covenants and default clauses that may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business strategies. A breach of any of these covenants or clauses could result in a default under the Loan Agreement, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable, including a makewhole amount and prepayment premium.

If we are unable to generate sufficient cash to repay our debt obligations when they become due and payable, we may not be able to obtain additional debt or equity financing on favorable terms, if at all, which may negatively affect our business operations and financial condition.

We will require 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 nonclinical and clinical development of our first commercial product, *Jelmyto*, and our lead product candidate UGN-102. As of September 30, 2022, we had cash and cash equivalents and marketable securities of $95.9 million. In January 2019, we completed an underwritten public offering in which we received net proceeds of approximately $161.4 million, after deducting the underwriting discounts and commissions and payment of other offering expenses. During the second quarter of 2020, we sold 700,000 ordinary shares under the sales agreement ("ATM Sales Agreement") with Cowen and Company, LLC ("Cowen"), for gross proceeds of approximately $16.6 million. The net proceeds to us after deducting sales commissions to Cowen and other issuance expenses were approximately $15.8 million. The remaining capacity under the ATM Sales Agreement is approximately $83.4 million. In March 2021, we announced a transaction with RTW Investments ("RTW") totaling $75 million in funding for our company, which was received in May 2021, to support the launch of *Jelmyto* and the development of UGN-102. In return for the upfront cash payment, RTW is entitled to receive tiered future payments based on global annual net product sales of *Jelmyto* and UGN-102, if approved. In addition, in March 2022, we entered into the Loan Agreement, pursuant to which the Lenders agreed to make the Term Loans to Borrower in an aggregate principal amount of up to $100 million to be funded in two tranches.

Based on our cash flow projections, we believe that our current cash and cash equivalents and marketable securities are sufficient to fund our planned operations for at least the next 12 months. 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 financings, 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 nonclinical 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 nonclinical 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 *Jelmyto* or any of our product candidates that obtain marketing approval.

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.

Covenants under our Pre-Paid Forward Contract with RTW restrict our ability to borrow additional capital.

In March 2021, we entered into a Pre-Paid Forward Contract (the "Forward Contract") with RTW, pursuant to which we are obligated to make tiered cash payments to RTW, based on the worldwide annual net product sales of *Jelmyto* and, subject to FDA approval, UGN-102 (together, the "Products"), subject to an aggregate revenue cap of $300 million.

Until the earlier of such time that (i) our aggregate worldwide annual net product sales of the Products reach a certain threshold or (ii) our market capitalization reaches a certain threshold, (a) we have granted RTW a security interest in the Products and the regulatory approvals, intellectual property, material agreements, proceeds and accounts receivable related to the Products (the "Product Collateral"), (b) we are subject to a negative pledge in respect of the Product Collateral and (c) we may not incur additional indebtedness secured by Product Collateral without such secured debt provider entering into a intercreditor agreement with RTW. Upon the occurrence of an insolvency event, as defined in the Forward Contract, any remaining payment obligations under the Forward Contract will be automatically accelerated.

The Forward Contract requires us to use a significant portion of our cash flow to make payments to RTW, limits our ability to borrow additional funds for working capital, capital expenditures or other general business purposes, limits our flexibility to plan for, or react to, changes in our business and industry, places us at a competitive disadvantage compared to our competitors not subject to similar restrictions and increases our vulnerability to the impact of adverse economic industry conditions.

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. To the extent that we raise additional capital through the sale of equity or convertible debt securities, including pursuant to the ATM Sales Agreement, 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 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, as well as other intellectual property advancements.

We seek patent protection for our product candidates, and we hold a broad collection of intellectual property comprised of issued patents, pending patent applications and trademarks covering our proprietary *RTGel* technology, the pharmaceutical compositions, methods of use and manufacturing aspects of our product candidates. In the United States, we currently hold approximately 18 granted patents that are directed to protect our approved product, *Jelmyto* and our lead product candidate, UGN-102, a proprietary *RTGel* technology, local compositions comprising different active ingredients, inter alia compositions comprising a Botulinum Toxin, UGN-201, the sequential use of UGN-201 and UGN-301, and our future product candidates that are under company research. These IP rights relate to certain aspects of cancer treatment. These issued patents are set to expire between 2024 and 2037. In total, our IP portfolio includes 40 granted patents worldwide, and more than 45 pending patent applications filed in the US, Europe, Israel, Japan, Canada, China, Mexico and Australia that are directed to cover various methods, systems and compositions for treating cancer locally, by intravesical means, utilize various active ingredients and the combinations thereof. These patent applications, if issued, are set to expire between 2031 and 2041.

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 known compounds and our patents and pending patent applications are directed inter alia to novel formulations of these known compounds with our proprietary *RTGel* technology. 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 of 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.

We will not necessarily seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

One or more of the patent applications that we filed, 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 granted patents are complex, lengthy and highly technical documents that are often prepared under 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 USPTO may be subject to reexamination and other challenges.

Pharmaceutical patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position. There is significant litigation activity in the pharmaceutical industry regarding patent and other intellectual property rights. Such litigation could result in substantial costs and be a distraction to management and other employees.

The patent positions of biotechnology and pharmaceutical companies can be highly uncertain and involve complex legal and factual questions. The interpretation and breadth of claims allowed in some patents covering pharmaceutical compositions may be uncertain and difficult to determine and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. 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 *Jelmyto*, UGN-102 and any of our other product candidates.

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

There can be no assurance that the patent applications will be granted. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained.

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 ("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 filed applications for trademarks (*Jelmyto* ®, *RTGel* ®, UroGen ® and Cystoject ™) that identify our branding elements, such as *Jelmyto* and our unique technology in the United States, Europe, Japan and China. 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 rights 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.

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 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 unknowingly infringe existing patents by commercialization of 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-102 satisfies the requirements under 505(b)(2) or if the requirements for our 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.

The Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), added 505(b)(2) to the FDCA. 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-102 and our other product candidates by potentially decreasing the amount of nonclinical 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 and, therefore, will not be treated as NCEs, the submission of an NDA under the 505(b)(2) 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 505(b)(2) pathway as anticipated, we may need to conduct additional nonclinical 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 505(b)(2) 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 505(b)(2) 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 505(b)(2) certain competitors and others have objected to the FDA's interpretation of 505(b)(2). If the FDA's interpretation of 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 505(b)(2). In addition, the pharmaceutical industry is highly competitive, and 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 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 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 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.

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, as amended by the Health Care and Education Reconciliation Act of 2010 (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 ("AMP") for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% 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, as defined by such law, and teaching hospitals and any ownership and investment interests held by such physicians and their immediate family members during the preceding calendar year, which will be expanded beginning in 2022 to include reporting obligations with respect to financial relationships with certain additional healthcare providers;
- 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, Congressional and executive branch challenges to certain aspects of the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 ("IRA") into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear any such challenges, other litigation and the healthcare reform measures of the Biden administration 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 included 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 until 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. 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, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's AMP, for single source and innovator multiple source drugs, beginning January 1, 2024. In addition, Congress is considering additional health reform measures

Additionally, there have been several recent U.S. presidential executive orders, 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 former Trump Administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the U.S. Department of Health and Human Services ("HHS") released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within 90 days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. 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.

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 regulations, guidance or interpretations will be changed, or what the impact of such changes on our operations, including the marketing approvals of UGN-102 or our other product candidates may be.

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, (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 exclusivity to *Jelmyto* for the treatment of UTUC, we may not receive orphan drug exclusivity for any of our other product candidates that have received orphan designation.

Although the FDA has granted Orphan Drug Designation to *Jelmyto* and UGN-201 for treatment of UTUC and CIS, respectively, 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.

Jelmyto 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 biotechnology 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. Conversely, even if we are granted orphan exclusivity, a competitor that demonstrates clinical superiority with the same active moiety may obtain approval prior to expiration of our exclusivity. 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.

Jelmyto and any of our product candidates that receive regulatory approval 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.

Jelmyto and any of our product candidates that receive regulatory approval will be subject to continual regulatory review by the FDA and/or foreign regulatory authorities. Additionally, *Jelmyto* and any of our product candidates that receive regulatory approval 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.

The FDA approval of *Jelmyto* is, and any regulatory approvals that we receive for our product candidates may be, subject to limitations on the approved indications for which the product may be marketed or to the conditions of approval. In addition, any regulatory approvals that we receive for our current or future product candidates may 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, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for *Jelmyto* is, and any of our product candidates that receive regulatory approval 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 products or 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 significant penalties.*

We are subject to various U.S. federal, state and foreign health care laws, including those intended to prevent health care fraud and abuse. These laws may impact, among other things, our clinical research, sales and marketing activities, and constrain the business or financial arrangements with healthcare providers, physicians, and other parties that have the ability to directly or indirectly influence the prescribing, ordering, marketing, or distribution of products for which we obtain marketing approval.

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 (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 pharmaceutical companies for, among other things, alleged violations of these anti-fraud statutes, based on among other things, 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 (“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 of 2009 (“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 as well as their covered subcontractors 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.

Our operations are also 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals (such as physician assistants and nurse practitioners) 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. In addition, we may be subject to certain foreign healthcare laws that are analogous to the U.S. healthcare laws described above. 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 FCPA 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.

We are subject to stringent and changing privacy, data protection and data security laws, contractual obligations, self-regulatory schemes, government regulation, and standards related to data privacy and security. The actual or perceived failure by us, our customers, partners or vendors to comply with such obligations could harm our reputation, subject us to significant fines and liability, or otherwise adversely affect our business.*

In the ordinary course of our business, we may collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (commonly known as processing) proprietary, confidential, and sensitive data, including personal data, intellectual property, and trade secrets (collectively, sensitive information). We are or may become subject to numerous domestic and foreign laws and regulations regarding privacy, data protection, and data security, the scope of which is changing, subject to differing applications and interpretations and may be inconsistent among countries, or conflict with other rules. We are also subject to the terms of our contractual obligations to customers and third parties related to privacy, data protection and data security.

In the United States, federal, state, and local governments have enacted numerous privacy, data protection, and data security laws, including data breach notification laws, personal data privacy laws, and consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act). For example, the California Consumer Privacy Act of 2018 ("CCPA") imposes obligations on covered businesses. These obligations include, but are not limited to, providing specific disclosures in privacy notices and affording California residents certain rights related to their personal data. The CCPA allows for statutory fines for noncompliance (up to $7,500 per violation). Although the CCPA exempts some data processed in the context of clinical trials, the CCPA may increase compliance costs and potential liability with respect to other personal data we maintain about California residents. In addition, it is anticipated that the California Privacy Rights Act of 2020 ("CPRA"), effective January 1, 2023, will expand the CCPA. The CPRA will, among other things, give California residents the ability to limit use of certain sensitive personal data, establish restrictions on the retention of personal data, and establish a new California Privacy Protection Agency to implement and enforce the CPRA, which could increase the risk of enforcement. Other states, such as Virginia, Colorado, Utah and Connecticut, have also passed comprehensive privacy laws, all of which become effective in 2023. In addition, privacy, data protection, and data security laws have been proposed at the federal, state, and local levels in recent years, which could further complicate compliance efforts. These laws demonstrate our vulnerability to the evolving regulatory environment related to personal data. As we expand our operations, these and similar laws may increase our compliance costs and potential liability.

Outside the United States, an increasing number of laws, regulations, and industry standards apply to privacy, data protection, and data security. For example, the European Union's General Data Protection Regulation ("EU GDPR") and the United Kingdom's GDPR ("UK GDPR") impose strict requirements for processing personal data. Our upcoming clinical trial will include sites in the EU, which will increase our exposure to potential liability under the EU GDPR. Penalties for non-compliance with the EU GDPR can be significant and include fines in the amount greater of €20 million or 4% of global turnover and restrictions or prohibitions on data processing, which could impair our ability to do business in the EU, interrupt our clinical trials, reduce demand for our services and adversely impact our business and results of operations. Further, the EU GDPR provides for private litigation related to the processing of personal data, which can be brought by classes of data subjects or consumer protection organizations authorized by law to represent the interests of such classes. 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 other countries in which we might operate, including the EU GDPR. Assisting our customers, partners, and vendors in complying with the EU GDPR or other foreign laws, or complying with such laws ourselves, may cause us to incur substantial operational costs or require us to change our business practices.

Moreover, many foreign laws, including the GDPR and data protection laws in the United Kingdom and Switzerland, impose restrictions on the transfer of personal data to the United States and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data. The European Commission released a set of Standard Contractual Clauses ("SCCs") that are designed to be a valid mechanism to facilitate personal data transfers out of the EEA to these jurisdictions. Currently, these SCCs are a valid mechanism to transfer personal data outside of the EEA. Additionally, the SCCs impose additional compliance burdens, such as conducting transfer impact assessments to determine whether additional security measures are necessary to protect the at-issue personal data. In addition, Switzerland and the UK similarly restrict personal data transfers outside of those jurisdictions to countries such as the United States that do not provide an adequate level of personal data protection, and certain countries outside Europe (e.g. China) have also passed or are considering laws requiring local data residency or otherwise impeding the transfer of personal data across borders, any of which could increase the cost and complexity of doing business. If we are unable to implement a valid compliance mechanism for cross-border personal data transfers, we may face increased exposure to regulatory actions, substantial fines and injunctions against processing or transferring personal data from Europe. Inability to import personal data from Europe to the United States may limit our ability to conduct clinical trial activities in Europe, limit our ability to collaborate with contract research organizations, service providers, contractors and other entities subject to European data protection laws, adversely impact our operations, product development and ability to provide our products, and require us to increase our data processing capabilities in Europe at significant expense.

Complying with these various laws, regulations and other obligations related to data privacy and protection could require us to incur substantial costs, take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, require us to change our business practices and compliance procedures in a manner adverse to our business, or, in some cases, impact our ability to operate in certain jurisdictions. Although we endeavor to comply with all applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. Moreover, despite our efforts, our personnel or third parties upon whom we rely may fail to comply with such obligations, which could negatively impact our business operations and compliance posture. For example, any failure by a third-party processor to comply with applicable law, regulations, or contractual obligations could result in adverse effects, including inability to or interruption in our ability to operate our business and proceedings against us by governmental entities or others. The actual or perceived failure by us, our customers, our vendors, or other relevant third parties to address or comply with these laws, regulations, and obligations could increase our compliance and operational costs, expose us to regulatory scrutiny, actions, fines, civil or criminal penalties, private litigation, cause regulators to reject, limit or disrupt our clinical trial activities, harm our reputation, and otherwise cause a material effect on our business, financial condition, and results of our operations. Moreover, inability to import personal data to the United States or other countries may disrupt or require us to change our business practices, interrupt our business operations, including clinical trials, and otherwise have a material financial impact on our business.

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 *Jelmyto*, 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. In October 2020, a Medicare C-Code was issued for *Jelmyto* and we have obtained pass-through status for two years, no more than three. CMS has established a permanent and product-specific J-code for *Jelmyto* that took effect on January 1, 2021. Our existing pass-through status is expiring in 2023, which could adversely affect the revenue we receive for *Jelmyto*.

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. Although our experience to date has demonstrated coverage for *Jelmyto*, we cannot be sure that adequate coverage will be available for 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. In addition, if inflation or other factors were to significantly increase our business costs, it may not be feasible to pass price increases on to our customers due to the process by which healthcare providers are reimbursed for our product candidates.

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. Our experience to date has demonstrated coverage with CMS and commercial payors for *Jelmyto*, and we have established written policies with certain commercial providers. However, 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. Moreover, for products administered under the supervision of a physician, obtaining and maintaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. 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 and maintaining 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.

Although we have observed written policy coverage in commercial plans as well as coverage for government plans for *Jelmyto* to date, we cannot be sure that adequate coverage or reimbursement will continue to be available for *Jelmyto*, or be available for 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 successfully commercialize *Jelmyto*, UGN-102 or our other product candidates, or achieve profitably at all, even if approved. Additionally, coverage policies and reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for any of our products or product candidates that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. For example, beginning on January 1, 2023, manufacturers will be required to pay quarterly refunds to CMS for discarded amounts of single-dose container and single-use package drugs covered under Medicare Part B. Rebates will be based on the discarded volume above 10% of the total allowed amount. However, in unique circumstances, CMS will increase the applicable threshold to 35%. At this time, CMS has determined that *Jelmyto* fits within this unique circumstance classification. If we are unable to obtain and maintain sufficient third-party coverage and adequate reimbursement for our products, the commercial success of our products may be greatly hindered and our financial condition and results of operations may be materially and adversely affected.

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-102 or any of our other product candidates and to produce, market, and distribute Jelmyto or any of our product candidates that receive clearance or approval.

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-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:

- the success of our launch and commercialization of *Jelmyto*;
- actual or anticipated variations in our and our competitors' results of operations and financial condition;
- physician and market acceptance of *Jelmyto* or any other approved product;
- the mix of products that we sell;
- any voluntary or mandatory recall of *Jelmyto* or any other approved product, or the imposition of any additional labeling, marketing or promotional restrictions;
- 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 nonclinical or clinical trials for *Jelmyto*, 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;
- the announcement of, or developments in, any litigation matters, including any product liability claims related to *Jelmyto* or any of our product candidates;
- 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, such as the COVID-19 pandemic, 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.

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.

In addition, our sale of additional ordinary shares or other 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. On December 20, 2019, we entered into the ATM Sales Agreement pursuant to which we may from time to time offer and sell our ordinary shares, having an aggregate offering price of up to $100.0 million, to or through Cowen, acting as sales agent or principal, in any manner deemed to be an "at-the market offering". The shares will be offered and sold pursuant to our shelf registration statement on Form S-3 filed with the SEC on December 20, 2019, which was declared effective on January 2, 2020. As of September 30, 2022, we had sold 700,000 shares under the sales agreement for total gross proceeds of $16.6 million, leaving up to $83.4 million available for sale under the ATM Sales Agreement.

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 a significant portion of our outstanding ordinary shares. 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.

If we are classified as a passive foreign investment company ("PFIC"), 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 PFIC for U.S. federal income tax purposes.

The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and the applicable law is subject to varying interpretation. In particular, the characterization of our assets as active or passive may depend in part on our current and intended future business plans, which are subject to change. In addition, for our current and future taxable years, the total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our ordinary shares from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into in the future and our corporate structure. The composition of our income and assets is also affected by how, and how quickly, we spend the cash we raise in any offering.

Based on our analysis of our estimated income, estimated assets, activities and market capitalization, we do not believe that we were a PFIC for the taxable year ended December 31, 2021. However, because the determination of whether or not we are a PFIC is a fact-intensive determination made on an annual basis, and because the applicable law is subject to varying interpretation, we cannot provide any assurances regarding our PFIC status for any past, current or future taxable years. Our U.S. tax counsel has not provided any opinion regarding our PFIC status in any taxable year.

If we are characterized as a PFIC, our U.S. shareholders 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. shareholders who are individuals, 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. shareholder 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. shareholder of a PFIC generally may mitigate these adverse U.S. federal income tax consequences by making a qualified electing fund ("QEF") election, or, in some circumstances, a "mark to market" election. However, there is no assurance that we will provide the information required by the Internal Revenue Service in order to enable U.S. shareholders to make a timely QEF election. Moreover, there is no assurance that we will have timely knowledge of our status as a PFIC in the future. Accordingly, U.S. shareholders may be unable to make a timely QEF election with respect to our ordinary shares

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, as well as tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, including those related to the Organisation for Economic Co-Operation and Development's ("OECD") Base Erosion and Profit Shifting ("BEPS") Project (including "BEPS 2.0") and 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.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could affect the tax treatment of our domestic and foreign earnings. Any new taxes could adversely affect our domestic and international business operations, and our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

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 "United States person" (as defined by the Internal Revenue Code of 1986, as amended (the "Code")) is treated as owning (directly, indirectly or constructively) at least 10% of the total combined voting power of all classes of our stock entitled to vote or 10% or more of the total value of all classes of our stock, such United States person may be treated as a "United States shareholder" with respect to each "controlled foreign corporation" (CFC) in our group (if any). Each United States shareholder of a CFC 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 the CFC, regardless of whether the CFC makes any distributions. In addition, a United States shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. An individual who is a United States shareholder with respect to a CFC 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. A non-U.S. corporation generally will be classified as a CFC for U.S. federal income tax purposes if United States shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. 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, attribution rules could cause them to be treated as CFCs with respect to any United States person owning (directly, indirectly or constructively) at least 10% of the value or voting power of our ordinary shares.

We cannot provide any assurances that we will assist investors in determining whether we or any non-U.S. subsidiaries that we may form or acquire in the future would be treated as a CFC or whether such investor would be treated as a United States shareholder with respect to any such CFC. Further, we cannot provide any assurances that we will furnish to any United States 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. shareholders should consult their tax advisors regarding the potential application of these rules to their investment in our ordinary shares.

Our ability to use our U.S. net operating loss carryforwards and certain other tax attributes to offset future taxable income and taxes may be limited.*

Under U.S. federal income tax law, federal net operating losses ("NOLs") incurred in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs in tax years beginning after December 31, 2020, is limited to 80% of taxable income. In addition, under Sections 382 and 383 of the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to utilize its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We have not performed a detailed analysis to determine whether an ownership change under Section 382 of the Code has occurred for UroGen Pharma, Inc. If we undergo or have undergone an ownership change, our ability to utilize NOLs and other tax attributes could be limited by Sections 382 and 383 of the Code. 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. 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. In addition, at the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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. 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, pandemic, 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 September 30, 2022, we had 40 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.

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 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, technical and commercial 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 September 30, 2022, we had 195 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, technical and commercial 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.

General Risk Factors

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.

Our business could be negatively affected as a result of actions of activist shareholders, and such activism could impact the trading value of our securities.

Shareholders may, from time to time, engage in proxy solicitations or advance shareholder proposals, or otherwise attempt to effect changes and assert influence on our board of directors and management. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition. A proxy contest would require us to incur significant legal and advisory fees, proxy solicitation expenses and administrative and associated costs and require significant time and attention by our board of directors and management, diverting their attention from the pursuit of our business strategy. Any perceived uncertainties as to our future direction and control, our ability to execute on our strategy, or changes to the composition of our board of directors or senior management team arising from a proxy contest could lead to the perception of a change in the direction of our business or instability which may result in the loss of potential business opportunities, make it more difficult to pursue our strategic initiatives, or limit our ability to attract and retain qualified personnel and business partners, any of which could adversely affect our business and operating results. If individuals are ultimately elected to our board of directors with a specific agenda, it may adversely affect our ability to effectively implement our business strategy and create additional value for our shareholders. We may choose to initiate, or may become subject to, litigation as a result of the proxy contest or matters arising from the proxy contest, which would serve as a further distraction to our board of directors and management and would require us to incur significant additional costs. In addition, actions such as those described above could cause significant fluctuations in our share price based upon temporary or speculative market perceptions or other factors that do not necessarily reflect the underlying fundamentals and prospects of our business.

Unstable market, economic and geo-political conditions may have serious adverse consequences on our business, financial condition and stock price.*

The global credit and financial markets have experienced extreme volatility and disruptions in the past. These disruptions can result in severely diminished liquidity and credit availability, increase in inflation, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment, higher inflation, or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Our portfolio of corporate and government bonds could also be adversely impacted. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our operations, growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn or rising inflation, which could directly affect our ability to attain our operating goals on schedule and on budget.

Other international and geo-political events could also have a serious adverse impact on our business. For instance, in February 2022, Russia initiated military action against Ukraine. In response, the United States and certain other countries imposed significant sanctions and trade actions against Russia and could impose further sanctions, trade restrictions, and other retaliatory actions. While we cannot predict the broader consequences, the conflict and retaliatory and counter-retaliatory actions could materially adversely affect global trade, currency exchange rates, inflation, regional economies, and the global economy, which in turn may increase our costs, disrupt our supply chain, impair our ability to raise or access additional capital when needed on acceptable terms, if at all, or otherwise adversely affect our business, financial condition, and results of operations.

Our business could be negatively impacted by environmental, social and corporate governance (ESG) matters or our reporting of such matters.*

There is an increasing focus from certain investors, employees, partners, and other stakeholders concerning ESG matters. We may be, or be perceived to be, not acting responsibly in connection with these matters, which could negatively impact us. For instance, the SEC has recently proposed climate change and ESG reporting requirements, which, if approved, would significantly increase our costs. In addition, we currently do not report our environmental emissions, and lack of reporting or future reporting could result in certain investors from declining to invest in our common stock.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

None.

Item 5. Other Information.

None.

Item 6. Exhibits.

The following exhibits are filed as part of this report:

Exhibit Number	Description
3.1	Articles of Association of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Form 6-K (File No. 001-38079), filed with the SEC on May 18, 2017).
10.1+	Manufacturing and Supply Agreement, dated May 30, 2020, by and between the Registrant and Isotopia Molecular Imaging Ltd. (the "Isotopia Agreement") and the extension to the Isotopia Agreement, dated August 25, 2022, by and between the Registrant and Isotopia Molecular Imaging Ltd.
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1#	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2#	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document – The instance document does not appear in the interactive data file because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	The cover page from the Company's Quarterly Report on Form 10-Q has been formatted in Inline XBRL

The information in Exhibits 32.1 and 32.2 shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act (including this Quarterly Report), unless the Registrant specifically incorporates the foregoing information into those documents by reference.

\+ Certain portions of this exhibit are omitted because they are not material and are the type that the Registrant treats as private and confidential.

Signatures

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

UroGen Pharma Ltd.

November 10, 2022 By: /s/ Elizabeth Barrett
Elizabeth Barrett
Chief Executive Officer
(Principal Executive Officer)

November 10, 2022 By: /s/ Don Kim
Don Kim
Chief Financial Officer
(Principal Financial and Accounting Officer)

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE AND CONFIDENTIAL.

Execution Version

MANUFACTURING AND SUPPLY AGREEMENT

This Manufacturing and Supply Agreement is made and entered into as of May 26, 2020 by and between **UroGen Pharma Ltd.**, with a principal place of business or an office at 9 HaTa'asiya Street, Ra'anana 4365007, Israel (the "**Buyer**") and **Isotopia Molecular Imaging Ltd.** with its principal place of business located at located at Alexander Yanai 39 Street Segula Industrial Park Petach Tikva 49277, Israel. (the "**Supplier**") (hereinafter referred to individually as a "**Party**" and collectively as the "**Parties**").

WHEREAS, Buyer is engaged in the development, production, formulation, sale and distribution of medical device and pharmaceutical products and is seeking a manufacturer to produce sterile vials of a Product (as defined below);

WHEREAS, Supplier maintains and operates a sterile manufacturing plant, cGMP certified by U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and Israeli Ministry of Health (MOH), which features Class D/C/B/A cleanrooms (equivalent to ISO 8/7/6/5 cleanrooms), and has manufacturing capacity, experience, and expertise in the manufacturing of sterile pharmaceutical products and has provided the Quote (as defined below) to carry out the Services (as defined below); and

WHEREAS, Buyer desires to have Supplier produce sterile filled vials or other pharmaceutical containers forms of the Product and supply them to Buyer, and Supplier is willing to manufacture and supply such sterile Product to Buyer.

NOW THEREFORE, in consideration of the foregoing premises, which are incorporated into and made part of this Agreement, and of the mutual covenants which are recited herein, the Parties agree as follows:

1. Definitions

In this Agreement, the following terms have the following respective meanings:

1.1 **"Adverse Event**" means in connection with the Product (as defined below) any product complaint, event that bears adverse effect or recall.

1.2 **"Adverse Event Costs**" means any expenses and costs related to Adverse Event investigation conclusions and relevant corrective actions resulting therefrom.

1.3 **"Affiliate**" means with respect to a Party, any company or entity controlled by, controlling, or under common control with such Party. For the purposes of this definition, the word "control" (including, with correlative meaning, the terms "controlled by" or "under the common control with") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of such entity, whether by the ownership of more than fifty percent (50%) of the voting stock of such entity, or by contract or otherwise.

1.4 **"Agreement**" means this Manufacturing and Supply Agreement and the exhibits and schedules hereto.

1.5 **"Audit**" means an inspection, scheduled or unscheduled, as required from time to time by an Auditor.

1.6 **"Auditor**" means the FDA, EMA, European Notified Body, Buyer-authorized representative, or other competent Regulatory Authorities.

1.7 **"Business Day**" means Sunday through Thursday except for days on which banking institutions in Tel Aviv, Israel are permitted or required to be closed.

1.8 **"Buyer Indemnitees**" means Buyer, its Affiliates, and their respective directors, officers, employees, and agents.

1.9 **"Buyer Intellectual Property**" means all Intellectual Property Rights (a) owned or controlled by Buyer as of the Effective Date and (b) developed by or on behalf of Buyer (including by Supplier or its Affiliates, representatives, or subcontractors) during the Term in connection with the Services under this Agreement, including all Inventions (as defined in Section 11.1) and Supplier's production processes and quality control.

1.10 **"Certificate of Analysis**" means a certificate evidencing all the acceptance criteria and tests for each batch of Deliverables in the form attached hereto as **Exhibit H**.

1.11 **"Certificate of Compliance**" means a document, signed by an authorized representative of Supplier, attesting that a particular batch was Manufactured in accordance with cGMPs, applicable laws, rules and regulations, and the Specifications.

1.12 **"cGMP**" means the current Good Manufacturing Practice as established by (a) the Israeli Ministry of Health, (b) ICH Guidelines cGMP, (c) Q7: Good Manufacturing Practice Guide For Active Pharmaceutical Ingredients; EudraLex - Volume 4 Good Manufacturing Practice (GMP) guidelines, (d) CFR 21 Part 211: Current Good Manufacturing Practice For Finished Pharmaceuticals and FDA Guideline; (e) Sterile Drug Products Produced by Aseptic Processing; and (f) all other relevant FDA and EMA cGMP guidelines or any successor agency.

1.13 **"Claims**" means all losses, damages, liabilities, costs, and expenses (including reasonable attorneys' fees and expenses).

1.14 **"Confidential Information**" means all confidential information of a Party that is designated as "Confidential," "Proprietary," or some similar designation, or which by its nature should be reasonably construed as being confidential, relating to any designs, know-how, technologies,

findings, inventions, chemical structures, mixtures, compounds, substances, molecules, coating compositions, specifications, technical data, ideas, concepts, uses, processes, methods, formulae, procedures, research and development activities, work in process, or any scientific, engineering, manufacturing, marketing plans, drawings, sketches, product schematic, documents, manuals, reports, studies, photographs, samples, programs, source codes, prototypes, improvements, algorithms, architectures, business plan or financial information relating to the disclosing Party, its present or future products, sales, prices, suppliers, customers, employees, investors or business, whether in oral, written, visual, graphic, electronic, or other form disclosed by the Parties prior to or during the Term (which is marked confidential or acknowledged as being confidential prior to disclosure whether or not patentable or protectable by copyright). Confidential Information shall also include any other information in oral, written, graphic, electronic, or other form which, given the nature thereof, would be considered confidential, whether or not marked or identified as confidential. For the avoidance of doubt, all materials, records, and documentation pertaining to the Deliverables, including any documents or reports from any authority, are Buyer's Confidential Information.

1.15 **"Dedicated Equipment**" means equipment and tools owned or purchased by Buyer or on its behalf and expense, validated by Supplier for Manufacture of the Products and Deliverables, and deposited in Supplier's possession as detailed in the list set forth in **Exhibit C**, as amended from time to time by mutual agreement of the Parties.

1.16 **"Deliverables**" means the Products ordered by Buyer under a certain Purchase Order, the Certificate of Analysis, the Certificate of Compliance, batch record, and other related documents and documentation requested in such Purchase Order.

1.17 **"Delivery**" means the moment at which Buyer's carrier takes control of the shipment at the EXW location as specified in Section 7.7 below.

1.18 **"Effective Date**" means the date first written above.

1.19 **"EMA**" means the European Medicines Agency and any successor agency thereto.

1.20 **"European Notified Body**" means an entity in the European Union that has been accredited by a member state of the European Union to assess whether a product to be placed on the market meets certain preordained standards.

1.21 **"Facility**" means the facility operated by Supplier located in Soreq, Yavne, Israel.

1.22 **"FDA**" means the United States Food and Drug Administration and any successor agency thereto.

1.23 **"Force Majeure Event**" means any cause beyond a Party's reasonable control, including acts of God, fire, explosion, weather, disease, war, insurrection, civil strike, riots, labor strike or lock-out, breakdown or malfunction of equipment (including Buyer's Dedicated Equipment) not due to said Party's action, omission, fault or responsibility, power failure, or energy shortages.

1.24 **"Information**" means all technical, scientific and other know-how and information, trade secrets, knowledge, technology, means, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, apparatuses, specifications, data, results and other material, including: biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, manufacturing and quality control data and information, including study designs and protocols, assays and biological methodology, in each case (whether or not confidential, proprietary, patented or patentable) in written, electronic or any other form now known or hereafter developed.

1.25 **"Intellectual Property Rights**" means all forms of intangible proprietary rights, title or interests recognized under any applicable laws, whether or not patentable or registerable, including trademarks, service marks, trade dress, logos, copyrights, rights of authorship, inventions, patents (including all applications and registrations with respect thereto), rights of inventorship, moral rights, rights of publicity and privacy, trade secrets, industrial design rights, rights under unfair competition and unfair trade practices laws, know how, show how, and all other intellectual and industrial property rights related thereto.

1.26 **"Latent Defect**" means any defect in a Deliverable that (a) is not reasonably discoverable at the time of Supplier's delivery of such Deliverable through Buyer's normal incoming goods inspection methods and procedures, which methods and procedures shall be in accordance with the Quality Agreement, or is not reasonably discoverable at the time of Supplier's delivery of such Deliverable to Buyer's contract manufacturer or other designee that receives the Deliverable, or (b) is discovered by Buyer's licensee to the extent such defect existed as of the time the Deliverable was delivered by Supplier to Buyer or its contract manufacturer or other designee pursuant to this Agreement.

1.27 **"Manufacture**" and "**Manufacturing**" means all activities conducted related to the managing and ordering of Raw Materials, testing, production, manufacture, processing, filling, packaging, labeling, shipping and holding of any product or any intermediate thereof, including process optimization and development, process qualification and validation, scale-up, pre-clinical, clinical and commercial manufacture and stability testing, quality assurance and quality control.

1.28 **"Manufacturing Process**" means all Information relating to the then-current process for the Manufacture of the Product.

1.29 **"MBR**" means the Master Batch Record provided by Supplier and approved in writing by Buyer and Supplier, as referenced in **Exhibit B**.

1.30 **"Nonconforming Deliverable**" means a batch of Deliverables that fails to meet the Specifications.

1.31 **"Product**" means Buyer's product meeting the Specifications set forth in **Exhibit A**.

1.32 **"Purchase Order**" means a written purchase order issued pursuant to terms of Section 7.2 and can be between [***] of the Binding Forecast (as defined in Section 7.1).

1.33 **"Quality Agreement**" means the Quality Agreement attached hereto as **Exhibit F**.

1.34 **"Quote**" means Supplier's quote for the Manufacture of released vials of the Product for use in clinical trials and for use in the manufacture of Buyer's finished product containing such released vials of Product, attached hereto as **Exhibit D**.

1.35 **"Raw Materials**" means any and all raw materials, consumables, packaging materials and components needed by Supplier to Manufacture

Product according to the terms and conditions of this Agreement and listed in the MBR.

1.36 **"Regulatory Authority**" means any applicable governmental authority or agency with jurisdiction or authority over the development, manufacture, commercialization, or other exploitation of pharmaceutical or biologic products in a particular country or other regulatory jurisdiction, including FDA, EMA and the Israeli Ministry of Health.

1.37 **"Services**" means the services listed in **Exhibit E**, including storage, Manufacturing, testing processes, and packaging of Product for use in clinical trials and for use in the manufacture of Buyer's finished product containing such released vials of Product for commercial supply and sale.

1.38 **"SOP**" means a Standard Operation Procedure of Supplier.

1.39 **"Specifications**" means the specifications for the product, minimum released quantity, product specifications and Manufacturing Process including testing, labeling, packaging and storing, which are listed hereto as **Exhibit A**.

1.40 **"Supplier Indemnitees**" means Supplier, its Affiliates and their respective, directors, officers, employees or agents.

1.41 **"Supplier Intellectual Property**" means all Intellectual Property Rights owned or controlled by Supplier as of the Effective Date and developed by or on behalf of Supplier (including its representatives and subcontractors) during the Term outside of the Services under this Agreement, including Supplier's production processes and quality control.

1.42 **"Term**" has the meaning set forth in Section 17.1 hereof.

2. **Scope of Agreement**

2.1 On and subject to the terms and conditions of this Agreement and the Specifications, Supplier shall Manufacture, store and deliver (as provided in Section 7.6 and Section 7.7) the Product to Buyer pursuant to one or more Purchase Orders.

2.2 Supplier shall provide the Services at the Facility as per the procedures specified in the Quote, all in accordance with the terms and conditions set forth in the Quality Agreement, MBR, the Specifications, and this Agreement.

2.3 Supplier shall Manufacture the Product in accordance with the Specifications and in compliance with all applicable laws, including cGMP.

2.4 Supplier shall not Manufacture any Product until Buyer has approved the Specifications, MBR, and relevant SOPs. Buyer shall deliver to Supplier written notice of any changes to the Specifications, MBR, and relevant SOPs and Supplier shall accommodate such changes; *provided*, that Buyer shall reimburse Supplier for [***]. Any changes to the Specifications by Buyer shall be incorporated to this Agreement as a written amendment to **Exhibit A** hereto and shall be implemented within the time frame set forth in the amended **Exhibit A**. It is agreed that any change in the Specifications will not apply to Purchase Orders already submitted by Buyer prior to any such change. Supplier may not make any changes to the Specifications, MBR, or the relevant SOPs without Buyer's prior written consent.

2.5 Buyer may review and comment on all SOPs applicable to the Manufacture of the Product and may comment on and approve any SOPs that are solely applicable to the Manufacture of the Product, if any. Supplier may not make any changes to the SOPs applicable to the Manufacture of the Product without Buyer's prior written consent.

2.6 Any modifications that may affect the provision of Services required by any applicable Regulatory Authority with jurisdiction to require such modifications shall be made in accordance therewith subject to mutual written agreement between the Parties as to timelines and terms under which such modifications shall be implemented. In case the change in the regulatory law or regulation prevents the provision of the Services, Supplier and Buyer shall promptly meet to discuss such change as it relates to the Services and Supplier shall stop any activity until such issue is resolved and a mutual agreement is reached. It is hereby clarified that in the event that an applicable regulatory requirement that applies only to the provision of the Services under this Agreement, may not be implemented by Supplier using [***], due to either (a) its excessive and unreasonable cost compared to the expected compensation payable pursuant to this Agreement, (b) its material adverse effect on the Facility's infrastructure or its (c) material adverse effect on other services provided by Supplier to other current and active clients, then Supplier and Buyer shall promptly negotiate in good faith a mechanism to share the costs of implementing such change or to address such material adverse effect, as applicable. In the event Supplier and Buyer are not able to agree upon such terms within [***] of starting such negotiations, then such dispute shall be resolved by [***] arbitration procedure in accordance with the provisions of **Exhibit G**. The decision of such arbitrator shall be final and binding on the Parties. For clarity, if the arbitrator determines that Supplier will not be obligated to implement the said requirement, then Buyer shall be entitled to terminate the Agreement immediately.

2.7 Supplier may not sub-contract with any third party to perform all or any part of the Services entrusted to it under this Agreement without Buyer's prior written consent and approval of any such arrangement. To the extent Buyer approves in writing in advance, Supplier shall, at Supplier's expense, qualify each of such sub-contractor prior to its involvement and remain fully responsible for the work of any such approved third party.

2.8 In the event of a conflict between the terms and conditions of this Agreement and the Quality Agreement, the terms and conditions of this Agreement shall prevail, except for technical quality responsibility issues, with respect to which the Quality Agreement shall prevail over this Agreement.

2.9 During the Initial Term, Buyer will purchase [***] of its total requirements of Product for commercial sale of Buyer's product referred to as UGN-101 during such time period; *provided, that*, the foregoing requirement shall no longer apply in the event Supplier is unable to timely supply Buyer's requested requirements of Product with conforming Product by the requested delivery date, including any failure due to a supply failure, quality concern or force majeure event. For clarity, in the event Buyer does not have any requirements of Product for commercial sale (e.g. the Product does not get approved or Buyer elects not to commercialize the Product), then Buyer shall have no obligation to submit purchase orders for any minimum quantity of Product pursuant to this Agreement.

3. **Supplier's Representations, Warranties and Covenants**

Supplier represents, warrants, and covenants that:

3.1 It shall perform all of its responsibilities pursuant to this Agreement in accordance with cGMP requirements and applicable laws;

3.2 Each batch of the Deliverables shall (i) be Manufactured in compliance with the terms of this Agreement, the Quality Agreement, applicable laws of jurisdictions agreed to by the Parties in writing, and cGMP; (ii) meet the Specifications; (iii) be packaged in accordance with the Specifications; and (iv) be free and clear of any liens or encumbrances of any kind; and (v) contain a Certificate of Analysis, a Certificate of Compliance, and a batch record;

3.3 The Services will be performed in a timely fashion and in a [***], and in accordance with the terms of this Agreement, the Quality Agreement (following the execution thereof), and the applicable law of the jurisdiction where the Product is Manufactured and any other jurisdiction mutually agreed to by the Parties in writing, and cGMP for clinical and commercial supply;

3.4 Any Intellectual Property Rights used by Supplier in connection with the Manufacture and supply of the Product is Supplier's property and does not, to the knowledge of Supplier, infringe any intellectual property right or proprietary right of any third party, whether or not registrable;

3.5 It shall perform the production of each batch under this Agreement according to MBR and the proper controls set forth in **Exhibit B**;

3.6 It lawfully maintains and operates the Facility, and that the Facility shall be maintained in accordance with applicable laws and cGMP and in such condition as will allow Supplier to perform the Services in compliance with this Agreement, the Quality Agreement, applicable laws of the jurisdiction where the Product is Manufactured and any other jurisdictions agreed to by the Parties in writing, and cGMP;

3.7 It has the knowledge, experience and competent personnel to carry out its undertakings pursuant to this Agreement in accordance with this Agreement, the Quality Agreement, applicable laws of the jurisdiction where the Product is Manufactured and any other jurisdictions agreed to by the Parties in writing, and cGMP;

3.8 It has the full power, right and authority to enter into, execute and deliver this Agreement;

3.9 It shall use the Dedicated Equipment and Buyer Intellectual Property solely to perform the Services, and that neither it nor its Affiliates, representatives, or subcontractors will use the Dedicated Equipment or Buyer Intellectual Property for any other purpose, without Buyer's prior written consent;

3.10 Neither it nor its Affiliates, representatives, or subcontractors will conduct any analysis, reverse engineering or modification of the Products;

3.11 It shall not, itself or through any third party, incorporate any Supplier Intellectual Property into any process step or Deliverables; and

3.12 It shall not develop or commercialize any Buyer Intellectual Property or any products that are developed, manufactured or produced using any Dedicated Equipment and Buyer Intellectual Property, in each case, except in connection with the performance of the Services in accordance with the terms and conditions set forth herein.

4. **Responsibilities of Supplier**

4.1 Without derogating from Supplier's undertakings pursuant to any other provision of this Agreement or the Quote, Supplier shall:

4.1.1 Purchase Raw Materials for the Services from manufacturers and suppliers qualified for cGMP purposes by Supplier and pre-approved by Buyer;

4.1.2 Store the Dedicated Equipment in accordance with the provisions of Section 8 below;

4.1.3 Assure that the required storage conditions of Manufacturing and storage rooms temperature for each batch of the Deliverables and the stability chambers storage condition are maintained in accordance with the Specifications and immediately notify Buyer of any deviation from said storage conditions;

4.1.4 Purchase, sample, conduct quality control testing, including taking and storing and releasing (or rejecting) of all production materials in accordance with the SOPs, methods and the Specifications, so as to ensure that the materials are suitable for their intended purpose;

4.1.5 Manufacture the Product according to the MBR and Specifications;

4.1.6 Perform quality control and quality assurance for all parts of the Manufacturing operations pursuant to this Agreement, the Quote, Specifications, and the Quality Agreement;

4.1.7 Provide Buyer a copy of the executed MBR, and raw data and Certificate of Analysis for those quality control tests performed by Supplier as detailed in the Quality Agreement, as reviewed and released (or rejected) by its quality assurance department for each batch of Deliverables. Supplier shall provide the batch documentation to Buyer for evaluation, prior to release and shipment of each batch, including Raw Material.

4.1.8 Obtain all Regulatory Authorities permits for the Facility and Deliverables and provide a copy thereof to Buyer upon its request;

4.1.9 Verify by visual identification and inspection the compounding, filling, capping, labeling, packaging of each batch of the Deliverables as described in the Quote, Specifications, and Quality Agreement;

4.1.10 Utilize a batch number as assigned by Buyer for each batch of Deliverables in accordance with the SOPs and as set forth in the Quote, Specifications, and Quality Agreement;

4.1.11 Perform environmental monitoring routinely and during provisions of the Services and track the environmental monitoring data in accordance with cGMP and Supplier SOPs;

4.1.12 Supply the items set forth in the Quote in quantities sufficient for the performance of the Services by Supplier;

4.1.13 Deliver the quantity of the Deliverables per each Purchase Order on the delivery date specified therein, as well as a sufficient amount for the retention of samples of the Deliverables by Supplier as set forth in the Quality Agreement;

4.1.14 Perform all final Product quality control testing at its Facility, other than those tests specifically stated in the Quality Agreement as being performed by Buyer or its designee;

4.1.15 Package and store the retained samples separately from the rest of the batch in accordance with the SOPs and Quality Agreement;

4.1.16 Maintain and archive all batch records and other documents in accordance with applicable SOPs, cGMP, good documentation practices as set forth in **Exhibit A**, applicable law, the Buyer documentation SOPs, the Supplier's SOPs requirement, and the Quality Agreement;

4.1.17 Transfer all batch records and other documents required to be maintained pursuant to Section 4.1.16 to Buyer upon Buyer's request;

4.1.18 Notify Buyer with immediate effect (no later than [***]) of all events, occurrences, reporting and investigations regarding the Deliverables as set forth in and the Quality Agreement;

4.1.19 Perform stability studies at intervals as planned according to Specifications at Supplier's cost, all subject to the respective provisions of the Quality Agreement. Supplier shall start each stability intervals testing on, but in any event no later than [***] after, the planned date. For the pivotal stability study, the Supplier shall utilize samples from [***] batches. With respect to each batch, the Supplier shall keep the stability batch)es) for a period of [***] as of production of the respective batch; and

4.1.20 Provide support, reasonably requested by Buyer, with respect to the chemistry, manufacturing and controls of the Product, as specified by the FDA or other applicable Regulatory Authorities ("**CMC**"), including by preparing and providing to Buyer CMC related regulatory materials, or portions thereof, for the Products.

4.1.21 Provide all assistance reasonably requested by Buyer to prepare for any meeting or teleconference with Regulatory Authorities and to respond to any requests from Regulatory Authorities with respect to the Product.

4.1.22 Notify Buyer of any critical deviations that occurred throughout the Manufacture and affect the Product no later than [***] from its discovery. If said deviation in manufacturing will cause low yield and the number of vials of Product to be released will be lower than the number set forth in the Purchase Order, then Sections 7.5 and 7.12 will apply.

4.2 Supplier shall be solely and exclusively responsible for the adequate conditions, but not less than applied to its own property, of all items provided to it by or on behalf of Buyer into its possession for purposes of this Agreement as though it were a paid custodian.

4.3 At all times, Supplier shall be adequately ready for an Audit as required from time to time by Auditor and shall (at its own expense) take all measures required to meet the criteria required and be approved by the respective Auditor. If Supplier is required to make any material changes to the Facility based on an Audit occurring after the Effective Date, Supplier shall implement such changes and the costs involved in such changes shall be borne, as follows:

4.3.1 If all corrective actions resulting from the Audit are related directly to the Manufacturing process or to the Quality Management System, or deriving therefrom, then Supplier will bear all cost and expenses;

4.3.2 If all corrective actions resulting from the Audit are related directly to Buyers product or process (for example the Dedicated Equipment), or deriving therefrom, then Buyer will bear all cost and expenses; and

4.3.3 If the corrective actions resulting from the Audit are equivocal and cannot be solely attributed under Section 4.3.1 or Section 4.3.2, [***].

4.4 Supplier shall notify Buyer in writing immediately upon learning any issue that may result in a supply interruption of greater than [***].

4.5 Supplier shall be responsible for inventory management, material planning and ordering of Raw Materials required to fulfill Buyer's Binding Forecasts and Purchase Orders. Upon the request of Buyer, Supplier shall order and maintain a safety stock of Raw Materials sufficient to meet a reasonably requested number of months within Buyer's then current Forecast ("**Safety Stock**"). Supplier shall timely increase the quantity of Safety Stock upon any corresponding increase in Buyer's Forecasts. Supplier shall track usage of Raw Materials pursuant to this Agreement (including usage of Safety Stock, if any) and shall timely provide written notice to Buyer recommending when additional Raw Materials should be ordered (which notice shall include the current inventory level, the recommended quantity to be ordered, the estimated delivery date if ordered and the applicable price). Upon Buyer's approval of any such recommendation and issuing a purchase order for such purchase of Raw Materials, Supplier shall promptly order such quantity of Raw Materials. Buyer shall be responsible for payment of all Raw Materials (including Safety Stock) properly ordered by Supplier in accordance with Section 10.2. Supplier shall not be responsible for any lack of inventory of Raw Materials to the extent such lack of inventory results from (a) Buyer's failure to timely approve Supplier's recommend order for Raw Materials in accordance with this Section 4.5 or (b) the applicable third party vendor's failure to timely supply the applicable Raw Materials timely ordered by Supplier or (c) Buyer's request to have such Raw Materials delivered to Buyer in accordance with the terms of this Section 4.5. Upon Buyer's written request and at Buyer's cost for shipping, Supplier shall deliver any requested portion of the Raw Materials in Safety Stock [***] at the Supplier's facility or such other delivery location in Israel designated by Supplier. Upon termination or expiration of this Agreement, Supplier shall deliver al unused Raw Materials in Safety Stock to Buyer [***] at the Supplier's facility or such other delivery location in Israel designated by Supplier.

5. **Responsibilities of Buyer**

Buyer shall:

5.1 Provide Supplier with all the written information required and reasonably requested by Supplier for the purpose of performing the Services.

5.2 Place Purchase Orders for each Product production, including batch, batches, or campaign; provided, that nothing herein requires Buyer to place any Purchase Orders with Supplier.

5.3 Notify Supplier within [***] of any problems that are reasonably likely, to the best of its judgment, pose a hazard to Supplier's premises, equipment, personnel, other materials or other products. Notwithstanding the foregoing, in emergency situations, when the contact should be made before implementing any action, such as recall, contact with the Supplier must be made [***] to discuss the situation and agree on an appropriate course of action. The data will be recorded in the Supplier's designated form, and it will describe the subject matter and the circumstances requiring it. The Buyer should contact the responsible person at the Supplier as follows:

Name: [***] (New product and CMO manager)

Telephone: [***]

Fax: [***]

Email: [***]

5.4 Pay all amounts due to Supplier according to this Agreement on a timely basis.

6. **Compliance**

6.1 Supplier shall Manufacture and test Product in the Facility unless otherwise agreed in advance and in writing by the Parties. Supplier shall, at its expense, maintain its Facility used for the Manufacture of Product in compliance with all applicable laws, rules and regulations, including cGMP and any applicable environmental, health and safety laws applicable on the Effective Date or thereafter during the Term.

6.2 Supplier shall, at its expense, obtain and maintain all permits and approvals from Regulatory Authorities that are required to perform the Services as contemplated hereunder. Supplier shall use best efforts to obtain and maintain an FDA approved cGMP facility and operation.

6.3 Supplier shall permit representatives of Buyer to visit the Facility for the purpose of observing the Manufacturing, including testing, labeling, packaging and storing of Products. Buyer shall give Supplier [***] notice, of no less than [***], of any proposed visit to the Facility. Any such visit shall be [***] and any information gathered during such visits shall be kept confidential.

6.4 Upon occurrence of an Adverse Event, Buyer shall coordinate the investigation, and, if required, inform the competent authorities and coordinate any recall of Product. Supplier shall reasonably cooperate with Buyer in performing its part of the investigation, including by making available to Buyer any relevant information and, if so requested by Buyer, permitting Buyer's personnel to visit or audit the Facility to attempt to resolve the complaint or adverse event. The Parties shall bear all and any expenses and costs related to such investigation, conclusions, and relevant corrective actions, as follows:

6.4.1 If Supplier is found responsible for the Adverse Event, then Supplier shall bear all Adverse Event Costs;

6.4.2 If Buyer is found responsible for the Adverse Event, then Buyer shall bear all Adverse Event Costs;

6.4.3 If the Adverse Event resulted from Force Majeure Event then, unless the Parties agree otherwise in good faith, Supplier and Buyer would bear the Adverse Event Cost in equal parts.

6.5 Supplier shall provide Buyer with all information, documentation and assistance that are reasonably necessary or useful in the preparation of comprehensive and complete regulatory applications for submission and any amendments and supplements.

6.6 Supplier covenants that it (a) will not, and will not permit any of its Affiliates, officers, directors, employees, agents or Affiliates (collectively "**Covered Persons**") to, directly or indirectly make any payment or gift to Government Officials, political parties or candidates for office in any country for the purposes of winning or keeping business; (b) will not, and will not permit any Covered Person to, directly or indirectly bribe or improperly influence any Government Official in any country in which it does business; (c) will not, and will not permit any Covered Person to, use bribes, kickbacks, or other means of obtaining undue or improper advantage, or engage in corrupt practices of any type; and (d) will otherwise comply in all respects with the U.S. Foreign Corrupt Practices Act of 1977, as amended, and any other anti-bribery, anti-corruption and anti-money-laundering applicable law. For purposes of this Section 6.6, a "**Government Official**" is any official, officer, director, employee, agent or representative of: (a) a federal, provincial, regional, territorial, state, district, municipal or local government or of any agency, board or instrumentality thereof; (b) an entity owned or controlled by a government entity; or (c) a public international organization.

6.7 In the event that Buyer reasonably suspects that any provision of Section 6.6 has been breached, Buyer will have the right to conduct an investigation of such suspected breach upon [***] to Supplier, and Supplier will provide all [***] to any investigation conducted by Buyer or its designees. Buyer will have the right to suspend any payment to Supplier or its Affiliates for the performance of Services implicated by such investigation for the pendency of such investigation.

7. **Annual Forecasts; Purchase Orders and Deliveries**

7.1 Not later than the [***] day of each month, Buyer will provide to Supplier in writing a rolling estimate of Buyer's orders for Product for the following [***] (or such longer period as Buyer may choose, in its discretion or a shorter period of time in the event the Agreement is set to expire prior to the end of such [***] period) (the "**Forecast**"), taking into consideration reasonable expectations for the [***] in question. The [***] of each Forecast shall be considered as a "**Binding Forecast**". Supplier shall be liable for failure to comply with a Binding Forecast or Purchase Order to the extent caused by lack of available inventory of Raw Materials as a result of Supplier's failure to properly manage

inventory of Raw Materials or Supplier's failure to timely recommend ordering or order Raw Materials in accordance with Section 4.5. Supplier shall not be liable for failure to comply with a Binding Forecast or a Purchase Order to the extent caused by lack of available inventory of the Raw Materials as a result of (a) Buyer's failure to timely approve Supplier's recommend order for Raw Materials in accordance with Section 4.5 or (b) the applicable third party vendor's failure to timely supply the applicable Raw Materials timely ordered by Supplier.

7.2 Buyer shall submit its Purchase Order to Supplier by e-mail whenever Buyer desires to purchase Product from Supplier. Each Purchase Order will specify the quantity of Product desired, and the required delivery date; provided, that the lead time for any Purchased Order, and the required delivery date specified therein, must be at least [***] after the date of the Purchase Order, or such other time period as may be mutually agreed upon by Buyer and Supplier in advance. In the event of any conflict between the provision of this Agreement and any Purchase Order, the provisions of this Agreement will control unless such Purchase Order expressly states that it prevails over this Agreement and is signed by duly authorized representatives of both Parties. Buyer may amend or postpone a certain Purchase Order [***] within [***] following its submission without incurring any penalty thereon. If Buyer cancels a certain Purchase Order upon written notice after its submission date and Buyer does not issue a new Purchase Order in lieu of the cancelled one, Buyer shall [***].

7.3 Buyer shall be responsible for submitting Purchase Orders for all batches of Product as required to comply with applicable regulatory requirements.

7.4 Purchase Orders submitted in accordance with this Section 7 will not be deemed accepted by Supplier unless Supplier informs Buyer that Supplier has accepted such Purchase Order within [***] after its receipt of the same; provided, however, that Supplier may not reject any Purchase Order and shall confirm acceptance within such [***] period of each Purchase Order issued in accordance with Section 7.1 and Section 7.2 and Supplier shall deliver (in accordance with Section 7.7) the quantities of Product ordered by the delivery date (that meets the lead time in Section 7.2) as specified in such accepted Purchase Order (the "**Delivery Date**"). If Supplier later becomes unable to deliver Product by the Delivery Date, it will immediately inform Buyer of same in writing and will provide alternate delivery dates when the unfilled portion of such Purchase Order may be delivered, which alternative delivery dates shall be as soon as practicable after the originally requested delivery date. If Supplier is unable to fill any portion of any Purchase Order that has been submitted to, and accepted by, Supplier in accordance with Section 7.2 and this Section 7.3, then, in Buyer's sole discretion, Buyer may, upon written notice to Supplier, immediately cancel the affected Purchase Order and the terms of Section 7.4 shall apply.

7.5 If Supplier is unable to deliver the quantity of Product ordered under a Purchase Order within [***] of the Delivery Date due to an act or omission by Supplier ("**Late Delivery**"), then Buyer will receive a credit from Supplier for such Late Delivery that will be applied against the purchase price under the next Purchase Order. The credit will be [***]. If not rectified by [***] of the Delivery Date, the credit shall increase to [***]. In the event there are [***] or more Late Deliveries in any [***] period due to any act or omission by Supplier, Buyer will have the right to terminate this Agreement immediately. Upon termination Supplier will be responsible for continuing to provide Product until such time that Buyer has secured and received approval for sourcing Product from another supplier. Supplier will also, at is sole expense, fully assist Buyer in sharing of pertinent information and technology transfer to a new supplier. For clarity, a Late Delivery will not include any delay in shipment of Product caused by a Force Majeure Event.

7.6 Supplier shall store and package the Deliverables in accordance with methods of packaging, preserving and monitoring as set forth in **Exhibit E**. Buyer shall arrange for the shipment of the Deliverables in coordination with Supplier.

7.7 All Product will be delivered [***] at the Supplier's facility or such other delivery location in Israel designated by Supplier. [***]. Unless otherwise agreed by the Parties, Supplier will select the method and manner of packaging of the Product, which will be carried out in accordance with Supplier's customary practices and the Specifications for the Product. At Buyer's request, Supplier shall assist Buyer with export and import formalities and procedures, including assisting Buyer with required documentation and communications with the applicable customs offices in connection with the export and import of Product.

7.8 Supplier will provide Buyer, together with each invoice, the results of all testing required to be run under the Specifications. Within [***] of the Buyer's receipt of the Deliverables, if Buyer does not approve or notify Supplier of any Nonconforming Deliverable, the Deliverables shall be deemed accepted; provided, however, with respect to any Nonconforming Deliverables containing a Latent Defect, Buyer will notify Supplier within [***] after discovery of such Latent Defects.

7.9 Any claims of non-conformance by Buyer regarding Product delivered shall specify in reasonable detail the nature and basis for the claim and cite the relevant batch numbers or other information to enable specific identification of the Product involved. Supplier agrees to review any written claim made by Buyer regarding the quality of the Product and to provide Buyer with the initial results of such review in writing within [***] of receiving Buyer's claim and the complete results within [***]. If such review and testing by Supplier confirms that a certain quantity of Product did not meet the Specifications, Buyer shall have the right to reject such batch. Buyer shall have the right to withhold payment for any Product during the review and testing by Supplier to confirm whether such Product met the Specifications and during any testing performed pursuant to Section 7.10.

7.10 If the Parties fail to agree as to whether or not a delivered Product complies with the Specifications at the time of delivery, the Parties shall:

7.10.1 Have the batch in dispute tested and where required further analyzed by an independent testing laboratory (with respect to compliance with the Specifications) mutually agreed to by the Parties, (i.e., a testing laboratory that is considered acceptable by the Supplier and Buyer). If the Parties do not agree on the identity of such laboratory, then Buyer shall propose at least [***] candidates and Supplier shall choose one (1) of the proposed candidates. If Supplier does not notify Buyer of its selection within [***] of the receipt of the candidates list from Buyer, then Buyer may choose the laboratory, and such election shall be final and binding upon the Parties.

7.10.2 The decision of the independent testing laboratory shall be deemed final as to any dispute over the Product quality.

7.10.3 Should the independent laboratory determine that delivered Product is Nonconforming Deliverable, Supplier shall bear all costs of the independent laboratory and Buyer shall have the right to reject such batch.

7.10.4 If said quantity of Product is determined by the independent laboratory to have met the Specifications, then it will be deemed accepted. [***].

7.11 If Buyer rejects a Product in accordance with Section 7.8 or 7.10 above and Supplier does not dispute such rejection, or if the independent testing laboratory determines that a delivered batch is Nonconforming Deliverable, (a) Supplier shall promptly replace such batch with conforming batch at Supplier's expense (including the cost of Raw Materials), in any event within [***] of Supplier's receipt of the Nonconforming Product (pending availability of Raw Materials; provided that Supplier shall use diligent efforts to promptly obtain such Raw Materials) and (b) if Buyer has not previously paid for the Nonconforming Deliverable at the time of rejection, then Buyer shall be liable to pay for the replacement conforming batch but shall not be liable to pay for the Nonconforming Deliverable. The provisions of this Agreement shall apply to the replacement batch, mutatis mutandis.

7.12 If Supplier fails to provide Buyer with the total quantity of Product ordered by Buyer pursuant to a Purchase Order, then (a) Supplier shall promptly deliver the balance of such ordered Product to Buyer within [***] of the original delivery date at no cost to Buyer and (b) Supplier shall indemnify Buyer for any losses incurred by Buyer as a result of Supplier's failure to meet its obligation to supply Buyer in accordance with Section 12.1.

8. Dedicated Equipment

8.1 Supplier shall purchase equipment for the performance of the Services and, if paid for by the Buyer, said equipment will be considered as Dedicated Equipment and owned by Buyer, including its documents, all receipts and invoices.

8.2 Supplier shall maintain and service the Dedicated Equipment in accordance the cGMP, the vendors' requirements, and Supplier's SOPs (as reviewed and approved by Buyer) at [***].

8.3 Supplier shall not use the Dedicated Equipment for any other internal or external business activities, unless such use is permitted in writing by the Buyer in advance.

8.4 All right and title in and to the Dedicated Equipment shall remain at all times with Buyer. Upon termination of this Agreement, the Supplier shall deliver the Dedicated Equipment to the Buyer free and clear from any liens or encumbrances.

8.5 Supplier shall deliver the Dedicated Equipment, including the Dedicated Equipment's maintenance and cleaning records, to Buyer at Buyer's expense, in good operating condition, with all assemblies in proper operating condition subject to reasonable wear and tear. The Supplier, at its expense, shall repair any damage to the Dedicated Equipment incurred due to use not in accordance with the terms of this Agreement or Buyer's written instructions.

9. Access and Inspection

9.1 Supplier shall permit Buyer's representatives or its designees to visit the Facility during normal working hours upon request and with [***], for the purpose of performing quality assurance audits at a mutually agreed time. Buyer may perform such audits annually, or at any time as set forth in the Quality Agreement. Buyer shall notify Supplier [***] regarding the expected audits [***].

9.2 Supplier shall permit, upon request, inspection of the Facility by any competent Regulatory Authority. Supplier shall immediately notify Buyer of any request for any such inspection, whether it is related to the Services or Deliverables, and Supplier shall coordinate any such inspection with Buyer. In such event, Buyer may send a representative to be present throughout so as to avoid any possible misunderstandings arising from the above described arrangements. Supplier shall consult with Buyer regarding any inspection, shall inform Buyer in writing of the results of any such inspection, and shall provide Buyer with a copy of any report or other written communication received from such competent Regulatory Authority with respect to any inspection at the Facility during the term of this Agreement. Buyer shall provide Supplier with an opportunity to compose, review, and comment on any responses required by Supplier to the applicable Regulatory Authority with respect to such inspection.

10. Price and Payment Terms

10.1 Supplier shall invoice Buyer, and Buyer shall pay for Product, in accordance with this Section 10 and as specified in the Quote. Supplier shall not change its prices for Product during the Initial Term. Thereafter, the Parties shall negotiate in good faith any change in the price of the Product.

10.2 For all Raw Materials and services ordered by Supplier following Buyer's approval, Supplier will receive approved purchase orders in accordance with Section 4.5 and before ordering the material or service., Supplier shall invoice Buyer directly for the costs of such Raw Materials (with reasonable documentation and packing slips associated with such costs) [***]. Buyer shall pay all such undisputed invoices provided by Supplier within [***] following the date of Buyer's receipt of the applicable invoice from Supplier. Buyer shall make each payment with no set-off against an invoice duly issued by Supplier, via wire transfer to a bank account to be indicated by Supplier. In the event the cost of any Raw Material increases by more than [***] from the last cost of such Raw Material paid by Buyer, then Supplier shall (a) provide prompt written notice of such cost increase to Buyer, (b) use diligent efforts to negotiate a lower price for such Raw Material and (c) at Buyer's request, allow Buyer to negotiate with the applicable supplier of such Raw Material on Supplier's behalf.

10.3 Supplier shall invoice Buyer for each Deliverable released by Supplier's quality assurance department in accordance with the Quality Agreement at the time such Deliverable is so released; provided, however, that the stated due date of each such invoice shall be no less than [***] following the date of Buyer's receipt of the applicable undisputed invoice from Supplier. Buyer shall make each payment with no set-off against an invoice duly issued by Supplier, via wire transfer to a bank account to be indicated by Supplier.

10.4 All prices specified in the Quote do not include local value added tax, taxes, charges, levies, assessments and other fees of any government or authority within the respective territory ("**Transfer Taxes**"), which shall be borne and paid by Supplier. The person(s) required by applicable law to file any necessary tax returns and other documentation with respect to Transfer Taxes shall file such tax returns and documentation provided that each Party shall use [***] to assist in the filing of such tax returns if necessary.

11. Intellectual Property Rights

11.1 Supplier owns all Supplier Intellectual Property. Buyer acknowledges and agrees that title to Supplier Intellectual Property shall always

remain with Supplier, and that Buyer shall not acquire any interest therein except as otherwise explicitly provided by this Agreement. Buyer shall not challenge, contest or otherwise impair Supplier's ownership of the Supplier Intellectual Property or the validity or enforceability of Supplier Intellectual Property Rights therein. Supplier hereby assigns to Buyer all of its right, title and interest in and to any invention or discovery, whether patentable or not, conceived or first reduced to practice in connection with or arising out of the performance of the Services, including in Manufacturing Process development or scale-up ("**Inventions**"). Supplier and its employees (including subcontractors and Affiliates) shall, upon Buyer's request [***], execute such documents and take such other actions as Buyer deems necessary for Buyer to obtain such ownership and to apply for, secure, and maintain patent or other proprietary protection of such Inventions. Supplier shall ensure that each of its employees, agents, personnel, and any subcontractors performing any part of the Services have a contractual obligation to assign all inventions and intellectual property rights therein created, discovered, or generated by such personnel as a result of performing the Services during the Term to Supplier so that Supplier can comply with its obligations under this Section 11.1, and Supplier shall promptly obtain such assignments.

11.2 Buyer owns all Buyer Intellectual Property. Supplier acknowledges and agrees that title to the Buyer Intellectual Property shall always remain with Buyer, and that Supplier shall not acquire any interest therein except as otherwise provided by this Agreement. Supplier shall not challenge, contest or otherwise impair Buyer's ownership of the Buyer Intellectual Property or the validity or enforceability of Buyer Intellectual Property Rights therein.

11.3 During the Term, Buyer hereby grants to Supplier a non-exclusive, limited license to use the Buyer Intellectual Property that is necessary for Supplier to perform its obligations under this Agreement, for the sole and limited purpose of Supplier's performance of the Services.

11.4 Supplier hereby grants to Buyer a non-exclusive, limited license to use the Supplier Intellectual Property that is necessary for Buyer to make or have made the Products if, notwithstanding Section 3.11, Supplier incorporates or relies upon Supplier Intellectual Property in developing the Manufacturing Process for or manufacturing the Products.

12. **Indemnification**

12.1 Supplier shall defend, indemnify and hold harmless Buyer Indemnitees from and against Claims in connection with any and all suits, investigations, claims or demands of any third party arising from or occurring as a result of (a) the breach of any representation or warranty made by Supplier hereunder; (b) the failure of Supplier to perform or observe any provision of this Agreement required to be performed or observed by Supplier hereunder (including the failure of Supplier to pay any Transfer Tax required to be paid and borne by Supplier pursuant to Section 10.3); or (c) Supplier's negligence, willful misconduct or violation of applicable laws, rules or regulations. Supplier shall not be obligated to indemnify the Buyer Indemnitees under this Section 12.1 if the applicable Claim was the direct result of a material breach of any covenant, warranty or representation made by Buyer under this Agreement.

12.2 Buyer shall indemnify, defend and hold harmless Supplier Indemnitees from and against all Claims in connection with any and all suits, investigations, claims or demands of any third party arising from or occurring as a result of (a) the breach of any of the representations or warranties made by Buyer hereunder; (b) the failure of Buyer to perform or observe any provision of this Agreement required to be performed or observed by Buyer hereunder; or (c) Buyer's negligence, willful misconduct or violation of applicable laws, rules or regulations. Buyer shall not be obligated to indemnify Supplier under this Section 12.2 if the applicable Claim was the direct result of a material breach of any covenant, warranty or representation made by Supplier under this Agreement.

12.3 The indemnified Party shall give the indemnifying Party prompt written notice within [***] of becoming aware of any Claim asserted or threatened against an indemnified Party that could give rise to a right of indemnification under this Agreement, and in no event shall the indemnifying Party be liable for any Claims to the extent such Claims result from any delay in providing such notice. The indemnifying Party may assume the defense of any Claim by giving written notice to the indemnified Party [***] after the indemnifying Party's receipt of an indemnification claim Notice. Any indemnified Party may participate in, but not control, the defense of a Claim and employ counsel of its choice for such purpose at its expense. The defending Party, but solely to the extent the defending Party is also the indemnifying Party, shall not agree to any settlement of such action, suit, proceeding or claim or consent to any judgment in respect thereof that does not include a complete and unconditional release of the indemnified Party from all liability with respect thereto or that imposes any liability or obligation on the indemnified Party without the prior written consent of the indemnified Party. The indemnified Party and its applicable indemnitees shall cooperate in the defense or prosecution of the Claim and shall furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith.

12.4 NEITHER PARTY SHALL BE LIABLE UNDER THIS AGREEMENT FOR ANY SPECIAL, INDIRECT, CONSEQUENTIAL, EXEMPLARY, PUNITIVE, OR INCIDENTAL DAMAGES (INCLUDING LOSS OF REVENUE, LOSS OF PROFITS, OR COMMERCIAL LOSS) ARISING OUT OF OR RELATED TO THE SALE OF THE PRODUCT, HOWEVER CAUSED AND UNDER ANY THEORY OF LIABILITY (INCLUDING, WITHOUT LIMITATION, NEGLIGENCE), EVEN IF SUCH PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES; *PROVIDED*, *HOWEVER*, THAT THE EXCLUSION OF LIABILITY SET FORTH IN THIS SECTION 12.4 SHALL NOT APPLY TO THE PARTIES' INDEMNIFICATION OBLIGATIONS SET FORTH IN SECTION 12.1 AND 12.2 OR TO DAMAGES RESULTING FROM BREACHES BY A PARTY OF ITS CONFIDENTIALITY AND NON-USE OBLIGATIONS UNDER SECTION 16.

13. **Records Retentions; Audits**

13.1 Supplier shall maintain, at its sole cost and expense, and will cause all of its subcontractors hereunder to maintain, complete, correct and accurate books and records relating to the Product Manufactured and sold hereunder (the "**Books and Records**"). Supplier shall keep such Books and Records for a period of [***] after the termination of this Agreement, or longer as may be required by applicable law.

13.2 Buyer (or any third party designated by Buyer), during the Term and for [***] thereafter, [***], may audit the Books and Records maintained by Supplier or any subcontractor hereunder to ensure Supplier's compliance with the terms of this Agreement; *provided*, *however*, that such audits may not (a) be conducted for [***], (b) be conducted more than [***] period (unless a previous audit during such [***] period revealed any material non-compliance by Supplier with the terms hereof and/or any overpayment by Buyer with respect to such period) or (c) be repeated for any [***]. Buyer (or, as applicable, Buyer's third party designee) will (i) be allowed to interview key Supplier employees with respect to the matters that are the subject of the audit and (ii) have access to, and be permitted to examine and copy (without charge), the Books and Records maintained by Supplier or any subcontractor hereunder for purposes of conducting such audit. The cost for any such audit of Books and Records will be borne by [***]; *provided*, *however*, that if the results of such audit disclose Buyer overpaid Supplier an amount

greater than [***] of the amount subject to audit as should have been paid according to this Agreement, Supplier shall promptly reimburse Buyer for [***] incurred by Buyer in connection with such audit. Buyer will be entitled to a refund in the amount of any overcharge or overpayment. At Buyer's discretion, the amount of any overcharge or overpayment may be credited to Buyer in anticipation of future payments by Buyer to Supplier. If the results of the audit disclose that Buyer has been undercharged, Supplier will invoice Buyer for the additional charge and Buyer will pay such invoice within [***] after receipt of such invoice.

14. **Manufacturing Technology Transfer.**

14.1 Upon Buyer's request, [***], Supplier shall effect a full transfer to Buyer or its designee (which designee may be an Affiliate or a third party manufacturer) of all Information included within the Manufacturing Process. Such technology transfer shall include, without limitation, providing Buyer or its designee with (a) any materials (as well as intermediates) used by Supplier or its Affiliates or subcontractors in the Manufacture of Products and (b) copies of the following documentation: all technical reports and materials for process development activities completed at the time of such transfer that are relevant to and would be required to manufacture the Product using the Manufacturing Process as performed by Supplier at such time (including but not limited to any recovery steps established, process validation, product identity assays, in-process-control, applicable computer software, relevant standard operating procedures, information regarding equipment thereof, etc.). Supplier will work diligently on such technology transfer and will use [***] to complete such technology transfer in [***]. Supplier shall keep Buyer regularly and fully informed of Supplier's progress in completing the technology transfer and the other related activities, including permitting appropriate Buyer employees or representatives to visit and inspect the Facility in connection with conducting such work. Supplier shall also use [***] to provide technical assistance and work with Buyer or its designee to implement the Manufacturing Process at facilities designated by Buyer or its designee. Buyer shall reimburse Supplier for its [***] to conduct the technology transfer and provide the assistance pursuant to this Section 14.1 at the rate set forth in Section 3(C) of **Exhibit D**. The transfer of the Manufacturing Process from Supplier shall be deemed complete when Buyer is able to, either itself or via its designee, Manufacture Products that meet the then-applicable Specifications.

14.2 Upon Buyer's [***] following the transfer of the Manufacturing Process, Supplier shall provide technical assistance to enable Buyer (or its Affiliate or designated third party manufacturer, as applicable) to implement, use and practice the Manufacturing Process

15. **Insurance**

15.1 During the Term and for a period of [***] thereafter, Supplier shall maintain at all times an adequate insurance program sufficient to adequately protect against the risks associated with its ongoing business, including the risks that may arise in connection with the transactions, obligations, and Services contemplated by this Agreement, as well as adequate product liability insurance, and in any event, Supplier shall maintain the following minimum required insurance coverage: (i) comprehensive general liability insurance coverage, including broad form contractual liability coverage, affording a limit of $[***] Bodily Injury/Property Damage Liability per occurrence and in the aggregate; and (ii) product liability insurance with minimum limits of $[***] per occurrence and $[***] annual aggregate, and in each case naming Buyer as an additional insured. This minimum required insurance coverage shall be kept in full force at all times during the Term of this Agreement. If any such insurance is written on a claims made basis, Supplier shall ensure continuity of coverage for any claims arising after the policy expiry date. Failure to maintain this minimum required insurance may be deemed a breach of this Agreement. At Buyer's request, Supplier will provide Buyer with a certificate of insurance evidencing this coverage.

15.2 In the event of any material change in Supplier's insurance situation, Supplier will promptly procure the appropriate insurance coverage to meet its obligations and shall provide Buyer with proof of such insurance coverage. In addition, Supplier agrees to provide at least [***] to Buyer of any non-renewal, cancellation or non-compliance with the insurance coverage required under Section 15.1.

16. **Confidentiality**

16.1 The receiving Party shall keep confidential and not disclose to others or use for any purpose, other than as authorized by this Agreement, all Confidential Information which was provided to it by the other Party. The restrictions of this Section 16.1 shall not apply to any Confidential Information which, as proved by reliable written evidence: (i) was already known to the receiving Party or in its possession without an obligation to keep it confidential, at the time of disclosure, as documented by written records in its files; (ii) was or became public knowledge through no fault of the recipient or becomes public domain not through the breach of this undertaking on the part of the receiving Party or by any other party who received Confidential Information from the receiving Party; (iii) was received from a third party having the lawful right to disclose the information; (iv) was independently developed by or for the receiving Party without use of or reference to the disclosing Party's Confidential Information, as can be substantiated by written records and completely apart from the disclosures hereunder; or (v) subject to Section 16.2, was required by law to be disclosed.

16.2 Unless otherwise agreed to in advance, in writing, by the disclosing Party or except as expressly permitted by this Agreement, the receiving Party will not disclose the disclosing Party's Confidential Information to third parties, provided, however, that the receiving Party may disclose the disclosing Party's Confidential Information if required by law, regulation or court order, including disclosure to the FDA or any other applicable governmental agency, as long as the receiving Party gives the disclosing Party prompt written notice of such requirement prior to such disclosure and reasonably assists the disclosing Party in obtaining a protective order. If prior notification is precluded by law or regulation or where enforcement action by applicable authority precludes prior notification, the receiving Party will limit the disclosure to the extent required by law and, to the extent permitted will notify the disclosing Party as soon as reasonably practical. If prior notification is precluded by law or regulation or where enforcement action by applicable authority precludes prior notification, in which case the receiving Party will limit the disclosure to the portion of such Confidential Information as is legally required and will notify the disclosing Party as soon as reasonably practicable.

16.3 The receiving Party may disclose Confidential Information of the disclosing Party only to those of its employees, consultants, contractors or sub-contractors who need to know such information. In addition, prior to any disclosure of such Confidential Information to any such employee or contractor, such employee or contractor shall be made aware of the confidential nature of the Confidential Information and shall execute, or shall already be bound by, a non-disclosure agreement containing terms and conditions consistent with the terms and conditions of this Agreement. In any event, the receiving Party shall be responsible for any breach of the terms and conditions of this Agreement by any of its employees, contractors or sub-contractors.

16.4 The receiving Party shall treat the disclosing Party Confidential Information with [***] and shall use the same degree of care to avoid disclosure of the disclosing Party's Confidential Information as the receiving Party employs with respect to its own Confidential Information

of like importance, [***].

16.5 This Agreement and the terms contained herein shall be deemed confidential and neither Party shall, without the prior written consent of the other Party, disclose in any manner to any third party the terms and conditions of this Agreement. Notwithstanding the foregoing, Buyer may disclose this Agreement to potential financial investors and sublicensees, provided, that, any such disclosure shall be made under a confidentiality agreement.

16.6 This Agreement does not constitute the conveyance of ownership with respect to or a license to any Confidential Information, except as otherwise provided in this Agreement.

16.7 Upon the termination or expiration of this Agreement for any reason, or upon the disclosing Party's earlier request, the receiving Party will deliver to the disclosing Party all of the disclosing Party's property or Confidential Information in tangible form that the receiving Party may have in its possession or control. The receiving Party may retain one copy of the Confidential Information in its legal files for a period no longer than [***] upon termination or expiration, provided that the receiving Party shall deliver as soon as practicable and within [***] following such termination or expiration to the disclosing Party a written acknowledgment that it has no rights of use in or to the disclosing Party property and Confidential Information after the expiration or termination date.

17. **Term and Termination**

17.1 This Agreement shall commence on the Effective Date and, unless earlier terminated in accordance with the provisions of this Section 17 below, shall remain in effect for an initial term until June 30, 2022 (the "**Initial Term**"). Upon the mutual written agreement of the Parties, the Initial Term may be extended for one or more additional periods of time as agreed upon by the Parties (each such agreed upon renewal term, a "**Renewal Term**" and the Initial Term with all Renewal Terms, the "**Term**").

17.2 In addition and without derogating from any other remedies that Buyer may have under the terms of this Agreement or at law, Buyer may terminate this Agreement as expressly set forth in this Agreement and may also terminate this Agreement immediately upon written notice to Supplier if (i) the Facility does not receive confirmation, permits or approvals from the competent Regulatory Authorities or (ii) Supplier is unable to perform the Services for a period of [***] due to the action of a competent Regulatory Authority.

17.3 Without derogating from any other remedies that either Party may have under the terms of this Agreement or at law, each Party may terminate this Agreement forthwith upon the occurrence of any of the following:

17.3.1 The commission of a material breach by the other Party hereto of its obligations hereunder, and such other Party's failure to remedy such breach within [***] after being requested in writing to do so by the non-breaching Party; or

17.3.2 The other Party's liquidation, whether voluntarily or otherwise, or its entering into any arrangement with its creditors or the appointment of a receiver.

17.4 Upon the effective date of termination of this Agreement, all legal obligations, rights and duties arising out of this Agreement shall terminate except for such legal obligations, rights and duties as shall have accrued prior to the effective date of termination and except as otherwise expressly provided in this Agreement. Termination or cancellation of this Agreement will not relieve the Parties of any obligation accruing prior to such termination or expiration including but not limited, to the confidentiality provisions herein.

17.5 Sections 1, 3 (to the extent relating to activities during the Term), 4.1.16, 4.3, 4.5 (the last sentence only), 6, 7.9, 7.10, 7.11, 7.12, 8, 11 (excluding 11.3), 12, 13, 14, 15, 16, 17.4, 17.5 and 18 shall survive any termination of this Agreement.

18. **Miscellaneous**

18.1 Notices. All notices or other communications hereunder shall be in writing and shall be given in person, by registered mail (registered international air mail if mailed internationally), by an overnight courier service that obtains a receipt to evidence delivery (provided that written confirmation of receipt is provided), postage prepaid, to addresses set forth below:

If to Buyer: UroGen Pharma Ltd.
9 HaTa'asiya Street
Ra'anana 4365405, Israel
Facsimile: [***]
E-mail: [***]
Attn: [***]

With copy to: [***]

If to Supplier: Isotopia Molecular Imaging Ltd.
Yanai Street Segula Industrial Park
Petach Tikva 49277, Israel
Facsimile: [***]
E-mail: [***]
Attn: [***]

All such notices and other communications shall be deemed to have been given and received (i) in the case of personal delivery, on the date of such delivery if delivered on a Business Day or if not delivered on a Business Day, the first Business Day after the delivery, (ii) in the case of delivery by nationally-recognized, overnight courier, on the [***] following dispatch, and (iii) in the case of mailing, on the [***] following such mailing.

18.2 Force Majeure. If either Party is prevented from performing any of its obligations hereunder due to a Force Majeure Event, such non-performing Party shall not be liable for breach of this Agreement with respect to such non-performance. Such non-performance shall be excused for [***] or until the termination of such event (whichever occurs sooner), provided that the non-performing Party gives written

notice to the other Party of the Force Majeure Event no later than [***] after becoming aware that the Force Majeure Event is reasonably likely prevent timely performance, and provided further that the non-performing Party shall use its [***] to avoid or remove such cause of non-performance and shall fulfil and continue performance hereunder with the utmost dispatch whenever and to the extent such cause or causes are removed. A Force Majeure Event affecting either Party does not excuse non-payment of amounts due for accepted Products ordered and delivered to the Buyer or for defective or recalled goods returned to the Supplier.

18.3 Law and Jurisdiction. This Agreement shall be governed by and construed in accordance with the laws of the state of Israel, without reference to any rules of conflict of laws. Subject to the foregoing, for purposes of this Agreement, each Party irrevocably and unconditionally submits to the exclusive jurisdiction of the courts of the District of Tel-Aviv - Jaffa, Israel for determining any dispute, claim or difference concerning this Agreement or any matter arising therefrom.

18.4 Injunctive Relief. Each of Buyer and Supplier acknowledge that a violation of Section 16 would cause immediate and irreparable harm for which money damages would be inadequate. Therefore, the harmed Party will be entitled to injunctive relief for the other Party's breach of any of its obligations under Section 16 without proof of actual damages and without the posting of bond or other security. Such injunctive relief is not the exclusive remedy for such violation, but is in addition to all other remedies available at law or in equity.

18.5 Entire Agreement. This Agreement represents the entire understanding and agreement between the Parties with respect to the subject matter hereof and can be amended, supplemented or changed, and any provision hereof can be waived, only by written instrument making specific reference to this Agreement signed by the Parties. This Agreement supersedes all prior agreements between the Parties relating to the subject matter hereof.

18.6 Other Instruments. Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof, or to better assure and confirm the rights and remedies of the other Party under this Agreement.

18.7 Severability. If at any time subsequent to the date hereof, any provision of this Agreement shall be held by any court of competent jurisdiction to be illegal, void or unenforceable, such provision shall be of no force and effect, but the illegality or unenforceability of such provision shall have no effect upon and shall not impair the enforceability of any other provision of this Agreement.

18.8 Successors and Assigns. This Agreement shall be binding upon and shall inure to the benefit of the Parties and their respective successors and assigns; provided, however, that this Agreement and all rights and obligations may not be assigned or transferred without the prior written consent of the other Party, except that Buyer may assign to an Affiliate. Notwithstanding the foregoing, Buyer may also assign or delegate all or any of its rights or obligations under this Agreement to a third party acquiring all of the business to which this Agreement relates without Supplier's consent provided that: (a) Buyer provides written notice to Supplier of such assignment; and (b) the assignee undertakes in writing to be bound by all of the terms of this Agreement and to perform the relevant obligations of Buyer hereunder.

18.9 Independent Contractors. Supplier is an independent company engaged by Buyer for the provision of the Services. Nothing in this Agreement shall constitute Supplier as an agent or general representative of Buyer. Neither Party has the right or authority to assume, create, or incur any liability or any obligation of any kind, express or implied, against, or in the name of or on behalf of, the other Party. This Agreement does not constitute, or create or in any way be interpreted as, a joint venture, partnership, or formal business organization of any kind.

18.10 Construction. Where specific language is used to clarify by example a general statement contained herein, such specific language shall not be deemed to modify, limit or restrict in any manner the construction of the general statement to which it relates. The language used in this Agreement shall be deemed to be the language chosen by the Parties to express their mutual intent, and no rule of strict construction shall be applied against any Party. The English language version of this Agreement shall prevail over any translation hereof.

18.11 Recitals & Exhibits. All recitals and exhibits and other ancillary documents referred to herein and/or attached hereto shall be and form an integral part of this Agreement. To the extent the terms and conditions of this Agreement do not address a particular circumstance or are otherwise unclear or ambiguous, the recitals are to be interpreted and construed in so far as to give effect to the goals and objectives which are sufficiently clearly set forth in them.

18.12 Descriptive Headings. The paragraph headings contained in this Agreement are for reference purposes only and shall not affect in any way the meaning or interpretation of this Agreement.

18.13 Nouns and Pronoun. Whenever the context may require, any pronouns used herein shall include the corresponding masculine, feminine or neuter forms, and the singular form of nouns and pronouns shall include the plural and vice-versa.

18.14 Counterparts. This Agreement may be executed in one or more counterparts by facsimile or e-mail by PDF, each of which shall be deemed an original, but all of which, taken together, shall constitute one and the same instrument.

[Intentionally left blank]

IN WITNESS WHEREOF, the Parties have caused this Manufacturing and Supply Agreement to be signed by their duly authorized representatives as of the Effective Date.

UroGen Pharma Ltd.		**Isotopia Molecular Imaging Ltd.**	
By:	/s/ Keren Stotzky	By:	/s/ Tzachi Levy
Name:	Keren Stotzky	Name:	Tzachi Levy
Title:	VP Manufacturing & Supply Chain	Title:	Head Of Sterile Plant
	5/27/2020		30/05/2020

LIST OF EXHIBITS

Exhibit A – Product and Specifications
Exhibit B – MBR
Exhibit C – Dedicated Equipment
Exhibit D – Quote
Exhibit E – Services, Storage, Packaging & Shipping
Exhibit F – Quality Agreement
Exhibit G – [***] Arbitration
Exhibit H – Certificate of Analysis

MANUFACTURING AND SUPPLY AGREEMENT - EXTENSION

Whereas, **Urogen Pharma Ltd.**, with a principal place of business or an office at 9 HaTa'asiya Street, Ra'anana 4365007, Israel (the "**Buyer**") and **Isotopia Molecular Imaging Ltd.** with its principal place of business located at Alexander Yanai 39 Street Segula Industrial Park Petach Tikva 49277, Israel. (the "**Supplier**") (hereinafter referred to individually as a "**Party**" and collectively as the "**Parties**") entered a Manufacturing and Supply Agreement with an Effective Date of May 26, 2020 (the "**Original Agreement**"); and

Whereas, the Original Agreement's Initial Term ended on June 30, 2022, and the Parties wish, according to Sec. 17.1 of the Original Agreement, to extend the Term with a Renewal Term beginning July 1, 2022 and ending December 31, 2025 (the "**First Renewal Term**"); and

Whereas, the Parties desire to make additional amendments to the Original Agreement as set forth below.

Now, therefore, in consideration of the mutual promises and covenants contained herein, the parties hereby agree as follows:

19. **Amendments of the Original Agreement**

19.1 In Sec. 10.2 of the Original Agreement, the sentence "Buyer shall pay all such undisputed invoices provided by Supplier within [***] following the date of Buyer's receipt of the applicable invoice from Supplier." shall be replaced by the following one:

"Buyer shall pay all such undisputed invoices provided by Supplier and received by Buyer by [***].".

19.2 In Sec. 10.3 of the Original Agreement, the sentence "provided, however, that the stated due date of each such invoice shall be no less than [***] following the date of Buyer's receipt of the applicable undisputed invoice from Supplier." shall be replaced by the following one:

"Provided, however, that the stated due date of each such invoices issued until the 15th day of each calendar month shall be the [***], and the due date of each such invoices issued after the 16th day of each calendar month shall be [***]".

19.3 Exhibits A,B,C,D and H of the Original Agreement are deleted in their entirety and replaced with Exhibits A,B,C,D,H to this Extension.

19.4 Supplier shall invoice Buyer directly for the costs of Raw Materials and related services (such as external storage, shipment expenses etc.). Reimbursement of such out of pocket expenses shall be paid by [***].

19.5 In accordance with Section 17 of the Original Agreement, the Parties hereby agree to extend the Term of the Agreement, beginning July 1, 2022 and ending December 31, 2025 (the "**First Renewal Term**").

19.6 Except as amended above, all other terms of and exhibits to the Original Agreement shall remain unchanged.

20. **Effective Date of Extension**

20.1 The effective date for this Extension shall be July 1, 2022.

IN WITNESS WHEREOF, this Extension has been signed by the following authorized representatives of the Parties hereto:

UROGEN PHARMA LTD.	ISOTOPIA MOLECULAR IMAGING LTD.
By: /s/ Keren Stotzky	By: /s/ Tzachi Levy
Name: Keren Stotzky	Name: Tzachi Levy
Title: VP Manufacturing & Supply Chain	Title: Head Of Sterile Plant
Date: 8/25/2022	Date: 8/25/2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Elizabeth Barrett, certify that:

1. I have reviewed this quarterly report on Form 10-Q of UroGen Pharma Ltd.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 10, 2022

By: /s/ Elizabeth Barrett
Elizabeth Barrett
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Don Kim, certify that:

1. I have reviewed this quarterly report on Form 10-Q of UroGen Pharma Ltd.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 10, 2022

By: /s/ Don Kim

Don Kim
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of UroGen Pharma Ltd. (the "Company") on Form 10-Q for the period ended September 30, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Elizabeth Barrett, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: November 10, 2022

By: /s/ Elizabeth Barrett
Elizabeth Barrett
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of UroGen Pharma Ltd. (the "Company") on Form 10-Q for the period ended September 30, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Don Kim, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: November 10, 2022

By: /s/ Don Kim

Don Kim
Chief Financial Officer
(Principal Financial and Accounting Officer)