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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington D.C. 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 June 30, 2019

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: 001-36294

uniQure N.V.
(Exact name of Registrant as specified in its charter)

The Netherlands	**Not applicable**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

Paasheuvelweg 25a,
1105 BP Amsterdam, The Netherlands
(Address of principal executive offices) (Zip Code)

+31-20-240-6000
(Registrant's telephone number, including area code)

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" and "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 ☒

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

Title of each class:	**Trading Symbol(s)**	**Name of each exchange on which registered**
Ordinary Shares	QURE	The Nasdaq Global Select Market

As of July 25, 2019, the registrant had 37,850,898 ordinary shares, par value €0.05, outstanding.

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SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains "forward-looking statements" as defined under federal securities laws. Forward-looking statements are based on our current expectations of future events and many of these statements can be identified using terminology such as "believes," "expects," "anticipates," "plans," "may," "will," "projects," "continues," "estimates," "potential," "opportunity" and similar expressions. These forward-looking statements may be found in Part II, Item 1A "Risk Factors," Part I, Item 2 "Management's Discussion and Analysis of Financial Condition and Results of Operations" and other sections of this Quarterly Report on Form 10-Q.

Forward-looking statements are only predictions based on management's current views and assumptions and involve risks and uncertainties, and actual results could differ materially from those projected or implied. The most significant factors known to us that could materially adversely affect our business, operations, industry, financial position or future financial performance include those discussed in Part II, Item 1A "Risk Factors," as well as those discussed in Part I, Item 2 "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this report, as well as other factors which may be identified from time to time in our other filings with the Securities and Exchange Commission ("SEC"), including our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 28, 2019, or in the documents where such forward-looking statements appear. You should carefully consider that information before you make an investment decision.

You should not place undue reliance on these statements, which speak only as of the date that they were made. Our actual results or experience could differ significantly from those anticipated in the forward-looking statements and from historical results, due to the risks and uncertainties described in this Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, and in our Annual Report on Form 10-K for the year ended December 31, 2018, including in "Part I, Item 1A. Risk Factors," as well as others that we may consider immaterial or do not anticipate at this time. These cautionary statements should be considered in connection with any written or oral forward-looking statements that we may make in the future or may file or furnish with the SEC. We do not undertake any obligation to release publicly any revisions to these forward-looking statements after completion of the filing of this Quarterly Report on Form 10-Q to reflect later events or circumstances or to reflect the occurrence of unanticipated events. All forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements.

In addition, with respect to all our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Part I – FINANCIAL INFORMATION

Item 1. Financial Statements

uniQure N.V.

UNAUDITED CONSOLIDATED BALANCE SHEETS

	June 30, 2019	December 31, 2018
	(in thousands, except share and per share amounts)	
Current assets		
Cash and cash equivalents	$ 184,095	$ 234,898
Accounts receivable and accrued income from related party	355	233
Prepaid expenses	3,511	1,116
Other current assets	580	329
Total current assets	**188,541**	**236,576**
Non-current assets		
Property, plant and equipment, net of accumulated depreciation of $25.8 million as of June 30, 2019, and $22.9 million as of December 31, 2018, respectively.	28,057	29,179
Operating lease right-of-use assets	27,173	—
Intangible assets, net	5,864	5,201
Goodwill	503	506
Restricted cash	2,940	2,444
Total non-current assets	**64,537**	**37,330**
Total assets	**$ 253,078**	**$ 273,906**
Current liabilities		
Accounts payable	$ 4,523	$ 3,792
Accrued expenses and other current liabilities	7,366	8,232
Current portion of operating lease liabilities	4,256	—
Current portion of deferred rent	—	311
Current portion of deferred revenue	7,223	7,634
Total current liabilities	**23,368**	**19,969**
Non-current liabilities		
Long-term debt	35,784	35,471
Operating lease liabilities, net of current portion	31,870	—
Deferred rent, net of current portion (see note 2.5)	—	8,761
Deferred revenue, net of current portion	26,354	28,861
Derivative financial instruments related party	3,251	803
Other non-current liabilities	395	435
Total non-current liabilities	**97,654**	**74,331**
Total liabilities	**121,022**	**94,300**
Commitments and contingencies		
Shareholders' equity		
Ordinary shares, €0.05 par value: 60,000,000 shares authorized at June 30, 2019 and December 31, 2018 and 37,839,833 and 37,351,653 ordinary shares issued and outstanding at June 30, 2019 and December 31, 2018, respectively.	2,327	2,299
Additional paid-in-capital	732,924	720,072
Accumulated other comprehensive loss	(8,518)	(7,259)
Accumulated deficit	(594,677)	(535,506)
Total shareholders' equity	**132,056**	**179,606**
Total liabilities and shareholders' equity	**$ 253,078**	**$ 273,906**

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
	(in thousands, except share and per share amounts)		(in thousands, except share and per share amounts)	
License revenues from related party	2,108	2,123	2,665	4,574
Collaboration revenues from related party	366	927	945	1,954
Total revenues	**2,474**	**3,050**	**3,610**	**6,528**
Operating expenses:				
Research and development expenses	(24,154)	(18,493)	(44,691)	(35,551)
Selling, general and administrative expenses	(7,870)	(5,896)	(15,937)	(12,197)
Total operating expenses	**(32,024)**	**(24,389)**	**(60,628)**	**(47,748)**
Other income	566	565	879	1,180
Other expense	(347)	(429)	(696)	(762)
Loss from operations	**(29,331)**	**(21,203)**	**(56,835)**	**(40,802)**
Interest income	728	583	1,170	836
Interest expense	(937)	(565)	(1,894)	(981)
Foreign currency (losses) / gains, net	(1,252)	2,255	1,022	2,433
Other non-operating loss, net	(607)	(1,301)	(2,634)	(598)
Loss before income tax expense	**(31,399)**	**(20,231)**	**(59,171)**	**(39,112)**
Income tax expense	—	(361)	—	(269)
Net loss	**$ (31,399)**	$ **(20,592)**	**$ (59,171)**	**$ (39,381)**
Other comprehensive income / (loss), net of income tax:				
Foreign currency translation adjustments net of tax impact of nil and $0.4 million for the three months ended June 30, 2019 and 2018, respectively, and nil and $0.3 million for the six months ended June 30, 2019 and 2018, respectively.	1,209	(3,376)	(1,259)	(2,692)
Total comprehensive loss	**$ (30,190)**	**$ (23,968)**	**$ (60,430)**	**$ (42,073)**
Basic and diluted net loss per ordinary share	$ (0.83)	(0.57)	$ (1.57)	$ (1.16)
Weighted average shares used in computing basic and diluted net loss per ordinary share	37,824,928	36,205,061	37,750,961	33,970,195

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
FOR THE THREE-MONTH PERIOD ENDED JUNE 30

	Ordinary shares		Additional paid-in capital	Accumulated other comprehensive (loss)/income	Accumulated deficit	Total shareholders' equity
	No. of shares	Amount				
	(in thousands, except share and per share amounts)					
Balance at March 31, 2018	**31,771,816**	**$ 1,971**	**$ 570,595**	**$ (1,312)**	**$ (470,991)**	**$ 100,263**
Loss for the period	—	—	—	—	(20,592)	(20,592)
Other comprehensive loss	—	—	—	(3,376)	—	(3,376)
Follow-on public offering	5,175,000	309	138,182	—	—	138,491
Exercise of share options	121,592	5	1,420	—	—	1,425
Restricted and performance share units distributed during the period	58,333	3	(3)	—	—	—
Share-based compensation expense	—	—	2,205	—	—	2,205
Balance at June 30, 2018	**37,126,741**	**$ 2,288**	**$ 712,399**	**$ (4,688)**	**$ (491,583)**	**$ 218,416**
Balance at March 31, 2019	**37,763,842**	**$ 2,322**	**$ 727,795**	**$ (9,727)**	**$ (563,278)**	**$ 157,112**
Loss for the period	—	—	—	—	(31,399)	(31,399)
Other comprehensive loss	—	—	—	1,209	—	1,209
Exercise of share options	52,847	4	454	—	—	458
Restricted and performance share units distributed during the period	21,400	1	(1)	—	—	—
Share-based compensation expense	—	—	4,592	—	—	4,592
Issuance of ordinary shares relating to employee stock purchase plan	1,744	—	84	—	—	84
Balance at June 30, 2019	**37,839,833**	**$ 2,327**	**$ 732,924**	**$ (8,518)**	**$ (594,677)**	**$ 132,056**

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
FOR THE SIX-MONTH PERIOD ENDED JUNE 30

	Ordinary shares		Additional paid-in capital	Accumulated other comprehensive (loss)/income	Accumulated deficit	Total shareholders' equity
	No. of shares	Amount				
	(in thousands, except share and per share amounts)					
Balance at December 31, 2017	**31,339,040**	**$ 1,947**	**$ 566,530**	**$ (3,800)**	**$ (475,318)**	**$ 89,359**
Cumulative effect of retroactive implementation of ASC 606 Revenue recognition	—	—	—	1,802	23,116	24,918
Loss for the period	—	—	—	—	(39,381)	(39,381)
Other comprehensive loss	—	—	—	(2,690)	—	(2,690)
Follow-on public offering	5,175,000	309	138,182	—		138,491
Exercise of share options	267,753	12	2,975	—	—	2,987
Restricted and performance share units distributed during the period	344,948	20	(20)	—	—	—
Share-based compensation expense	—	—	4,732	—	—	4,732
Balance at June 30, 2018	**37,126,741**	**$ 2,288**	**$ 712,399**	**$ (4,688)**	**$ (491,583)**	**$ 218,416**
Balance at December 31, 2018	**37,351,653**	**$ 2,299**	**$ 720,072**	**$ (7,259)**	**$ (535,506)**	**$ 179,606**
Loss for the period	—	—	—	—	(59,171)	(59,171)
Other comprehensive loss	—	—	—	(1,259)	—	(1,259)
Hercules warrants exercise	37,175	2	1,271	—	—	1,273
Exercise of share options	236,654	14	2,542	—	—	2,556
Restricted and performance share units distributed during the period	209,481	12	(12)	—	—	—
Share-based compensation expense	—	—	8,886	—	—	8,886
Issuance of ordinary shares relating to employee stock purchase plan	4,870	—	165	—	—	165
Balance at June 30, 2019	**37,839,833**	**$ 2,327**	**$ 732,924**	**$ (8,518)**	**$ (594,677)**	**$ 132,056**

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF CASH FLOWS

	Six months ended June 30,	
	2019	2018
	(in thousands)	
Cash flows from operating activities		
Net loss	$ (59,171)	$ (39,381)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	3,217	3,211
Share-based compensation expense	8,886	4,732
Change in fair value of derivative financial instruments and contingent consideration	2,634	517
Unrealized foreign exchange gains	(386)	(3,417)
Change in deferred taxes	-	269
Change in lease incentives	-	(52)
Changes in operating assets and liabilities:		
Accounts receivable and accrued income, prepaid expenses and other current assets	(2,779)	(202)
Accounts payable	283	717
Accrued expenses, other liabilities and operating leases	(658)	208
Deferred revenue	(2,683)	(4,579)
Net cash used in operating activities	(50,657)	(37,977)
Cash flows from investing activities		
Purchases of intangible assets	(996)	(1,445)
Purchases of property, plant and equipment	(1,432)	(1,197)
Net cash used in investing activities	(2,428)	(2,642)
Cash flows from financing activities		
Proceeds from issuance of shares related to employee stock option and purchase plans	2,721	2,987
Proceeds from public offering of shares, net of issuance costs	-	138,491
Proceeds from exercise of warrants	500	-
Net cash generated from financing activities	3,221	141,478
Currency effect cash, cash equivalents and restricted cash	(443)	(1,071)
Net (decrease) / increase in cash, cash equivalents and restricted cash	(50,307)	99,787
Cash, cash equivalents and restricted cash at beginning of period	237,342	161,851
Cash, cash equivalents and restricted cash at the end of period	**$ 187,035**	**$ 261,638**
Cash and cash equivalents	$ 184,095	$ 259,180
Restricted cash related to leasehold and other deposits	$ 2,940	$ 2,458
Total cash, cash equivalents and restricted cash	**$** 187,035	**$** 261,638
Supplemental cash flow disclosures:		
Cash paid for interest	$ (1,544)	$ (851)
Non-cash increases / (decreases) in accounts payables related to purchase of intangible assets and property, plant and equipment	$ 473	$ 316

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

1 General business information

uniQure (the "Company") was incorporated on January 9, 2012 as a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) under the laws of the Netherlands. The Company is a leader in the field of gene therapy and seeks to deliver to patients suffering from rare and other devastating diseases single treatments with potentially curative results. The Company's business was founded in 1998 and was initially operated through its predecessor company, Amsterdam Molecular Therapeutics (AMT) Holding N.V ("AMT"). In 2012, AMT undertook a corporate reorganization, pursuant to which uniQure B.V. acquired the entire business and assets of AMT and completed a share-for-share exchange with the shareholders of AMT. Effective February 10, 2014, in connection with its initial public offering, the Company converted into a public company with limited liability (*naamloze vennootschap*) and changed its legal name from uniQure B.V. to uniQure N.V.

The Company is registered in the trade register of the Chamber of Commerce (*Kamer van Koophandel*) in Amsterdam, the Netherlands under number 54385229. The Company's headquarters are in Amsterdam, the Netherlands, and its registered office is located at Paasheuvelweg 25a, Amsterdam 1105 BP, the Netherlands and its telephone number is +31 20 240 6000.

The Company's ordinary shares are listed on the NASDAQ Global Select Market and trades under the symbol "QURE".

2 Summary of significant accounting policies

2.1 Basis of preparation

The Company prepared these unaudited consolidated financial statements in compliance with generally accepted accounting principles in the United States of America ("U.S. GAAP") and applicable rules and regulations of the SEC regarding interim financial reporting. Any reference in these notes to applicable guidance is meant to refer to authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

The unaudited consolidated financial statements are presented in U.S. dollars, except where otherwise indicated. Transactions denominated in currencies other than U.S. dollars are presented in the transaction currency with the U.S. dollar amount included in parenthesis, converted at the foreign exchange rate as of the transaction date.

2.2 Unaudited interim financial information

The interim financial statements and related disclosures are unaudited, have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for a fair statement of the financial position, results of operations and changes in financial position for the period presented.

Certain information and footnote disclosures normally included in annual financial statements prepared in accordance with U.S. GAAP have been omitted. The results of operations for the six months ended June 30, 2019, are not necessarily indicative of the results to be expected for the full year ending December 31, 2019, or for any other future year or interim period. The accompanying financial statements should be read in conjunction with the audited financial statements and the related notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on February 28, 2019.

2.3 Use of estimates

The preparation of the financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of revenues and expenses during the reporting periods. Actual results could differ from those estimates.

2.4 Accounting policies

The principal accounting policies applied in the preparation of these unaudited consolidated financial statements are described in the Company's audited financial statements as of and for the year ended December 31, 2018, and the notes thereto, which are included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on February 28, 2019. There have been no material changes in the Company's significant accounting policies during the six months ended June 30, 2019, other than the adoption of accounting pronouncements discussed below.

2.5 Recent accounting pronouncements

Recently Adopted Accounting Pronouncements

ASC 842 – Leases

In February 2016, the FASB issued ASU 2016-02, "Leases (Topic 842)". In July 2018, the FASB issued ASU No. 2018-10, "Codification Improvements to Topic 842, Leases" (ASU 2018-10), which provides narrow amendments to clarify how to apply certain aspects of the new lease standard, and ASU No. 2018-11, "Leases (Topic 842) – Target Improvements" (ASU 2018-11), which address implementation issues related to the new lease standard. The standard is effective for interim and annual reporting periods beginning after December 15, 2018. Under the new standard, lessees are required to recognize the right-of-use assets and lease liabilities that arise from operating leases on the consolidated balance sheet. The Company adopted the standard using the modified retrospective approach with an effective date as of the beginning of the Company's fiscal year, January 1, 2019, to operating leases that existed on that date. Prior year comparative financial information was not recast under the new standard and continues to be presented under ASC 840. The Company elected to utilize the package of practical expedients available for expired or existing contracts which allowed the Company to carryforward historical assessments of (1) whether contracts are or contain leases, (2) lease classification, and (3) initial direct costs. The Company performed an assessment and identified the lease facilities as material leases to be accounted for under ASC 842 as of January 1, 2019. The Company elected to implement ASC 842 by applying the modified retrospective approach, which allows the Company to restrict the application of the new guidance to operating leases as of January 1, 2019. The impact of implementing ASC 842 is summarized below:

- Recognized a $19.0 million operating right-of-use asset and a $28.1 million operating lease liability in relation to the facilities leased at the Amsterdam and Lexington sites in the consolidated balance sheet as of January 1, 2019;
- Presented deferred rent of $9.1 million as of December 31, 2018, as a reduction of the right-of-use asset as from January 1, 2019 onwards in the consolidated balance sheet and as a change within operating cash flows within accrued expense, other liabilities and operating leases;

The Company measured the lease liability at the present value of the future lease payments as of January 1, 2019. The Company used an incremental borrowing rate to discount the lease payments. The Company derived the discount rate, adjusted for differences in the term and payment patterns, from the Company's loan from Hercules Capital, which was refinanced immediately prior to the January 1, 2019 adoption date in December 2018. The right-of-use asset is valued at the amount of the lease liability reduced by the remaining December 31, 2018 balance of lease incentives received. The lease liability is subsequently measured at the present value of the future lease payments as of the reporting date with a corresponding adjustment to the right-to-use asset. Absent a lease modification, the Company will continue to utilize the January 1, 2019, incremental borrowing rate.

The Company will continue to recognize lease cost on a straight-line basis and will continue to present these costs as operating expenses within the Consolidated statements of operations and comprehensive loss. The Company will continue to present lease payments within cash flows from operations within the Consolidated statements of cash flows.

The financial results for the three and six months ended June 30, 2019, are presented under the new standard, while the comparative periods presented are not adjusted and continue to be reported in accordance with the Company's historical accounting policy.

Refer to note 5, "Right-of-use asset and lease liabilities" for further information.

In March 2019, the FASB issued ASU 2019-01, "Codification Improvements" to Leases (Topic 842). This pronouncement did not have a material impact on the Company.

Recent Accounting Pronouncements Not Yet Effective

There have been no new accounting pronouncements or changes to accounting pronouncements during the six months ended June 30, 2019, as compared to the recent accounting pronouncements described in Note 2.3.23 of the Company's Annual Report on Form 10-K for the year ended December 31, 2018, which could be expected to materially impact the Company's unaudited condensed consolidated financial statements.

3 Collaboration arrangements and concentration of credit risk

BMS collaboration

In May 2015, the Company entered into a collaboration and license agreement (the "BMS CLA") and various related agreements with Bristol-Myers Squibb ("BMS") that provide BMS with exclusive access to the Company's gene therapy technology platform for the research, development and commercialization of therapeutics aimed at multiple targets in cardiovascular and other diseases ("Collaboration Targets"). During the initial research term of the agreement, the Company supported BMS in discovery, non-clinical, analytical and process development efforts in respect of the Collaboration Targets. For any Collaboration Targets that may be advanced, the Company will be responsible for manufacturing of clinical and commercial supplies using the Company's vector technologies and industrial, proprietary insect-cell based manufacturing platform. BMS reimbursed the Company for all its research and development costs in support of the collaboration during the research term, and will lead development, regulatory and commercial activities for any Collaboration Targets that may be advanced. The agreement provides that the companies may collaborate on up to ten Collaboration Targets in total. The Company has agreed to certain restrictions on its ability to work independently of the collaboration, either directly or indirectly through any affiliate or third party, on certain programs that would be competitive with the collaboration programs.

BMS initially designated four Collaboration Targets, including S100A1 for congestive heart failure ("AMT-126"). In October 2018, the Company and BMS completed a heart function proof-of-concept study of AMT-126 in a pre-clinical, diseased animal model. The study demonstrated deoxyribonucleic acid delivery and expression of S100A1 in the myocardium, thereby validating the Company's vector delivery platform in the animal model. The data did not show a benefit on heart function at six months and, consequently, the Joint Steering Committee for the collaboration decided to discontinue work on S100A1. In April 2019, BMS designated a new cardiovascular Collaboration Target to replace S100A1. BMS has not designated or reserved any additional Collaboration Targets as of June 30, 2019.

The initial four-year research term under the collaboration terminated on May 21, 2019. In February 2019, BMS requested a one-year extension of the research term. In April 2019, following an assessment of the progress of this collaboration and the Company's expanding proprietary programs, the Company notified BMS that the Company did not intend to agree to an extension of the research term.

Accordingly, the Company is currently in discussions with BMS potentially to amend the BMS CLAs. It is currently uncertain whether an amendment to the BMS CLA will be agreed and, if agreed, what the specific terms of any such amendment may be. As a consequence, the Company has not taken into account the impact of such amendment, if any, on the timing of recognition of the prepaid License Revenue. The Company will account for potential changes in the timing of recognition of the prepaid License Revenue if and when the agreements have been amended.

The Company evaluated the BMS CLA and determined that its performance obligations are as follows:

(i) Providing access to its technology and know-how in the field of gene therapy as well as actively contributing to the selection of Collaboration Targets, the collaboration as a whole, the development during the pre-clinical and the clinical phase through participating in joint steering committee and other governing bodies ("License Revenue");

(ii) Providing pre-clinical Collaboration Target specific, non-clinical, analytical and process development services during the initial research term, which ended on May 21, 2019 ("Collaboration Revenue"); and

(iii) Providing clinical and commercial manufacturing services for Collaboration Targets ("Manufacturing Revenue"). To date the Company has not generated any Manufacturing Revenue.

Amounts owed by BMS in relation to Collaboration Revenue are as follows:

	June 30, 2019	December 31, 2018
	(in thousands)	
Bristol Myers Squibb	$ 355	$ 233
Total	**$ 355**	**$ 233**

License Revenue

The Company recognized $2.1 million and $2.7 million of License Revenue for the three and six months ended June 30, 2019, respectively, compared to $2.1 million and $4.6 million during the same periods in 2018 in relation to a $60.1 million upfront payment recorded on May 21, 2015, as well as $15.0 million received in relation to the designation of the second, third and fourth Collaboration Target in August 2015.

The Company would be entitled to an aggregate $16.5 million in target designation payments upon the selection of the fifth to tenth Collaboration Targets. The Company would also be eligible to receive research, development and regulatory milestone payments of up to $254.0 million for a lead Collaboration Target and up to $217.0 million for each of the other selected Collaboration Targets, if defined milestones are achieved. The Company would include the variable consideration related to the selection of the fifth to tenth Collaboration Targets, or any of the milestones, in the transaction price once it is considered probable that including these payments in the transaction price would not result in the reversal of cumulative revenue recognized. The Company would recognize significant amounts of License Revenue for services performed in prior periods if and when the Company considers this probable. Due to the significant uncertainty surrounding the development of gene-therapy product candidates and the dependence on BMS's performance and decisions, the Company does not currently consider this probable.

Additionally, the Company is eligible to receive net sales-based milestone payments and tiered mid-single to low double-digit royalties on product sales. The royalty term is determined on a licensed-product-by-licensed-product and country-by-country basis and begins on the first commercial sale of a licensed product in a country and ends on the expiration of the last to expire of specified patents or regulatory exclusivity covering such licensed product in such country or, with a customary royalty reduction, ten years after the first commercial sale if there is no such exclusivity. These revenues will be recognized when performance obligations are satisfied.

The Company recognizes License Revenue over the expected performance period based on its measure of progress towards the completion of certain activities related to its services. The Company determines such progress by comparing activities performed at the end of each reporting period with total activities expected to be performed. The Company estimates total expected activities using a number of unobservable inputs, such as the probability of BMS designating additional targets, the probability of successfully completing each phase and estimated time required to provide services during the various development stages. If available, the Company uses product candidate-specific research and development plans. Alternatively, the Company assumes that completion of the pre-clinical phase requires an average of four years and that clinical development and commercial launch on average require 8.5 years.

The estimation of total services at the end of each reporting period involves considerable judgement. The estimated number of Collaboration Targets that BMS will pursue significantly impacts the amount of License Revenue the Company recognizes. For example, if the Company would increase the probability of all additional Collaboration Targets being designated by 10% then the revenue for the six months ended June 30, 2019 would have decreased by approximately $1.9 million, as the Company would be required to render more services in relation to the consideration received.

4 Fair value measurement

The Company measures certain assets and liabilities at fair value, either upon initial recognition or for subsequent accounting or reporting. U.S. GAAP requires disclosure of methodologies used in determining the reported fair values, and establishes a hierarchy of inputs used when available. The three levels of the fair value hierarchy are described below:

- Level 1 - Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company can access at the measurement date.
- Level 2 - Valuations based on quoted prices for similar assets or liabilities in markets that are not active or models for which the inputs are observable, either directly or indirectly.
- Level 3 - Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and are unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amount of cash and cash equivalents, accrued income from related parties, prepaid expenses, other assets, accounts payable, accrued expenses and other current liabilities reflected in the consolidated balance sheets approximate their fair values due to their short-term maturities.

The following table sets forth the Company's assets and liabilities that are required to be measured at fair value on a recurring basis as of June 30, 2019, and December 31, 2018:

	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)	Total	Classification in consolidated balance sheets
			(in thousands)		
At December 31, 2018					
Assets:					
Cash, cash equivalents and restricted cash	$ 237,342	$ —	$ —	$ 237,342	Cash and cash equivalents; restricted cash
Total assets	$ 237,342	$ —	$ —	$ 237,342	
Liabilities:					
Derivative financial instruments - debt	$ —	$ —	$ 572	$ 572	Accrued expenses and other current liabilities
Derivative financial instruments - related party	—	—	803	803	
Total liabilities	$ —	$ —	$ 1,375	$ 1,375	
At June 30, 2019					
Assets:					
Cash, cash equivalents and restricted cash	$ 187,035	$ —	$ —	$ 187,035	Cash and cash equivalents; restricted cash
Total assets	$ 187,035	$ —	$ —	$ 187,035	
Liabilities:					
Derivative financial instruments - related party	—	—	3,251	3,251	
Total liabilities	$ —	$ —	$ 3,251	$ 3,251	

Changes in Level 3 items during the six months ended June 30, 2019, are as follows

	Derivative financial instruments
	(in thousands)
Balance at December 31, 2018	**$ 1,375**
Losses recognized in profit or loss	2,634
Exercise of warrants	(770)
Currency translation effects	12
Balance at June 30, 2019	**$ 3,251**

Derivative financial instruments

The Company issued derivative financial instruments related to its collaboration with Bristol-Meyers Squibb Company and in relation to the issuance of the Hercules Technology Growth Corp. ("Hercules") loan facility. The Hercules warrants were exercised as of February 1, 2019. The Company issued 37,175 ordinary shares at $34.25 following the exercise of all Hercules warrants and receipt of $0.5 million from Hercules.

The fair value of the BMS derivative financial instruments ("BMS warrants") as of June 30, 2019, was $3.3 million compared to a fair value of both the BMS and Hercules derivative financial instruments of $1.4 million as of December 31, 2018. Changes in the fair value of the BMS warrants are primarily impacted by changes in the Company's share price, whereby an increase in share price generally results in an increase of the fair value. These BMS warrants are described in more detail below.

BMS warrants

Pursuant to the BMS CLA, the Company granted BMS two warrants:

- A warrant allowing BMS to purchase a specific number of uniQure ordinary shares such that its ownership will equal 14.9% immediately after such purchase. The warrant can be exercised on the later of (i) the date on which the Company receives from BMS the Target Designation Fees (as defined in the BMS CLA) associated with the first six new targets (a total of seven Collaboration Targets); and (ii) the date on which BMS designates the sixth new target (the seventh Collaboration Target).
- A warrant allowing BMS to purchase a specific number of uniQure ordinary shares such that its ownership will equal 19.9% immediately after such purchase. The warrant can be exercised on the later of (i) the date on which uniQure receives from BMS the Target Designation Fees associated with the first nine new targets (a total of ten Collaboration Targets); and (ii) the date on which BMS designates the ninth new target (the tenth Collaboration Target).

Pursuant to the terms of the BMS CLA, the exercise price in respect of each warrant is equal to the greater of (i) the product of (A) $33.84, multiplied by (B) a compounded annual growth rate of 10% (or approximately $49.93 as of June 30, 2019) and (ii) the product of (A) 1.10 multiplied by (B) the VWAP for the 20 trading days ending on the date that is five trading days prior to the date of a notice of exercise delivered by BMS.

As of June 30, 2019, BMS had designated a total of four Collaboration Targets, and as such, the warrants were not exercisable. The Company had estimated the exercise of warrants to occur within two and four years after the balance sheet date.

The Company conducted a sensitivity analysis to assess the impact on changes in assumptions on the fair value. Specifically, the Company examined the impact on the fair market value of the warrants by increasing the volatility by 10% to 82.5%. A further sensitivity analysis was performed assuming the warrants would be exercised a year later than currently estimated. The table below illustrates the impact on the fair market valuation associated with these changes in assumptions as of June 30, 2019.

	Total warrants (in thousands)
Base case	$ 3,251
Increase volatility by 10% to 82.5%	687
Extend exercise dates by one year	(38)

5 Right-of-use asset and lease liabilities

The Company adopted ASU 2016-02 “Leases (Topic 842)” as well as ASU 2018-10 and ASU 2018-11, which both relate to improvements to ASC 842. The Company adopted the standard using the modified retrospective approach with an effective date as of the beginning of the Company’s fiscal year, January 1, 2019. The standard requires the balance sheet recognition for leases. Prior year interim periods were not recast under the new standard and therefore, those amounts are not presented below. The Company elected to utilize practical expedients available for expired or existing contracts which allowed the Company to carryforward historical assessments of (1) whether contracts are or contain leases, (2) lease classification, and (3) initial direct costs.

The Company leases various office space and laboratory space under the following operating lease agreements:

Lexington, Massachusetts / United States

In July 2013, the Company entered into a lease for a facility in Lexington, Massachusetts, United States. The term of the lease commenced in November 2013, was set for 10 years starting from the 2014 rent commencement date and is non-cancellable. Originally, the lease for this facility had a termination date of 2024. In November 2018, the term was expanded by five years to June 2029. The lease continues to be renewable for two subsequent five-year terms. Additionally, the lease was expanded to include an additional 30,655 square feet within the same facility and for the same term. The lease of the expansion space commenced on June 1, 2019.

The contractually fixed annual increases of lease payments through 2029 for both the extension and expansion lease have been included in the lease payments.

Amsterdam / The Netherlands

In March 2016, the Company entered into a 16-year lease for a facility in Amsterdam, the Netherlands, and amended this agreement in June 2016. The lease for this facility terminates in February 2032, with an option to extend in increments of five-year periods. The lease contract includes variable lease payments related to annual increases in payments based on a consumer price index.

On December 1, 2017, the Company entered into an agreement to sub-lease three of the seven floors of its Amsterdam facility for a ten-year term ending on December 31, 2027, with an option for the sub-lessee to extend until December 31, 2031. The fixed lease payments to be received during the remaining term amount to $9.1 million (EUR 8.0 million) as of June 30, 2019.

Operating lease liabilities

As no implicit rate in relation to the three above facility leases was readily available, the Company used an incremental borrowing rate to discount the lease payments. The Company derived the discount rates, adjusted for differences in the term and payment patterns, from the Company’s loan from Hercules Capital, which was refinanced in December 2018.

The components of lease cost were as follows:

	Three months ended June 30, 2019	Six months ended June 30, 2019
	(in thousands)	
Operating lease cost	$ 1,022	$ 1,919
Variable lease cost	101	182
Sublease income	(264)	(532)
Total lease cost	**$ 859**	**$ 1,569**

The rent expense for the three and six months ended June 30, 2018 was $0.7 million and $1.4 million, respectively.

The table below presents the lease-related assets and liabilities recorded on the Consolidated balance sheet.

	June 30, 2019 (in thousands)
Assets	
Operating lease right-of-use assets	**$ 27,173**
Liabilities	
Current	
Current operating lease liabilities, net of $1.5 million landlord incentive payments expected to be collected within 12 months	4,256
Non-current	
Non-current operating lease liabilities	31,870
Total lease liabilities	**$ 36,126**

Other information

The weighted-average remaining lease term as of June 30, 2019 is 10.9 years and the weighted-average discount rate as of this date is 11.35%.

The table below presents supplemental cash flow and non-cash information related to leases.

	Three months ended June 30, 2019 (in thousands)	Six months ended June 30, 2019 (in thousands)
Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows for operating leases	$ 603	$ 2,016
Right-of-use asset obtained in exchange for lease obligation		
Operating lease [1)]	$ 8,634	$ 8,634

([1)] The Company capitalized $19.0 million of operating right-of-use assets upon adoption of the new lease standard on January 1, 2019 that are not included in the movement for the six months ended June 30, 2019.)

Undiscounted cash flows

The table below reconciles the undiscounted cash flows as of June 30, 2019, for each of the first five years and the total of the remaining years to the operating lease liabilities recorded on the Consolidated balance sheet as of June 30, 2019.

	Lexington	Amsterdam[1)] (in thousands)	Total
2019 (six months remaining)	$ 1,650	$ 1,438	$ 3,088
2020	3,360	1,918	5,278
2021	3,455	1,918	5,373
2022	3,552	1,918	5,470
2023	3,650	1,918	5,568
Thereafter	24,892	15,343	40,235
Total lease payments	$ 40,559	$ 24,453	$ 65,012
Less: amount of lease payments representing interest payments	(17,728)	(11,158)	(28,886)
Present value of lease payments	22,831	13,295	36,126
Less: current operating lease liabilities	(1,859)	(2,397)	(4,256)
Non-current operating lease liabilities	**$ 20,972**	**$ 10,898**	**$ 31,870**

([1)] Payments are due in EUR and have been translated at the foreign exchange rate as of June 30, 2019, of $1.13709 / €1.00)

As of December 31, 2018, aggregate minimum lease payments under the historical accounting standard ASC 840 for the calendar years were as follows:

	Lexington	Amsterdam[1)]	Total
		(in thousands)	
2019	$ 2,707	$ 1,963	$ 4,670
2020	3,360	1,970	5,330
2021	3,455	1,970	5,425
2022	3,552	1,970	5,522
2023	3,650	1,970	5,620
Thereafter	24,892	16,085	40,977
Total minimum lease payments	**$ 41,616**	**$ 25,926**	**$ 67,544**

([1)] Payments are due in EUR and have been translated at the foreign exchange rate as of December 31, 2018, of $1.14449 / €1.00)

6 Accrued expenses and other current liabilities

Accrued expenses and other current liabilities include the following items:

	June 30, 2019	December 31, 2018
	(in thousands)	
Accruals for services provided by vendors-not yet billed	$ 2,933	$ 1,999
Personnel related accruals and liabilities	4,433	5,688
Derivative financial liability warrants	—	545
Total	**$ 7,366**	**$ 8,232**

7 Long-term debt

On June 14, 2013, the Company entered into a venture debt loan facility with Hercules, which was amended and restated on June 26, 2014, and again on May 6, 2016 (“2016 Amended Facility”). The 2016 Amended Facility extended the maturity date from June 30, 2018, to May 1, 2020. The interest rate was adjustable and was the greater of (i) 8.25% or (ii) 8.25% plus the prime rate less 5.25%. Under the 2016 Amended Facility, the interest rate initially was 8.25% per annum. The interest-only payment period was extended by 12 months to November 30, 2018 as a result of raising more than $50.0 million in equity financing in October 2017.

On December 6, 2018, the Company signed an amendment to the Second Amended and Restated Loan and Security Agreement that both refinanced the existing $20 million 2016 Amended Facility and provided an additional commitment of $30 million (of which $15 million is subject to the discretion of Hercules) (the “2018 Amended Facility”). At signing, the Company drew down an additional $15 million for a total of $35 million outstanding. The Company has the right to draw another $15 million through June 30, 2020 subject to the terms of the 2018 Amended Facility. The 2018 Amended Facility extends the loan’s maturity date from May 1, 2020 until June 1, 2023. The interest-only period is extended from November 2018 to January 1, 2021, or in the event that specified conditions are met, the interest-only period may be extended to January 1, 2022. The Company is required to repay the facility in equal monthly installments of principal and interest between the end of the interest-only period and the maturity date. The interest rate continues to be adjustable and is the greater of (i) 8.85% or (ii) 8.85% plus the prime rate less 5.50% per annum.

Under the 2018 Amended Facility, the Company paid a facility fee of 0.50% of the $35 million outstanding as of signing and owes a back-end fee of 4.95% of the outstanding debt. In addition, in May 2020 the Company owes a back-end fee of 4.85% of $20 million, which is the amount of debt raised under the 2016 Amended Facility.

The amortized cost (including interest due presented as part of accrued expenses and other current liabilities) of the 2018 Amended Facility was $36.0 million as June 30, 2019, compared to $35.7 million as of December 31, 2018, and is recorded net of discount and debt issuance costs. The foreign currency gain on the loan in the three months ended June 30, 2019, was $0.5 million and the foreign currency loss in the six months ended June 30, 2019, was $0.2 million, compared to a foreign currency loss of $1.1 million and $0.6 million during the same periods in 2018.

Interest expense associated with the 2018 Amended Facility during the three and six months ended June 30, 2019 was $0.9 million and $1.9 million, respectively, compared to $0.5 million and $0.9 million associated with the 2016 Amended Facility during the same periods in 2018.

As a covenant in the 2018 Amended Facility, the Company has periodic reporting requirements and is required to keep a minimum cash balance deposited in bank accounts in the United States, equivalent to the lesser of the outstanding 65% balance of principal due or 100% of worldwide cash reserves. This restriction on the cash reserves only relates to the location of the cash reserves, and such cash reserves can be used at the discretion of the Company. In combination with other covenants, the 2018 Amended Facility restricts the Company's ability to, among other things, incur future indebtedness and obtain additional debt financing, to make investments in securities or in other companies, to transfer assets, to perform certain corporate changes, to make loans to employees, officers and directors, and to make dividend payments and other distributions. The Company secured the facilities by pledging the shares in its subsidiaries, substantially all its receivables, moveable assets as well as the equipment, fixtures, inventory and cash of uniQure Inc.

The 2018 Amended Facility contains provisions that include the occurrence of a material adverse effect, as defined therein, which would entitle Hercules to declare all principal, interest and other amounts owed by the Company immediately due and payable. As of June 30, 2019, the Company was in compliance with all covenants and provisions.

8 Share-based compensation

The Company's share-based compensation plans include the 2014 Amended and Restated Share Option Plan (the "2014 Plan") and inducement grants under Rule 5653(c)(4) of the NASDAQ Global Select Market with terms similar to the 2014 Plan (together the "2014 Plans"). At the annual general meeting of shareholders in June 2018, the Company's shareholders approved amendments of the 2014 Plan, increasing the shares authorized for issuance by 3,000,000 to a total of 8,601,471. The Company previously had a 2012 Equity Incentive Plan ("2012 Plan"). As of June 30, 2019, 14,000 fully vested share options are outstanding (December 31, 2018: 32,567) under the 2012 Plan.

a) 2014 Plan

Share-based compensation expense recognized by classification included in the Consolidated statements of operations and comprehensive loss in relation to the 2014 Plan was as follows:

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
	(in thousands)			
Research and development	$ 2,119	$ 993	$ 4,099	$ 1,799
Selling, general and administrative	2,457	1,212	4,755	2,933
Total	**$ 4,576**	**$ 2,205**	**$ 8,854**	**$ 4,732**

Share-based compensation expense for the six months ended June 30, 2019 increased by $4.1 million when compared to six months ended June 30, 2018 as a result of the appreciation of the share price and increase in number of grants. Share-based compensation expense for the three months ended June 30, 2019 increased by $2.4 million when compared to three months ended June 30, 2018 as a result of the appreciation of the share price.

Share-based compensation expense recognized by award type was as follows:

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
	(in thousands)			
Award type				
Share options	$ 2,004	$ 1,096	$ 4,080	$ 2,155
Restricted share units ("RSUs")	995	540	1,925	1,286
Performance share units ("PSUs")	1,577	569	2,849	1,291
Total	**$ 4,576**	**$ 2,205**	**$ 8,854**	**$ 4,732**

As of June 30, 2019, the unrecognized share-based compensation expense related to unvested awards under the 2014 Plans were:

Award type	Unrecognized share-based compensation expense (in thousands)	Weighted average remaining period for recognition (in years)
Share options	$ 21,695	3.08
Restricted share units	6,955	2.10
Performance share units	9,867	2.12
Total	**$ 38,517**	**2.66**

The Company satisfies the exercise of share options and vesting of RSUs and PSUs through newly issued ordinary shares.

Share options

The following table summarizes option activity for the six months ended June 30, 2019:

	Options	
	Number of ordinary shares	Weighted average exercise price
Outstanding at December 31, 2018	**2,673,712**	**$ 15.09**
Granted	530,276	$ 36.05
Forfeited	(41,602)	$ 11.88
Expired	(543)	$ 12.26
Exercised	(218,087)	$ 11.45
Outstanding at June 30, 2019	**2,943,756**	**$ 19.16**
Fully vested and exercisable at June 30, 2019	1,264,254	$ 12.37
Outstanding and expected to vest at June 30, 2019	1,679,502	$ 24.27
Total weighted average grant date fair value of options issued during the period (in $ millions)		$ 11.2
Proceeds from option sales during the period (in $ millions)		$ 2.5

Share options are priced on the date of grant and, except for certain grants made to non-executive directors, vest over a period of four years, the first 25% vests after one year from the grant date and the remainder vests in equal quarterly installments, over years two, three and four. Any options that vest must be exercised by the tenth anniversary of the grant date.

The fair value of each option issued is estimated at the respective grant date using the Hull & White option pricing model with the following weighted-average assumptions:

	Three months ended June 30,		Six months ended June 30,	
Assumptions	**2019**	**2018**	**2019**	**2018**
Expected volatility	75%	75%	75%	75%
Expected terms	10 years	10 years	10 years	10 years
Risk free interest rate	2.17% - 2.63%	2.99% - 3.07%	2.17% - 2.87%	2.77% - 3.07%
Expected dividend yield	0%	0%	0%	0%

Restricted share units

The following table summarizes the RSUs activity for the six months ended June 30, 2019:

	RSU	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2018	**412,321**	**$ 16.49**
Granted	145,004	$ 33.62
Vested	(186,417)	$ 12.78
Forfeited	(14,516)	$ 12.90
Non-vested at June 30, 2019	**356,392**	**$ 25.55**
Total weighted average grant date fair value of RSUs granted during the period (in $ millions)		$ 4.9

RSUs vest over one to three years. RSUs granted to non-executive directors will vest one year from the date of grant.

Performance share units

The following table summarizes the PSUs activity for the six months ended June 30, 2019:

	PSU	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2018	**377,169**	**$ 16.73**
Granted	132,362	$ 31.71
Vested	(23,064)	$ 5.76
Non-vested at June 30, 2019	**486,467**	**$ 17.80**
PSUs awarded but not yet earned	96,389	$ 78.15
Total non-vested and discretionary PSUs	582,856	$ 27.78
Total weighted average grant date fair value of PSUs granted and awarded during the period (in $ millions)		$ 11.7

In January 2019, the Company awarded PSUs to its executives and other members of senior management. These PSUs are earned based on the Board's assessment of the level of achievement of agreed upon performance targets through December 31, 2019.

b) Employee Share Purchase Plan ("ESPP")

In June 2018 the Company's shareholders adopted and approved an ESPP allowing the Company to issue up to 150,000 ordinary shares. The ESPP is intended to qualify under Section 423 of the Internal Revenue Code of 1986. Under the ESPP, employees are eligible to purchase ordinary shares through payroll deductions, subject to any plan limitations. The purchase price of the shares on each purchase date is equal to 85% of the lower of the closing market price on the offering date or the closing market price on the purchase date of each three-month offering period. During the six months ended June 30, 2019 4,870 shares were issued. As of June 30, 2019, a total of 142,539 ordinary shares remains available for issuance under the ESPP plan.

9 Income taxes

Deferred tax assets and deferred tax liabilities are recognized based on the expected future tax consequences of temporary differences between the financial statement carrying amounts and the income tax basis of assets and liabilities, using current statutory rates. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all the deferred tax assets will not be realized. Due to the uncertainty surrounding the realization of the favorable tax attributes in future tax returns, the Company has recorded a full valuation allowance against the Company's otherwise recognizable net deferred tax assets.

10 Basic and diluted earnings per share

Diluted earnings per share are calculated by adjusting the weighted average number of ordinary shares outstanding, assuming conversion of all potentially dilutive ordinary shares. As the Company has incurred a loss, all potentially dilutive ordinary shares would have an antidilutive effect, if converted, and thus have been excluded from the computation of loss per share.

The potentially dilutive ordinary shares are summarized below:

	June 30,	
	2019	2018
	(ordinary shares)	
BMS warrants	8,435,000	7,530,000
Stock options under 2014 Plans	2,943,756	2,694,741
Non-vested RSUs and earned PSUs	842,859	943,853
Stock options under 2012 Plan	14,000	33,467
Warrants (exercised February 1, 2019)	—	37,175
Employee share purchase plan	596	—
Total potential dilutive ordinary shares	**12,236,211**	**11,239,236**

11 Subsequent event

None.

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

The following Management's Discussion and Analysis of Financial Condition and Results of Operations ("MD&A") is intended to help the reader understand our results of operations and financial condition. This MD&A is provided as a supplement to, and should be read in conjunction with, our unaudited condensed consolidated financial statements and the accompanying notes thereto and other disclosures included in this Quarterly Report on Form 10-Q, including the disclosures under Part II, Item 1A "Risk Factors", and our audited financial information and the notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2018, which was filed with the Securities and Exchange Commission (the "SEC"), on February 28, 2019. Our unaudited condensed consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the US ("U.S. GAAP") and unless otherwise indicated are presented in U.S. dollars.

Overview

We are a leader in the field of gene therapy, seeking to develop single treatments with potentially curative results for patients suffering from genetic and other devastating diseases. We are advancing a focused pipeline of innovative gene therapies. We have established clinical proof-of-concept in our lead indication, hemophilia B, and achieved preclinical proof-of-concept in Huntington's disease. We believe our validated technology platform and manufacturing capabilities provide us distinct competitive advantages, including the potential to reduce development risk, cost and time to market. We produce our adeno-associated virus ("AAV") -based gene therapies in our own facilities with a proprietary, commercial-scale, current good manufacturing practices ("cGMP")-compliant, manufacturing process. We believe our Lexington, Massachusetts-based facility is one of the world's leading, most versatile, gene therapy manufacturing facilities.

Business Developments

Below is a summary of our recent significant business developments:

Hemophilia B program (AMT-061)

AMT-061 is our lead gene therapy candidate, and includes an AAV5 vector incorporating the Factor IX-Padua variant. We are currently enrolling a pivotal study in patients with severe and moderately-severe hemophilia B. AMT-061 has been granted Breakthrough Therapy Designation by the United States Food and Drug Administration ("FDA") and access to the PRIME initiative by the European Medicines Agency ("EMA").

In February 2019, we announced the dosing of the first patient in our Phase III HOPE-B hemophilia B pivotal trial. The trial is a multinational, multi-center, open-label, single-arm study to evaluate the safety and efficacy of AMT-061. After the six-month lead-in period, patients will receive a single intravenous administration of AMT-061. The primary endpoint of the study will be based on the Factor IX ("FIX") activity level achieved following the administration of AMT-061, and the secondary endpoints will measure annualized FIX replacement therapy usage, annualized bleed rates and safety. Patients enrolled in the HOPE-B trial will be tested for the presence of pre-existing neutralizing antibodies to AAV5 but will not be excluded from the trial based on their titers.

In February, May and July 2019, we presented updated data from our Phase IIb dose-confirmation study of AMT-061. The Phase IIb study is an open-label, single-dose, single-arm, multi-center trial being conducted in the United States. The objective of the study was to evaluate the safety and tolerability of AMT-061 and confirm the dose based on FIX activity at six weeks after administration. Three patients with severe hemophilia were enrolled in this study and received a single intravenous infusion of $2x10^{13}$ gc/kg.

Data from the Phase IIb study of AMT-061 show that all three patients experienced increasing and sustained FIX levels after a one-time administration of AMT-061. Mean FIX activity was 45% of normal at 36 weeks of follow-up, exceeding threshold FIX levels generally considered sufficient to significantly reduce the risk of bleeding events. Specifically, the first patient achieved FIX activity of 54% of normal, the second patient achieved FIX activity of 30% of normal, and the third patient achieved FIX activity of 51% of normal. Through 36 weeks of follow-up, no patient experienced a material loss of FIX activity, reported any bleeding events or required any infusions of FIX replacement therapy for bleeds. One patient underwent hip surgery due to a pre-existing condition and was treated perioperatively with short-acting factor replacement. This was reported by the investigator as a serious adverse event unrelated to AMT-061.

In July 2019, we also presented three-and-a-half-year follow-up data related to our first-generation hemophilia B program, AMT-060, which incorporated a wild-type Factor IX gene. All 10 patients enrolled in the Phase I/II study continue to show long-term meaningful clinical impact, including sustained increases in FIX activity and improvements in their disease state as measured by reduced usage of FIX replacement therapy and decreased bleeding frequency. At up to 3.5 years of follow-up, AMT-060 continues to be safe and well-tolerated, with no new serious adverse events and no development of inhibitors since the last reported data.

All five patients in the second dose cohort of $2x10^{13}$ gc/kg continue to be free of routine FIX replacement therapy at up to three years after treatment. During the last 12 months of observation, the mean annualized bleeding rate was 0.7 bleeds, representing an 83% reduction compared with the year prior to treatment. During this same period, the usage of FIX replacement therapy declined 96% compared with the year prior to treatment. Steady state mean yearly FIX activity at three years was 7.9%, compared with 7.1% in the first year and 8.4% in the second year.

Huntington's disease program (AMT-130)

AMT-130 is our gene therapy candidate targeting Huntington's disease and utilizes an AAV vector carrying a microRNA ("miRNA") specifically designed to silence the huntingtin gene. AMT-130 has received orphan drug designation from the FDA and Orphan Medicinal Product Designation from the EMA.

In January 2019, our Initial New Drug ("IND") application for AMT-130 was cleared by the FDA, thereby enabling us to initiate our planned Phase I/II clinical study. The Phase I/II study is expected to be a randomized, double-arm, blinded, imitation surgery-controlled trial conducted at three surgical sites in the U.S., and at least two non-surgical sites. The primary objective of the study is to evaluate the safety, tolerability and efficacy of AMT-130 at two doses.

Also in January 2019, the U.S. Patent and Trademark Office issued U.S. Patent 10,174,321 and in May 2019 the European Patent Office issued EP 3237618, both with granted claims that cover the RNA constructs specifically designed to target exon1 and the embedding of these Huntington's disease RNA sequences into the miR451 scaffold, which we exclusively license from Cold Spring Harbor Laboratory (CSHL). The claims also cover certain expression cassettes comprising the RNA constructs and the use of gene therapy vectors including AAV vectors encompassing the described expression cassettes.

In February 2019, we presented new preclinical data at the 14th Annual CHDI Huntington's disease Therapeutics Conference that illustrate the therapeutic potential of AMT-130 in restoring function of damaged brain cells in Huntington's disease and providing a safe and sustained reduction of mutant huntingtin protein.

In April 2019, we announced that the FDA granted fast track designation for AMT-130.

Hemophilia A program (AMT-180)

In May 2019, we presented preclinical proof-of-concept data at the American Society of Gene and Cell Therapy ("ASGCT") Annual Meeting, demonstrating that our gene therapy candidate AMT-180 for hemophilia A induced clinically relevant thrombin activation, and up to 29% of Factor VIII-independent activity, in FVIII-depleted human plasma. The studies further demonstrated that a single intravenous administration of AMT-180 resulted in sustained, dose-dependent hemostatic effect as measured by one-stage clotting assay, and that AMT-180 shows activation kinetics similar to native FIX and is not hyperactive. A pilot study in non-human primates demonstrated that administration of AMT-180 resulted in sufficient FIX protein expression that translates to clinically relevant Factor VIII-independent activity in humans. No elevation of coagulation activation markers or signs of thrombi formation were observed.

Spinocerebellar Ataxia Type 3 (AMT-150)

At the 2019 American Academy of Neurology (AAN) Annual Meeting, we presented preclinical data on AMT-150 for the treatment of Spinocerebellar Ataxia Type 3 ("SCA3"). The data featured at the conference demonstrated mechanistic proof-of-concept of the non-allele-specific ataxin-3 protein-silencing approach by using artificial microRNA candidates engineered to target the ataxin-3 gene in a SCA3 knock-in mouse model. The proof-of-concept study demonstrated that a single AMT-150 injection in the cerebrospinal fluid resulted in strong AAV transduction and significant mutant ataxin-3 lowering at the primary sites of disease neuropathology, the cerebellum (up to 53%) and the brainstem (up to 65%).

Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) (AMT-160)

In February 2019, we published results from preclinical studies showing the potential for significant silencing, or knockdown, of the mutated gene most commonly known to lead to onset of amyotrophic lateral sclerosis ("ALS") and frontotemporal dementia ("FTD"), two devastating neurodegenerative diseases. The proof-of-concept studies utilized the Company's proprietary, next-generation gene-silencing platform miQURE™.

Fabry program (AMT-190)

We also presented at the ASGCT conference preclinical data on AMT-190, our novel AAV5 gene therapy candidate for Fabry disease that comprises a recombinant AAV5 vector incorporating a proprietary, exclusively licensed, modified NAGA (ModNAGA) variant. AMT-190 provides expression of ModNAGA, which shows a high structural resemblance to α-gal. We believe that this approach may have several advantages over α-gal therapies, including higher stability in blood, better biodistribution in the target organs, secondary toxic metabolite reduction and improved cross-correction of neighboring cells. ModNAGA might also be effective in the presence of α-gal antibodies. Data from in vitro and in vivo studies show that AMT-190 has the potential to become a one-time treatment option that could be an improvement upon the enzyme replacement standard of care with more efficient uptake in the kidney and heart and an improved immunogenicity profile.

BMS collaboration

We entered into a collaboration and license agreement with BMS in May 2015. We have been supporting BMS in the discovery, non-clinical, analytical and process development efforts of Collaboration Targets. For any Collaboration Targets that are advanced, we will be responsible for manufacturing of clinical and commercial supplies using our vector technologies and industrial, proprietary insect-cell based manufacturing platform. BMS has been reimbursing us for all our research and development costs in support of the collaboration during the research term. BMS will lead the development, regulatory and commercial activities for all four currently active Collaboration Targets as well as additional Collaboration Targets that may be advanced.

In February 2019, BMS requested a one-year extension of the research term. In April 2019, following an assessment of the progress of this collaboration and our expanding proprietary programs, we notified BMS that we did not intend to agree to an extension of the research term. Accordingly, the initial four-year research term under the collaboration terminated on May 21, 2019. We are currently in discussions with BMS potentially to amend the collaboration and license agreement and other related agreements following the expiration of the research term.

Financial Overview

Key components of our results of operations include the following:

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
	(in thousands)		(in thousands)	
Total revenues	$ 2,474	$ 3,050	$ 3,610	$ 6,528
Research and development expenses	(24,154)	(18,493)	(44,691)	(35,551)
Selling, general and administrative expenses	(7,870)	(5,896)	(15,937)	(12,197)
Net loss	(31,399)	(20,592)	(59,171)	(39,381)

As of June 30, 2019, and December 31, 2018, we had cash and cash equivalents of $184.1 million and $234.9 million, respectively. We had a net loss of $31.4 million and $59.2 million in the three and six months ended June 30, 2019, respectively, compared to $20.6 million and $39.4 million for the same periods in 2018. As of June 30, 2019, and December 31, 2018, we had accumulated deficits of $594.7 million and $535.5 million, respectively. We anticipate that our loss from operations will increase in the future as we:

- Advance our AMT-061 pivotal trial;
- Advance the clinical development of AMT-130 for our Huntington's disease gene therapy program;
- Build-out our commercial infrastructure and seek marketing approval for any product candidates (including AMT-061) that successfully complete clinical trials;
- Advance multiple research programs related to gene therapy candidates targeting liver-directed and central nervous system ("CNS") diseases;

- Continue to build-out our clinical, medical and regulatory capabilities;
- Continue to expand, enhance and optimize our technology platform, including our manufacturing capabilities, next-generation viral vectors and promoters, and other enabling technologies;
- Acquire or in-license rights to new therapeutic targets or product candidates; and
- Maintain, expand and protect our intellectual property portfolio, including in-licensing additional intellectual property rights from third parties;

See “Results of Operations” below for a discussion of the detailed components and analysis of the amounts above.

Critical Accounting Policies and Estimates

In preparing our consolidated financial statements in accordance with U.S. GAAP and pursuant to the rules and regulations promulgated by the SEC, our management makes assumptions, judgments and estimates that can have a significant impact on our net income/loss and affect the reported amounts of certain assets, liabilities, revenue and expenses, and related disclosures. On an ongoing basis, we evaluate our estimates and judgments, including those related to recognition of License Revenue in accordance with ASC 606, BMS warrants and share-based payments. We base our assumptions, judgments and estimates on historical experience and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not clear from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies. With the exception of ASC 842 Leases, during the six months ended June 30, 2019, there were no material changes to our critical accounting policies as reported in our Annual Report on Form 10-K for the year ended December 31, 2018, which was filed with the SEC on February 28, 2019.

We believe that the assumptions, judgments and estimates involved in the recognition of License Revenue in accordance with ASC 606, BMS warrants and share-based payments to be our critical accounting policies during the year ended December 31, 2018, as well as during the three and six months ended June 30, 2019. We also consider the accounting for our operating leases including the Lexington expansion lease that commenced on June 1, 2019, to be among our critical accounting policies.

Adoption of ASC 842 Leases on January 1, 2019

On January 1, 2019, we adopted ASC 842, “Leases (Topic 842)”. We adopted the standard using the modified retrospective approach with an effective date as of the beginning of the fiscal year, January 1, 2019, to operating leases that existed on that date. Prior year comparative financial information was not recast under the new standard and continues to be presented under ASC 840. We elected to utilize the package of practical expedients available for expired or existing contracts which allowed us to carryforward historical assessments of (1) whether contracts are or contain leases, (2) lease classification, and (3) initial direct costs. We performed an assessment and identified the lease facilities as material leases to be accounted for under ASC 842 as of January 1, 2019. The impact of implementing ASC 842 is summarized below:

- Recognized a $19.0 million operating right-of-use asset and a $28.1 million operating lease liability in relation to the facilities leased at the Amsterdam and Lexington sites in the consolidated balance sheet as of January 1, 2019;
- Presented deferred rent of $9.1 million as of December 31, 2018, as a reduction of the right-of-use asset as from January 1, 2019 onwards in the consolidated balance sheet and as a change within operating cash flows within accrued expense, other liabilities and operating leases;

We measured the lease liability at the present value of the future lease payments as of January 1, 2019. We used an incremental borrowing rate to discount the lease payments. We derived the discount rate, adjusted for differences in the term and payment patterns, from our Hercules loan which was refinanced immediately prior to the January 1, 2019 adoption date in December 2018. We valued the right-of-use asset at the amount of the lease liability reduced by the remaining December 31, 2018 balance of lease incentives received. We subsequently measure the lease liability at the present value of the future lease payments as of the reporting date with a corresponding adjustment to the right-to-use asset. Absent a lease modification we will continue to utilize the January 1, 2019, incremental borrowing rate.

We will continue to recognize lease cost on a straight-line basis and will continue to present these costs as operating expenses within our Consolidated statements of operations and comprehensive loss. We will continue to present lease payments within cash flows from operations within our Consolidated statements of cash flows.

Revenues

We recognize Collaboration Revenues associated with pre-clinical Collaboration Target specific, non-clinical, analytical and process development activities that are reimbursable by BMS under our collaboration agreement during the research term.

We recognize License Revenues associated with the amortization of the non-refundable upfront payment, target designation fees and research and development milestone payments we received or might receive from BMS. The timing of these cash payments may differ from the recognition of revenue, as revenue is deferred and recognized over the duration of the performance period. We recognize other revenue, such as sales milestone payments, when earned.

Research and development expenses

We expense research and development costs ("R&D") as incurred. Our R&D expenses generally consist of costs incurred for the development of our target candidates, which include:

- Employee-related expenses, including salaries, benefits, travel and share-based compensation expense;
- Costs incurred for laboratory research, preclinical and nonclinical studies, clinical trials, statistical analysis and report writing, and regulatory compliance costs incurred with clinical research organizations and other third-party vendors;
- Costs incurred to conduct consistency and comparability studies;
- Costs incurred for the validation of our Lexington facility;
- Costs incurred for the development and improvement of our manufacturing processes and methods;
- Costs associated with our research activities for our next-generation vector and promoter platform;
- Changes in the fair value of the contingent consideration related to our acquisition of InoCard (up to September 30, 2018) as well as the impairment of in process research and development acquired (in the three-month period ended September 30, 2018);
- Facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies; and
- Amortization of intangible assets.

Our research and development expenses primarily consist of costs incurred for the research and development of our product candidates, which include:

- *AMT-061 (hemophilia B)*. We have incurred costs related to the research, development and production of AMT-061 for the treatment of hemophilia B. In June 2018, we initiated a pivotal study of AMT-061 and in August and September 2018, we completed dosing patients in our Phase IIb dose-confirmation study.
- *AMT-130 (Huntington's disease).* We have incurred costs related to preclinical and nonclinical studies of AMT-130 and started incurring costs related to our Phase I/II trial;
- *Preclinical research programs*. We incur costs related to the research of multiple preclinical gene therapy product candidates with the potential to treat certain rare and other serious medical conditions; and
- *Technology platform development and other related research*. We incur significant research and development costs related to manufacturing and other enabling technologies that are applicable across all our programs.

Our research and development expenses may vary substantially from period to period based on the timing of our research and development activities, including manufacturing campaigns, regulatory submissions and enrollment of patients in clinical trials. The successful development of our product candidates is highly uncertain. Estimating the nature, timing or cost of the development of any of our product candidates involves considerable judgement due to numerous risks and uncertainties associated with developing gene therapies, including the uncertainty of:

- the scope, rate of progress and expense of our research and development activities;
- our ability to successfully manufacture and scale-up production;

- clinical trial protocols, speed of enrollment and resulting data;
- the effectiveness and safety of our product candidates;
- the timing of regulatory approvals; and
- our ability to agree to ongoing development budgets with collaborators who share the costs of our development programs.

A change in the outcome of any of these variables with respect to our product candidates that we may develop could mean a significant change in the expenses and timing associated with the development of such product candidate.

Selling, general and administrative expenses

Our general and administrative expenses consist principally of employee, office, consulting, legal and other professional and administrative expenses. We incur expenses associated with operating as a public company, including expenses for personnel, legal, accounting and audit fees, board of directors' costs, directors' and officers' liability insurance premiums, NASDAQ listing fees, expenses related to investor relations and fees related to business development and maintaining our patent and license portfolio.

Other items, net

Our other income consists of payments to subsidize our research and development efforts as well as income from the sublicensing of our Amsterdam facility.

Our other expense consists of expenses we incur in relation to our sublicensing income.

Results of Operations

Comparison of the three months ended June 30, 2019 and 2018

The following table presents a comparison of the three months ended June 30, 2019 and 2018.

	Three months ended June 30,		
	2019	2018	2019 vs 2018
	(in thousands)		
Total revenues	$ 2,474	$ 3,050	$ (576)
Operating expenses:			
Research and development expenses	(24,154)	(18,493)	(5,661)
Selling, general and administrative expenses	(7,870)	(5,896)	(1,974)
Total operating expenses	**(32,024)**	**(24,389)**	**(7,635)**
Other income	566	565	1
Other expense	(347)	(429)	82
Loss from operations	**(29,331)**	**(21,203)**	**(8,128)**
Other non-operating items, net	(2,068)	972	(3,040)
Loss before income tax benefit	**(31,399)**	**(20,231)**	**(11,168)**
Income tax expense	—	(361)	361
Net loss	**$ (31,399)**	**$ (20,592)**	**$ (10,807)**

Revenue

Our revenue for the three months ended June 30, 2019 and 2018 was as follows:

	Three months ended June 30,		
	2019	2018	2019 vs 2018
	(in thousands)		
License Revenue	$ 2,108	$ 2,123	$ (15)
Collaboration Revenue	366	927	(561)
Total revenues	**$ 2,474**	**$ 3,050**	**$ (576)**

We recognize License Revenue related to upfront payments and target designation fees received from BMS in 2015. We recognized $2.1 million of BMS License Revenue in the three months ended June 30, 2019, compared to $2.1 million for the same period in 2018.

We recognized Collaboration Revenue from BMS during the initial research term that ended on May 21, 2019. We recognized $0.4 million in the three months ended June 30, 2019, compared to $0.9 million for the same period in 2018. The decrease in Collaboration Revenue was primarily related to the discontinuation of S100A1 research in the fourth quarter of 2018.

Research and development expenses

Research and development expenses for the three months ended June 30, 2019 were $24.2 million, compared to $18.5 million for the same period in 2018.

- We incurred $9.1 million in personnel and consulting expenses in the three months ended June 30, 2019, compared to $7.6 million for the same period in 2018. Our costs during the three months ended June 30, 2019 increased by $1.5 million as a result of the recruitment of personnel to support the preclinical and clinical development of our product candidates;
- We incurred $2.1 million in share-based compensation expenses in the three months ended June 30, 2019, compared to $1.0 million for the same period in 2018 primarily driven by the appreciation of our share price;
- We incurred $8.9 million in external services and costs related to the development of our product candidates in the three months ended June 30, 2019, compared to $6.9 million in the same period in 2018. The increase was a result of our continued enrollment of patients into our pivotal Phase III trial of AMT-061 that commenced at the end of June 2018, as well as expenses incurred in relation to our ongoing Phase IIb dose-confirmation studies for AMT-061; and
- We incurred $3.6 million in operating expenses and depreciation expenses related to our rented facilities in the three months ended June 30, 2019, compared to $3.0 million in the same period in 2018. Our costs during the three months ended June 30, 2019 increased as a result of extending and expanding the lease of our Lexington facility.

Selling, general and administrative expenses

Selling, general and administrative expenses for the three months ended June 30, 2019 were $7.9 million, compared to $5.9 million for the same period in 2018.

- We incurred $2.4 million in personnel and consulting expenses in the three months ended June 30, 2019, compared to $2.3 million in the same period in 2018;
- We incurred $2.4 million of share-based compensation expenses in the three months ended June 30, 2019, compared to $1.2 million in the same period in 2018. The increase was primarily driven by the appreciation of our share price; and
- We incurred $1.3 million in professional fees in the three months ended June 30, 2019, compared to $1.0 million in the same period in 2018.

Other items, net

We recognized $0.3 million of income from payments received from European authorities to subsidize our research and development efforts in the Netherlands in the three months ended June 30, 2019, compared to $0.2 million for the same period in 2018.

Other non-operating items, net

We recognize interest income associated with our cash and cash equivalents.

We hold monetary items and enter into transactions in foreign currencies, predominantly in euros and U.S. dollars. We recognize foreign exchange results related to changes in these foreign currencies.

We issued warrants to Hercules in 2013 and to BMS in 2015. We recognize changes in the fair value of these warrants within other non-operating (expense) / income. Following the exercise of the warrants by Hercules in February 2019 we no longer recognize changes in the fair value of these warrants within other non-operating (expense) / income.

Our other non-operating items, net, for the three months ended June 30, 2019 and 2018 were as follows:

	Three months ended June 30,		
	2019	2018	2019 vs 2018
	(in thousands)		
Interest income	$ 728	$ 583	$ 145
Interest expense - Hercules long-term debt	(937)	(565)	(372)
Foreign currency (losses) / gains, net	(1,252)	2,255	(3,507)
Other non-operating loss	(607)	(1,301)	694
Total other non-operating (expense) / income, net	**$ (2,068)**	**$ 972**	**$ (3,040)**

We recognized a net foreign currency loss related to our borrowings from Hercules and our cash and cash equivalents of $1.3 million during the three months ended June 30, 2019, compared to a net gain of $2.3 million during the same period in 2018.

In the three months ended June 30, 2019, we recognized a loss of $0.6 million related to changes of fair value of warrants compared to a loss of $1.3 million for the same period in 2018. The three months ended June 30, 2018, include a loss related to the Hercules warrants.

Comparison of the six months ended June 30, 2019, and 2018

The following table presents a comparison of the six months ended June 30, 2019 and 2018.

	Six months ended June 30,		
	2019	2018	2019 vs 2018
	(in thousands)		
Total revenues	$ 3,610	$ 6,528	$ (2,918)
Operating expenses:			
Research and development expenses	(44,691)	(35,551)	(9,140)
Selling, general and administrative expenses	(15,937)	(12,197)	(3,740)
Total operating expenses	**(60,628)**	**(47,748)**	**(12,880)**
Other income	879	1,180	(301)
Other expense	(696)	(762)	66
Loss from operations	**(56,835)**	**(40,802)**	**(16,033)**
Non-operating items, net	(2,336)	1,690	(4,026)
Loss before income tax expense	**(59,171)**	**(39,112)**	**(20,059)**
Income tax benefit / (expense)	—	(269)	269
Net loss	**$ (59,171)**	**$ (39,381)**	**$ (19,790)**

Revenue

Our revenue for the six months ended June 30, 2019 and 2018 was as follows:

	Six months ended June 30,		
	2019	2018	2019 vs 2018
	in thousands		
License revenue	$ 2,665	$ 4,574	$ (1,909)
Collaboration revenue	945	1,954	(1,009)
Total revenues	**$ 3,610**	**$ 6,528**	**$ (2,918)**

We recognize License Revenue related to upfront payments and target designation fees received from BMS in 2015. We recognized $2.7 million of BMS License Revenue in the six months ended June 30, 2019, compared to $4.6 million for the same period in 2018. The change in License Revenue is a result of adjustments to the expected performance period based on its measure of progress towards the completion of certain activities related to its services.

We recognized Collaboration Revenue from BMS during the initial research term that ended on May 21, 2019. We recognized $0.9 million in the six months ended June 30, 2019, compared to $2.0 million for the same period in 2018. The decrease in Collaboration Revenue was primarily related to the discontinuation of S100A1 research in the fourth quarter of 2018.

Research and development expenses

Research and development expenses for the six months ended June 30, 2019 were $44.7 million, compared to $35.6 million for the same period in 2018.

- We incurred $18.0 million in personnel and consulting expenses in the six months ended June 30, 2019, compared to $15.4 million for the same period in 2018. Our costs during the six months ended June 30, 2019 increased by $2.6 million as a result of the recruitment of personnel to support the preclinical and clinical development of our product candidates;
- We incurred $4.1 million in share-based compensation expenses in the six months ended June 30, 2019, compared to $1.8 million for the same period in 2018 primarily driven by the appreciation of our share price and increase in number of grants;
- We incurred $14.8 million in external services and costs related to the development of our product candidates in the six months ended June 30, 2019, compared to $11.9 million in the same period in 2018. The increase was a result of our continued enrollment of patients into our pivotal Phase III trial of AMT-061 that commenced at the end of June 2018, as well as expenses incurred in relation to our ongoing Phase IIb dose-confirmation for AMT-061; and
- We incurred $6.9 million in operating expenses and depreciation expenses related to our rented facilities in the six months ended June 30, 2019, compared to $6.0 million in the same period in 2018. Our costs during the six months ended June 30, 2019 increased as a result of extending and expanding the lease of our Lexington facility.

Selling, general and administrative expenses

Selling, general and administrative expenses for the six months ended June 30, 2019 were $15.9 million, compared to $12.2 million for the same period in 2018.

- We incurred $5.1 million in personnel and consulting expenses in the six months ended June 30, 2019, compared to $4.4 million in the same period in 2018 driven by increase in personnel related and consulting related expenses;
- We incurred $4.8 million of share-based compensation expenses in the six months ended June 30, 2019, compared to $2.9 million in the same period in 2018. The increase was primarily driven by the appreciation of our share price and increase in number of grants; and
- We incurred $2.9 million in professional fees in the six months ended June 30, 2019, compared to $2.2 million in the same period in 2018.

Other items, net

We recognized $0.3 million of income from payments received from European authorities to subsidize our research and development efforts in the Netherlands in the six months ended June 30, 2019, compared to $0.5 million for the same period in 2018.

Other non-operating items, net

We recognize interest income associated with our cash and cash equivalents.

We hold monetary items and enter into transactions in foreign currencies, predominantly in euros and U.S. dollars. We recognize foreign exchange results related to changes in these foreign currencies.

We issued warrants to Hercules in 2013 and to BMS in 2015. We recognize changes in the fair value of these warrants within other non-operating (expense) / income. Following the exercise of the warrants by Hercules in February 2019 we no longer recognize changes in the fair value of these warrants within other non-operating (expense) / income.

Our other non-operating items, net, for the six months ended June 30, 2019 and 2018 were as follows:

	Six months ended June 30,		
	2019	2018	2019 vs 2018
	(in thousands)		
Interest income	$ 1,170	$ 836	$ 334
Interest expense - Hercules debt	(1,894)	(981)	(913)
Foreign currency gains, net	1,022	2,433	(1,411)
Other non-operating expense	(2,634)	(598)	(2,036)
Total non-operating (expense) / income, net	**$ (2,336)**	**$ 1,690**	**$ (4,026)**

We recognized a net foreign currency gain related to our borrowings from Hercules and our cash and cash equivalents of $1.0 million during the six months ended June 30, 2019, compared to a net gain of $2.4 million during the same period in 2018.

In the six months ended June 30, 2019, we recognized a loss of $2.6 million related to changes of fair value of warrants compared to a loss of $0.6 million for the same period in 2018.

Financial Position, Liquidity and Capital Resources

As of June 30, 2019, we had cash, cash equivalents and restricted cash of $187.0 million. We currently expect that our cash and cash equivalents will be sufficient to fund operations into 2021. The table below summarizes our consolidated cash flow data for the six months ended June 30, 2019, and 2018.

	Six months ended June 30,	
	2019	2018
	(in thousands)	
Cash, cash equivalents and restricted cash at the beginning of the period	$ 237,342	$ 161,851
Net cash used in operating activities	(50,657)	(37,977)
Net cash used in investing activities	(2,428)	(2,642)
Net cash generated from financing activities	3,221	141,478
Foreign exchange impact	(443)	(1,071)
Cash, cash equivalents and restricted cash at the end of period	**$ 187,035**	$ **261,638**

We have incurred losses and cumulative negative cash flows from operations since our business was founded by our predecessor entity AMT Therapeutics (“AMT”) Holding N.V. in 1998. We had a net loss of $31.4 million and $59.2 million during the three and six months ended June 30, 2019, respectively, compared to a net loss of $20.6 million and $39.4 million during the same periods in 2018, respectively. As of June 30, 2019, we had an accumulated deficit of $594.7 million.

Sources of liquidity

From our first institutional venture capital financing in 2006 through June 30, 2019, we funded our operations primarily through private and public placements of equity securities and convertible and other debt securities as well as payments from our collaboration partners.

On December 6, 2018, we signed an amendment to the Second Amended and Restated Loan and Security Agreement with Hercules Technology Growth Capital Inc. (“Hercules”) that both refinanced our existing $20 million credit facility and provided us with an additional commitment of $30 million (of which $15 million is subject to the discretion of Hercules) (the “Amended Facility”). At signing, we drew down an additional $15 million, for a total outstanding amount of $35 million. We have the right to draw another $15 million through June 30, 2020 subject to the terms of the Amended Facility.

The Amended Facility extends the loan's maturity date until June 1, 2023. This includes extending the interest-only period from November 2018 up to January 1, 2022, upon achieving certain specified conditions. As of June 30, 2019 and December 31, 2018, $35 million was outstanding. We are required to repay the facility in equal monthly installments of principal and interest between the end of the interest-only period and the maturity date. The variable interest rate is equal to the greater of (i) 8.85% or (ii) 8.85% plus the prime rate less 5.50%. Under the Amended Facility, we paid a facility fee equal to 0.50% of the $35 million loan outstanding and will owe a back-end fee of 4.95% of the outstanding debt.

On May 7, 2018, we completed a follow-on public offering of 5,175,000 ordinary shares at $28.50 per ordinary share, resulting in gross proceeds to us of approximately $147.5 million. The net proceeds to us from this offering were approximately $138.5 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us. We capitalized $0.2 million of expenses (which are presented as a reduction of additional paid-in capital) related to this offering.

We expect to continue to incur losses and to generate negative cash flows. We have no firm sources of additional funding. Until such time, if ever, as we can generate substantial cash flows from successfully commercializing our product candidates, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution and licensing arrangements.

We are subject to covenants under our Loan Agreement with Hercules and may become subject to covenants under any future indebtedness that could limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely impact our ability to conduct our business. In addition, our pledge of assets as collateral to secure our obligations under the Hercules loan agreement may limit our ability to obtain debt financing. To the extent we need to finance our cash needs through equity offerings or debt financings, such financing may be subject to unfavorable terms including without limitation, the negotiation and execution of definitive documentation, as well as credit and debt market conditions, and we may not be able to obtain such financing on terms acceptable to us or at all. If financing is not available when needed, including through debt or equity financings, or is available only on unfavorable terms, we may be unable to meet our cash needs. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or 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, which could have a material adverse effect on our business, financial conditions, results of operations and cash flows.

Net Cash used in operating activities

Net cash used in operating activities was $50.7 million for the six months ended June 30, 2019, and consisted of a net loss of $59.2 million adjusted for non-cash items, including depreciation and amortization expense of $3.2 million, share-based compensation expense of $8.9 million, fair value loss of derivative financial instruments of $2.6 million, unrealized foreign exchange gain of $0.4 million, and a decrease in unamortized deferred revenue of $2.7 million. Net cash used in operating activities also included changes in operating assets and liabilities of $3.1 million. These changes primarily related to an increase in accounts receivable and accrued income, prepaid expenses and other current assets of $2.8 million driven by an increase in prepaid expenses related to our AMT-061 and AMT-130 trials.

Net cash used in operating activities was $38.0 million for the six months ended June 30, 2018, and consisted of a net loss of $39.4 million adjusted for non-cash items, including depreciation and amortization expense of $3.2 million, share-based compensation expense of $4.7 million, fair value loss of derivative financial instruments and contingent consideration of $0.5 million, unrealized foreign exchange gain of $3.4 million, deferred tax expense of $0.3 million, a decrease in lease incentive of $0.1 million, and a decrease in unamortized deferred revenue of $4.6 million . Net cash used in operating activities also included changes in operating assets and liabilities of $0.7 million primarily related to an increase in accounts payable.

Net cash used in investing activities

In the six months ended June 30, 2019, we used $2.4 million in our investing activities compared to $2.6 million for the same period in 2018.

	Six months ended June 30,	
	2019	2018
	(in thousands)	
Build out of Lexington site	$ (930)	$ (818)
Build out of Amsterdam site	(502)	(379)
Acquisition of licenses and patents	(996)	(1,445)
Total investments	**$ (2,428)**	**$ (2,642)**

Net cash generated from financing activities

During the six months ended June 30, 2019, we received $2.7 million from the exercise of options to purchase ordinary shares in relation to our share incentive plans compared to $3.0 million in the same period 2018.

We received net proceeds of $138.5 million associated with our follow-on offering in May 2018.

Funding requirements

We believe our cash and cash equivalents as of June 30, 2019 will enable us to fund our operating expenses including our debt repayment obligations as they become due and capital expenditure requirements into early 2021. Our future capital requirements will depend on many factors, including but not limited to:

- the scope, timing, results and costs of our current and planned clinical trials, including those for AMT-061 in hemophilia B and AMT-130 in Huntington's disease;
- the scope, timing, results and costs of preclinical development and laboratory testing of our additional product candidates;
- the need for any additional tests, studies, or trials beyond those originally anticipated to confirm the safety or efficacy of our product candidates and technologies;
- the cost, timing and outcome of regulatory reviews associated with our product candidates;
- the cost and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution of any of our product candidates for which we receive marketing approval in the future;
- the amount and timing of revenue, if any, we receive from commercial sales of any product candidates for which we, or our collaboration partner, receives marketing approval in the future;
- our ability to enter into collaboration arrangements in the future;
- the costs and timing of preparing, filing, expanding, acquiring, licensing, maintaining, enforcing and prosecuting patents and patent applications, as well as defending any intellectual property-related claims;
- the repayments of the principal amount of our venture debt loan with Hercules, which will contractually start in January 2021 and will run through June 2023;
- the extent to which we acquire or in-license other businesses, products, product candidates or technologies; and
- the costs associated with maintaining quality compliance and optimizing our manufacturing processes, including the operating costs associated with our Lexington, Massachusetts manufacturing facility.

Contractual obligations and commitments

The table below sets forth our contractual obligations and commercial commitments as of June 30, 2019, that are expected to have an impact on liquidity and cash flows in future periods.

	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years	Total
			(in thousands)		
Debt obligations (including $11.6 million interest payments)	$ 4,119	$ 9,403	$ 33,111	$ —	$ 46,633
Operating lease obligations	5,758	5,364	16,772	37,613	65,507
Total	**$ 9,877**	**$ 14,767**	**$ 49,883**	**$ 37,613**	**$ 112,140**

We also have obligations to make future payments to third parties that become due and payable on the achievement of certain development, regulatory and commercial milestones (such as the start of a clinical trial, filing of a Biologics License Application, approval by the FDA or product launch). We have not included these commitments on our balance sheet or in the table above because the achievement and timing of these milestones is not fixed and determinable.

We enter into contracts in the normal course of business with clinical research organizations (“CROs”) for preclinical research studies and clinical trials, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Off-Balance Sheet Arrangements

As of June 30, 2019, we did not have any off-balance sheet arrangements as defined in Item 303(a) (4) of Regulation S-K.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to a variety of financial risks in the normal course of our business, including market risk (including currency, price and interest rate risk), credit risk and liquidity risk. Our overall risk management program focuses on preservation of capital and the unpredictability of financial markets and has sought to minimize potential adverse effects on our financial performance and position.

Our market risks and exposures to such market risks during the six months ended June 30, 2019, have not materially changed from our market risks and our exposure to market risk discussed in Part II, Item 7A of our Annual Report on Form 10-K for the year ended December 31, 2018, which was filed with the SEC on February 28, 2019.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive and chief financial officer ("CEO"), evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) as of June 30, 2019. Based on such evaluation, our CEO has concluded that as of June 30, 2019, our disclosure controls and procedures were effective to ensure that information required to be disclosed by it in reports the Company files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and that such material information is accumulated and communicated to the Company's management, including its Principal Executive Officer and Principal Financial Officer, to allow timely decisions regarding required disclosure. Because of the inherent limitations in all control systems, any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management necessarily is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Furthermore, the Company's controls and procedures can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of such control, and misstatements due to error or fraud may occur and not be detected on a timely basis.

Changes in Internal Control over Financial Reporting

During the second quarter of 2019, there was no change in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) that materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Part II – OTHER INFORMATION

Item 1. Legal Proceedings

None.

Item 1A. Risk Factors

An investment in our ordinary shares involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Quarterly Report on Form 10-Q, including our financial statements and related notes thereto, and the risk factors discussed in Part I, Item 1A "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on February 28, 2019, before deciding to invest in our ordinary shares. We operate in a dynamic and rapidly changing industry that involves numerous risks and uncertainties. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the value of our securities to decline, and you may lose all or part of your investment.

Risks Related to the Development of Our Product Candidates

None of our product candidates have been approved for commercial sale and they might never receive regulatory approval or become commercially viable. We have never generated any revenue from product sales and may never be profitable.

All of our product candidates are in research or development. We have not generated any revenues from the sale of products and do not expect to do so for at least the next several years. Our lead product candidates, AMT-061 and AMT-130, and any of our other potential product candidates will require extensive preclinical and/or clinical testing and regulatory approval prior to commercial use. Our research and development efforts may not be successful. Even if our clinical development efforts result in positive data, our product candidates may not receive regulatory approval or be successfully introduced and marketed at prices that would permit us to operate profitably.

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates.

Clinical and non-clinical development is expensive, time-consuming and uncertain as to outcome. Our product candidates are in different stages of clinical or preclinical development, and there is a significant risk of failure or delay in each of these programs. We cannot guarantee that any preclinical tests or clinical trials will be completed as planned or completed on schedule, if at all. A failure of one or more preclinical tests or clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include, but are not limited to:

- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations ("CROs") and clinical trial sites;
- delays in receiving regulatory authorization to conduct the clinical trials or a regulatory authority decision that the clinical trial should not proceed;
- delays in obtaining required IRB approval at each clinical trial site;
- imposition of a clinical hold by regulatory agencies after an inspection of our clinical trial operations or trial sites;
- failure by CROs, other third parties or us to adhere to clinical trial requirements or otherwise properly manage the clinical trial process, including meeting applicable timelines, properly documenting case files, including the retention of proper case files, and properly monitoring and auditing clinical sites;
- failure of sites or clinical investigators to perform in accordance with Good Clinical Practice or applicable regulatory guidelines in other countries;
- difficulty or delays in patient recruiting into clinical trials;
- delays or deviations in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites;
- delays in having patients' complete participation in a study or return for post-treatment follow-up;

- clinical trial sites or patients dropping out of a study;
- occurrence of serious adverse events associated with a product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols, undertaking additional new tests or analyses or submitting new types or amounts of clinical data.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Such trials and regulatory review and approval take many years. It is impossible to predict when or if any of our clinical trials will demonstrate that product candidates are effective or safe in humans.

If the results of our clinical trials are inconclusive, or fail to meet the level of statistical significance required for approval or if there are safety concerns or adverse events associated with our product candidates, we may:

- be delayed in or altogether prevented from obtaining marketing approval for our product candidates;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes with the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Because of the nature of the gene therapies we are developing, regulators may also require us to demonstrate long-term gene expression, clinical efficacy and safety, which may require additional or longer clinical trials, and which may not be able to be demonstrated to the regulatory authorities' standards.

Our ability to recruit patients for our trials is often reliant on third parties, such as clinical trial sites. Clinical trial sites may not have the adequate infrastructure established to handle gene therapy products or may have difficulty finding eligible patients to enroll into a trial.

In addition, we or any collaborators we may have may not be able to locate and enroll enough eligible patients to participate in these trials as required by the FDA, the EMA or similar regulatory authorities outside the United States and the European Union. This may result in our failure to initiate or continue clinical trials for our product candidates, or may cause us to abandon one or more clinical trials altogether. Because our programs are focused on the treatment of patients with rare or orphan or ultra-orphan diseases, our ability to enroll eligible patients in these trials may be limited or slower than we anticipate considering the small patient populations involved and the specific age range required for treatment eligibility in some indications. In addition, our potential competitors, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions, may seek to develop competing therapies, which would further limit the small patient pool available for our studies. Also, patients may be reluctant to enroll in gene therapy trial where there are other therapeutic alternatives available or that may become available, which may be for various reasons including uncertainty about the safety or effectiveness of the therapeutic and the possibility that treatment with the therapeutic would preclude future gene therapy treatments.

Any inability to successfully initiate or complete preclinical and clinical development could result in additional costs to us or impair our ability to receive marketing approval, to generate revenues from product sales or obtain regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, including changes in the vector or manufacturing process used, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may materially harm our business, financial conditions and results of operations.

Our progress in early-stage clinical trials may not be indicative of long-term efficacy in late-stage clinical trials, and our progress in trials for one product candidate may not be indicative of progress in trials for other product candidates.

Study designs and results from previous studies are not necessarily predictive of our future clinical study designs or results, and initial results may not be confirmed upon full analysis of the complete study data. Our product candidates may fail to show the required level of safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies. In 2017, we announced our plans to advance AMT-061, which includes an AAV5 vector carrying the FIX-Padua transgene, into a pivotal study. While we believe AMT-061 and AMT-060, our product candidate that was previously studied in a Phase I/II study, have been demonstrated to be materially comparable in nonclinical studies and manufacturing quality assessments, it is possible that ongoing or future clinical studies of AMT-061 may show unexpected differences from AMT-060. Should these differences have an unfavorable impact on clinical outcomes, they may adversely impact our ability to achieve regulatory approval or market acceptance of AMT-061.

In our Phase I/II clinical study of AMT-060, we screened patients for preexisting anti-AAV5 antibodies to determine their eligibility for the trial. Three of the ten patients screened for the study tested positive for anti-AAV5 antibodies on reanalysis using a more sensitive antibody assay. Since we did not observe any ill-effects or correlation between the level of anti-AAV5 antibodies and clinical outcomes, patients who have anti-AAV5 antibodies will be permitted to enroll in our planned pivotal study of AMT-061. Since we only have been able to test a limited number of patients and have limited clinical and pre-clinical data, it is possible that ongoing or future clinical studies may not confirm these results, and if so, negatively impact the outcome of our study.

In advance of treating patients in the pivotal study of AMT-061, we conducted a short study to confirm the dose expected to be used in the pivotal trial. The dose-confirmation study enrolled three patients, who were administered a single dose of $2x10^{13}$ gc/kg. We have relied on the short-term data from this study, including FIX activity and safety outcomes during the weeks following administration of AMT-061, to confirm the dose to be used in the pivotal study. Following the results of this study, our Data Monitoring Committee confirmed the dose of $2x10^{13}$ gc/kg for administration in the pivotal study. Given the limited number of patients and short follow-up period, data from this study may differ materially from the future results of our planned pivotal study of AMT-061.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later-stage clinical trials even after achieving promising results in early-stage clinical trials. If a larger population of patients does not experience positive results during clinical trials, if these results are not reproducible or if our products show diminishing activity over time, our product candidates may not receive approval from the FDA or EMA. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may encounter regulatory delays or rejections because of many factors, including changes in regulatory policy during the period of product development. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our products in later-stage clinical trials with larger patient populations could have a material adverse effect on our business, financial condition and results of operations.

Fast track product, breakthrough therapy, priority review, or Regenerative Medicine Advanced Therapy ("RMAT") designation by the FDA, or access to the PRIME scheme by the EMA, for our product candidates may not lead to faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We have obtained and may in the future seek one or more of fast track designation, breakthrough therapy designation, RMAT designation, PRIME scheme access or priority review designation for our product candidates. A fast track product designation is designed to facilitate the clinical development and expedite the review of drugs intended to treat a serious or life-threatening condition and which demonstrate the potential to address an unmet medical need. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A RMAT designation is designed to accelerate approval for regenerative advanced therapies. Priority review designation is intended to speed the FDA marketing application review timeframe for drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. PRIME is a scheme provided by the EMA, similar to the FDA's Breakthrough Therapy Designation, to enhance support for the development of medicines that target an unmet medical need.

For drugs and biologics that have been designated as fast track products or breakthrough therapies, or granted access to the PRIME scheme, interaction and communication between the regulatory agency and the sponsor of the trial can help to identify the most efficient path for clinical development. Sponsors of drugs with fast track products or breakthrough therapies may also be able to submit marketing applications on a rolling basis, meaning that the FDA may review portions of a marketing application before the sponsor submits the complete application to the FDA, if the sponsor pays the user fee upon submission of the first portion of the marketing application. For products that receive a priority review designation, the FDA's marketing application review goal is shortened to six months, as opposed to ten to twelve months under standard review. RMAT designations will accelerate approval, but the exact mechanisms have not yet been announced by FDA.

Designation as a fast track product, breakthrough therapy, RMAT, PRIME, or priority review product is within the discretion of the regulatory agency. Accordingly, even if we believe one of our product candidates meets the relevant criteria, the agency may disagree and instead determine not to make such designation. In any event, the receipt of such a designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional regulatory procedures and does not assure ultimate marketing approval by the agency. In addition, regarding fast track products and breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification as either a fast track product, RMAT, or a breakthrough therapy or, for priority review products, decide that period for FDA review or approval will not be shortened.

We may not be successful in our efforts to use our gene therapy technology platform to build a pipeline of additional product candidates.

An element of our strategy is to use our gene therapy technology platform to expand our product pipeline and to progress these candidates through preclinical and clinical development ourselves or together with collaborators. Although we currently have a pipeline of programs at various stages of development, we may not be able to identify or develop product candidates that are safe and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. Research programs to identify new product candidates require substantial technical, financial and human resources. We or any collaborators may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. If we do not continue to successfully develop and commercialize product candidates based upon our technology, we may face difficulty in obtaining product revenues in future periods, which could result in significant harm to our business, results of operations and financial position and materially adversely affect our share price.

Our strategy of obtaining rights to key technologies through in-licenses may not be successful.

We seek to expand our product pipeline from time to time in part by in-licensing the rights to key technologies, including those related to gene delivery, genes and gene cassettes. The future growth of our business will depend in significant part on our ability to in-license or otherwise acquire the rights to additional product candidates or technologies, particularly through our collaborations with academic research institutions. However, we may be unable to in-license or acquire the rights to any such product candidates or technologies from third parties on acceptable terms or at all. The in-licensing and acquisition of these technologies is a competitive area, and many more established companies are also pursuing strategies to license or acquire product candidates or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be competitors may be unwilling to license rights to us. Furthermore, we may be unable to identify suitable product candidates or technologies within our areas of focus. If we are unable to successfully obtain rights to suitable product candidates or technologies, our business, financial condition and prospects could suffer.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain marketing approvals for our product candidates.

Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. The risk of cancer remains a concern for gene therapy, and we cannot assure that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material.

As of June 30, 2019, a total of three patients reported serious adverse events related to the treatment of AMT-060 in our Phase I/II hemophilia B trial, including one patient with a short, self-limiting fever in the first 24 hours after treatment and two patients with mild, asymptomatic elevations in liver transaminases. Additionally, one patient in our

ongoing Phase IIb study of AMT-061 underwent hip surgery due to a pre-existing condition and was treated perioperatively with short-acting factor replacement. This was reported by the investigator as a serious adverse event unrelated to AMT-061.

Adverse events in our clinical trials or those conducted by other parties (even if not ultimately attributable to our product candidates), and the resulting publicity, could result in increased governmental regulation, unfavorable public perception, failure of the medical community to accept and prescribe gene therapy treatments, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. If any of these events should occur, it may have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Our Manufacturing

Our manufacturing facility is subject to significant government regulations and approvals. If we fail to comply with these regulations or maintain these approvals our business will be materially harmed.

Our manufacturing facility in Lexington is subject to ongoing regulation and periodic inspection by the FDA, EMA and other regulatory bodies to ensure compliance with current Good Manufacturing Practices ("cGMP"). Any failure to follow and document our adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical study, may result in the termination of or a hold on a clinical study, or may delay or prevent filing or approval of marketing applications for our products.

Failure to comply with applicable regulations could also result in the FDA, EMA or other applicable authorities taking various actions, including levying fines and other civil penalties; imposing consent decrees or injunctions; requiring us to suspend or put on hold one or more of our clinical trials; suspending or withdrawing regulatory approvals; delaying or refusing to approve pending applications or supplements to approved applications; requiring us to suspend manufacturing activities or product sales, imports or exports; requiring us to communicate with physicians and other customers about concerns related to actual or potential safety, efficacy, and other issues involving our products; mandating product recalls or seizing products; imposing operating restrictions; and seeking criminal prosecutions. Any of the foregoing could materially harm our business, financial condition and results of operations.

Gene therapies are complex and difficult to manufacture. We could experience production or technology transfer problems that result in delays in our development or commercialization schedules or otherwise adversely affect our business.

The insect-cell based manufacturing process we use to produce our products and product candidates is highly complex and in the normal course is subject to variation or production difficulties. Issues with any of our manufacturing processes, even minor deviations from the normal process, could result in insufficient yield, product deficiencies or manufacturing failures that result in adverse patient reactions, lot failures, insufficient inventory, product recalls and product liability claims. Additionally, we may not be able to scale up some or all of our manufacturing processes that may results in delays in regulatory approvals or otherwise adversely affect our ability to manufacture sufficient amounts of our products.

Many factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including raw materials shortages, raw material failures, growth media failures, equipment malfunctions, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, or acts of god beyond our control. We also may encounter problems in hiring and retaining the experienced specialized personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing processes or facilities could make us a less attractive collaborator for academic research institutions and other parties, which could limit our access to additional attractive development programs, result in delays in our clinical development or marketing schedules and materially harm our business.

Our use of viruses, chemicals and other hazardous materials requires us to comply with regulatory requirements and exposes us to significant potential liabilities.

Our development and manufacturing processes involve the use of viruses, chemicals, other (potentially) hazardous materials and produce waste products. Accordingly, we are subject to national, federal, state and local laws and regulations in the United States and the Netherlands governing the use, manufacture, distribution, storage, handling, treatment and disposal of these materials. In addition to ensuring the safe handling of these materials, applicable requirements require increased safeguards and security measures for many of these agents, including controlling access and screening of entities and personnel who have access to them, and establishing a comprehensive

national database of registered entities. In the event of an accident or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for damages that result, and any such liability could exceed our assets and resources, and could result in material harm to our business, financial condition and results of operations.

Risks Related to Regulatory Approval of Our Products

We cannot predict when or if we will obtain marketing approval to commercialize a product candidate.

The development and commercialization of our product candidates, including their design, testing, manufacture, safety, efficacy, purity, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States, the EMA and other regulatory agencies of the member states of the European Union, and similar regulatory authorities in other jurisdictions. Failure to obtain marketing approval for a product candidate in a specific jurisdiction will prevent us from commercializing the product candidate in that jurisdiction.

The process of obtaining marketing approval for our product candidates in the United States, the European Union and other countries is expensive and may take many years, if approval is obtained at all. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application, may decide that our data are insufficient for approval, may require additional preclinical, clinical or other studies and may not complete their review in a timely manner. Further, any marketing approval we ultimately obtain may be for only limited indications, or be subject to stringent labeling or other restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining marketing approval for any of our product candidates in the United States or other countries, the commercial prospects of our other product candidates may be harmed and our ability to generate revenues will be materially impaired.

The risks associated with the marketing approval process are heightened by the status of our products as gene therapies.

We believe that all our current product candidates will be viewed as gene therapy products by the applicable regulatory authorities. While there are a number of gene therapy product candidates under development, in the United States, FDA has only approved a limited number of gene therapy products, to date. Accordingly, regulators, like FDA, may have limited experience with the review and approval of marketing applications for gene therapy products.

Both the FDA and EMA have demonstrated caution in their regulation of gene therapy treatments, and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of our product candidates that are difficult to predict. The FDA and the EMA have issued various guidance documents pertaining to gene therapy products, with which we likely must comply to gain regulatory approval of any of our product candidates in the United States or European Union, respectively. The close regulatory scrutiny of gene therapy products may result in delays and increased costs, and may ultimately lead to the failure to obtain approval for any gene therapy product.

Regulatory requirements affecting gene therapy have changed frequently and continue to evolve, and agencies at both the U.S. federal and state level, as well as congressional committees and foreign governments, have sometimes expressed interest in further regulating biotechnology. In the United States, there have been a number of changes relating to gene therapy development over the last year. By example, FDA issued a number of new guidance documents on human gene therapy development, one of which was specific to human gene therapy for hemophilia and another of which was specific to rare diseases. Moreover, the U.S. National Institutes of Health, which also has authority over research involving gene therapy products, issued a proposed rule in October 2018, seeking to streamline the oversight of such protocols and reduce duplicative reporting requirements that are already captured within existing regulatory frameworks. Moreover, the European Commission conducted a public consultation in early 2013 on the application of EU legislation that governs advanced therapy medicinal products, including gene therapy products, which could result in changes in the data we need to submit to the EMA for our product candidates to gain regulatory approval or change the requirements for tracking, handling and distribution of the products which may be associated with increased costs. In addition, divergent scientific opinions among the various bodies involved in the review process may result in delays, require additional resources and ultimately result in rejection. The FDA, EMA, and other regulatory authorities will likely continue to revise and further update its approach to gene therapies in the coming

years. These regulatory agencies, committees and advisory groups and the new regulations and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenues to maintain our business.

Our failure to obtain or maintain orphan product exclusivity for any of our product candidates for which we seek this status could limit our commercial opportunity, and if our competitors are able to obtain orphan product exclusivity before we do, we may not be able to obtain approval for our competing products for a significant period.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the relevant indication, the product is entitled to a period of market exclusivity, which precludes the FDA or EMA from approving another marketing application for the same drug for the same indication for that period. The FDA and EMA, however, may subsequently approve a similar drug for the same indication during the first product's market exclusivity if the FDA or EMA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if the incidence and prevalence of patients who are eligible to receive the drug in these markets materially increase. The inability to obtain or failure to maintain adequate product exclusivity for our product candidates could have a material adverse effect on our business prospects, results of operations and financial conditions.

As appropriate, we intend to seek all available periods of regulatory exclusivity for our product candidates. However, there is no guarantee that we will be granted these periods of regulatory exclusivity or that we will be able to maintain these periods of exclusivity.

The FDA grants product sponsors certain periods of regulatory exclusivity, during which the agency may not approve, and in certain instances, may not accept, certain marketing applications for competing drugs. For example, biologic product sponsors may be eligible for twelve years of exclusivity from the date of approval, seven years of exclusivity for drugs that are designated to be orphan drugs, and/or a six-month period of exclusivity added to any existing exclusivity period or patent life for the submission of FDA requested pediatric data. While we intend to apply for all periods of market exclusivity that we may be eligible for, there is no guarantee that we will receive all such periods of market exclusivity. Additionally, under certain circumstances, the FDA may revoke the period of market exclusivity. Thus, there is no guarantee that we will be able to maintain a period of market exclusivity, even if granted. In the case of orphan designation, other benefits, such as tax credits and exemption from user fees may be available. If we are not able to obtain or maintain orphan drug designation or any period of market exclusivity to which we may be entitled, we will be materially harmed, as we will potentially be subject to greater market competition and may lose the benefits associated with programs.

Risks Related to Commercialization

If we are unable to successfully commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

Our ability to generate product revenues will depend on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on many factors, including:

- successful completion of preclinical studies and clinical trials;
- receipt and maintenance of marketing approvals from applicable regulatory authorities;
- our ability to timely manufacture sufficient quantities according to required quality specifications;
- obtaining and maintaining patent and trade secret protection and non-patent, orphan drug exclusivity for our product candidates;
- obtaining and maintaining regulatory approvals using our manufacturing facility in Lexington, Massachusetts;
- launch and commercialization of our products, if approved, whether alone or in collaboration with others;
- identifying and engaging effective distributors or resellers on acceptable terms in jurisdictions where we plan to utilize third parties for the marketing and sales of our product candidates;

- acceptance of our products, if approved, by patients, the medical community and third-party payers;
- effectively competing with existing therapies and gene therapies based on safety and efficacy profile;
- achieve value-based pricing levels based on durability of expression, safety and efficacy;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- complying with any applicable post-approval requirements and maintaining a continued acceptable overall safety profile; and
- obtaining adequate reimbursement for the total patient population and each subgroup to sustain a viable commercial business model in US and EU markets.

Failure to achieve or implement any of these elements could result in significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business.

The affected populations for our gene therapies may be smaller than we or third parties currently project, which may affect the size of our addressable markets.

Our projections of the number of people who have the diseases we are seeking to treat, as well as the subset of people with these diseases who have the potential to benefit from treatment with our therapies, are estimates based on our knowledge and understanding of these diseases. The total addressable market opportunities for these therapies will ultimately depend upon many factors, including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient consent, patient access and product pricing and reimbursement.

Prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward-looking and speculative. The use of such data involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of the diseases we seek to address. The number of patients with the diseases we are targeting may turn out to be lower than expected or may not be otherwise amenable to treatment with our products, reimbursement may not be sufficient to sustain a viable business for all sub populations being studied, or new patients may become increasingly difficult to identify or access, any of which would adversely affect our results of operations and our business.

The addressable markets for AAV-based gene therapies may be impacted by the prevalence of neutralizing antibodies to the capsids, which are an integral component of our gene therapy constructs. Patients that have pre-existing antibodies to a particular capsid may not be eligible for administration of a gene therapy that includes this particular capsid. For example, our AMT-061 gene therapy candidate for hemophilia B patients incorporates an AAV5 capsid. In our Phase I/II clinical study of AMT-060, we screened patients for preexisting anti-AAV5 antibodies to determine their eligibility for the trial. Three of the ten patients screened for the study tested positive for anti-AAV5 antibodies on reanalysis. However, we did not observe any ill-effects or correlation between the level of anti-AAV5 antibodies and clinical outcomes in these three patients, suggesting that patients who have anti-AAV5 antibodies may still be eligible for AAV5-based gene therapies. Since we only have been able to test a limited number of patients and have limited clinical and pre-clinical data, it is possible that future clinical studies may not confirm these results. This may limit the addressable market for AMT-061 and any future revenues derived from the sale of the product, if approved.

Any approved gene therapy we seek to offer may fail to achieve the degree of market acceptance by physicians, patients, third party payers and others in the medical community necessary for commercial success.

Doctors may be reluctant to accept a gene therapy as a treatment option or, where available, choose to continue to rely on existing treatments. The degree of market acceptance of any of our product candidates that receive marketing approval in the future will depend on many factors, including:

- the efficacy and potential advantages of our therapies compared with alternative treatments;
- our ability to convince payers of the long-term cost-effectiveness of our therapies and, consequently, the availability of third-party coverage and adequate reimbursement;
- the cost of treatment with gene therapies, including ours, in comparison to traditional chemical and small-molecule treatments
- the limitations on use and label requirements imposed by regulators;
- the convenience and ease of administration of our gene therapies compared with alternative treatments;
- the willingness of the target patient population to try new therapies, especially a gene therapy, and of physicians to administer these therapies;
- the strength of marketing and distribution support;

- the prevalence and severity of any side effects;
- limited access to site of service that can perform the product preparation and administer the infusion; and
- any restrictions by regulators on the use of our products.

A failure to gain market acceptance for any of the above reasons, or any reasons at all, by a gene therapy for which we receive regulatory approval would likely hinder our ability to recapture our substantial investments in that and other gene therapies and could have a material adverse effect on our business, financial condition and results of operation.

We face substantial competition, and others may discover, develop or commercialize competing products before or more successfully than we do.

The development and commercialization of new biotechnology and biopharmaceutical products, including gene therapies, is highly competitive. We may face intense competition with respect to our product candidates, as well as with respect to any product candidates that we may seek to develop or commercialize in the future, from large and specialty pharmaceutical companies and biotechnology companies worldwide, who currently market and sell products or are pursuing the development of products for the treatment of many of the disease indications for which we are developing our product candidates. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. In recent years, there has been a significant increase in commercial and scientific interest and financial investment in gene therapy as a therapeutic approach, which has intensified the competition in this area.

We are aware of numerous companies focused on developing gene therapies in various indications, including Applied Genetic Technologies Corp, Abeona Therapeutics, Adverum Biotechnologies, Allergan, Ally Therapeutics, Asklepios BioPharmaceutical, Audentes Therapeutics, AVROBIO, Axovant Sciences, Bayer, Biogen, BioMarin, bluebird bio, CRISPR Therapeutics, Editas Medicine, Expression Therapeutics, Freeline Therapeutics, Generation Bio, Genethon, GlaxoSmithKline, Homology Medicines, Intellia Therapeutics, Johnson & Johnson, Krystal Biotech, LogicBio Therapeutics, Lysogene, MeiraGTx, Milo Biotechnology, Mustang Bio, Novartis, Orchard Therapeutics, Oxford Biomedica, Pfizer, REGENXBIO, Renova Therapeutics, Rocket Pharmaceuticals, Sangamo BioSciences, Sanofi, Selecta Biosciences, Sarepta, Shire, Solid Biosciences, Spark Therapeutics, Takeda, Ultragenyx, Vivet Therapeutics, and Voyager, as well as several companies addressing other methods for modifying genes and regulating gene expression. We may also face competition with respect to the treatment of some of the diseases that we are seeking to target with our gene therapies from protein, nucleic acid, antisense, RNAi and other pharmaceuticals under development or commercialized at pharmaceutical and biotechnology companies such as Alnylam, Amgen, Bayer, Biogen, BioMarin, CSL Behring, Dicerna, Ionis, Novartis, Novo Nordisk, Pfizer, Translate Bio, Roche, Sanofi, Shire, Sobi, Wave Biosciences and numerous other pharmaceutical and biotechnology firms.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than the products that we develop. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market. Because we expect that gene therapy patients may generally require only a single administration, we believe that the first gene therapy product to enter the market for a particular indication will likely enjoy a significant commercial advantage, and may also obtain market exclusivity under applicable orphan drug regimes.

Many of the companies with which we are competing or may compete in the future have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Risks Related to Our Dependence on Third Parties

We rely on third parties for important aspects of our development programs. If these parties do not perform successfully or if we are unable to enter into or maintain key collaboration or other contractual arrangements, our business could be adversely affected.

We have in the past entered into, and expect in the future to enter into, collaborations with other companies and academic research institutions with respect to important elements of our development programs.

Any collaboration, may pose several risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- we may have limited or no control over the design or conduct of clinical trials sponsored by collaborators;
- we may be hampered from entering into collaboration arrangements if we are unable to obtain consent from our licensors to enter into sublicensing arrangements of technology we have in-licensed;
- if any collaborator does not conduct the clinical trials they sponsor in accordance with regulatory requirements or stated protocols, we will not be able to rely on the data produced in such trials in our further development efforts;
- collaborators may not perform their obligations as expected;
- collaborators may also have relationships with other entities, some of which may be our competitors;
- collaborators may not pursue development and commercialization of any product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus 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 develop, independently or with third parties, products that compete directly or indirectly with our products or product candidates, if, for instance, 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;
- our collaboration arrangements may impose restrictions on our ability to undertake other development efforts that may appear to be attractive to us;
- 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 that achieves regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including over proprietary rights, contract interpretation or the preferred course of development, could cause delays or termination of the research, development or commercialization of product candidates, lead to additional responsibilities for us, delay or impede reimbursement of certain expenses or result in litigation or arbitration, any of which would 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 rights 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 in some cases be terminated for the convenience of the collaborator and, if terminated, we could be required to expend additional funds to pursue further development or commercialization of the applicable product or product candidates.

If any collaboration does not result in the successful development and commercialization of products or if a collaborator were to terminate an agreement with us, we may not receive future research funding or milestone or royalty payments under that collaboration, and we may lose access to important technologies and capabilities of the collaboration. All the risks relating to product development, regulatory approval and commercialization described herein also apply to the activities of any development collaborators.

Risks Related to Our Intellectual Property

We rely on licenses of intellectual property from third parties, and such licenses may not provide adequate rights or may not be available in the future on commercially reasonable terms or at all, and our licensors may be unable to obtain and maintain patent protection for the technology or products that we license from them.

We currently are heavily reliant upon licenses of proprietary technology from third parties that is important or necessary to the development of our technology and products, including technology related to our manufacturing process, our vector platform, our gene cassettes and the therapeutic genes of interest we are using. These and other licenses may not provide adequate rights to use such technology in all relevant fields of use. Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. In addition, if third parties who license patents to us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

The agreements under which we license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business and financial condition.

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose rights that are important to our business.

Our licensing arrangements with third parties impose diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our counterparties may have the right to terminate these agreements either in part or in whole, in which case we might not be able to develop, manufacture or market any product that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or amended agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our ability to successfully commercialize our products may be impaired.

We rely, in part, upon a combination of forms of intellectual property, including in-licensed and owned patents to protect our intellectual property. Our success depends in a large part on our ability to obtain and maintain this protection in the United States, the European Union and other countries, in part by filing patent applications related to our novel technologies and product candidates. Our patents may not provide us with any meaningful commercial protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. For example, patents we own currently are and may become subject to future patent opposition or similar proceedings, which may result in loss of scope of some claims or the entire patent. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

Successful challenges to our patents may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products.

The patent prosecution process is expensive, time-consuming and uncertain, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Additionally, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, EU patent law with respect to the patentability of methods of treatment of the human body is more limited than U.S. law. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after their priority date, or in some cases at all. Therefore, we cannot know with certainty whether we were the first to make the inventions or that we were the first to file for patent protection of the inventions claimed in our owned or licensed patents or pending patent applications. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the European Union, the United States or other countries may diminish the value of our patents or narrow the scope of our patent protection. Our inability to obtain and maintain appropriate patent protection for any one of our products could have a material adverse effect on our business, financial conditions and results of operations.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property or third parties may assert their intellectual property rights against us, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our owned or licensed patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, maintained in more narrowly amended form or interpreted narrowly.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, increase our operating losses, reduce available resources and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, which could have an adverse effect on the price of our ordinary shares.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. For example, outside of the United States two of the patents we own are subject to patent opposition. If these or future oppositions are successful or if we are found to otherwise infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. We may not be able to obtain the required license on commercially reasonable terms or at all. Even if we could obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product or otherwise to cease using the relevant intellectual property. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease or materially modify some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

For example, we are aware of patents owned by third parties that relate to some aspects of our programs that are still in development. In some cases, because we have not determined the final methods of manufacture, the method of administration or the therapeutic compositions for these programs, we cannot determine whether rights under such third party patents will be needed. In addition, in some cases, we believe that the claims of these patents are invalid or not infringed, or will expire before commercialization. However, if such patents are needed and found to be valid and infringed, we could be required to obtain licenses, which might not be available on commercially reasonable terms, or to cease or delay commercializing certain product candidates, or to change our programs to avoid infringement.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.

In addition to seeking patent protection, we also rely on other proprietary rights, including protection of trade secrets, know-how and confidential and proprietary information. To maintain the confidentiality of our trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, collaborators and other third parties who have access to our trade secrets. Our agreements with employees also provide that any inventions conceived by the individual in the course of rendering services to us will be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. In addition, in the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our confidential information including a breach of our confidentiality agreements. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time consuming, and the outcome is unpredictable. In addition, some courts in and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. The disclosure of our trade secrets or the independent development of our trade secrets by a competitor or other third party would impair our competitive position and may materially harm our business, financial condition, results of operations, stock price and prospects.

Our reliance on third parties may require us to share our trade secrets, which could increase the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we collaborate from time to time with various organizations and academic research institutions on the advancement of our gene therapy platform, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, materials transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, if we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements.

Some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us.

Risks Related to Pricing and Reimbursement

We face uncertainty related to insurance coverage of, and pricing and reimbursement for product candidates for which we may receive marketing approval.

We anticipate that the cost of treatment using our product candidates will be significant. We expect that most patients and their families will not be capable of paying for our products themselves. There will be no commercially viable market for our product candidates without reimbursement from third party payers, such as government health administration authorities, private health insurers and other organizations. Even if there is a commercially viable market, if the level of third-party reimbursement is below our expectations, most patients may not be able to afford treatment with our products and our revenues and gross margins will be adversely affected, and our business will be harmed.

Government authorities and other third-party payers, such as private health insurers and health maintenance organizations, decide for which medications they will pay and, subsequently, establish reimbursement levels. Reimbursement systems vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. Government authorities and third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and procedures. Increasingly, third party payers require drug companies to provide them with predetermined discounts from list prices, are exerting influence on decisions regarding the use of particular treatments and are limiting covered indications. Additionally, in the United States and some foreign jurisdictions, pending or potential legislative and regulatory changes regarding the healthcare system and insurance coverage, could result in more rigorous coverage criteria and downward pressure on drug prices, and may affect our ability to profitably sell any products for which we obtain marketing approval.

The pricing review period and pricing negotiations for new medicines take considerable time and have uncertain results. Pricing review and negotiation usually begins only after the receipt of regulatory marketing approval, and some authorities require approval of the sale price of a product before it can be marketed. In some markets, particularly the countries of the European Union, prescription pharmaceutical pricing remains subject to continuing direct governmental control and to drug reimbursement programs even after initial approval is granted and price reductions may be imposed. Prices of medical products may also be subject to varying price control mechanisms or limitations as part of national health systems if products are considered not cost-effective or where a drug company's profits are deemed excessive. In addition, pricing and reimbursement decisions in certain countries can lead to mandatory price reductions or additional reimbursement restrictions in other countries. Because of these restrictions, any product candidates for which we may obtain marketing approval may be subject to price regulations that delay or prohibit our or our partners' commercial launch of the product in a particular jurisdiction. In addition, we or any collaborator may elect to reduce the price of our products to increase the likelihood of obtaining reimbursement approvals. If countries impose prices, which are not sufficient to allow us or any collaborator to generate a profit, we or any collaborator may refuse to launch the product in such countries or withdraw the product from the market. If pricing is set at unsatisfactory levels, or if the price decreases, our business could be harmed, possibly materially. If we fail to obtain and sustain an adequate level of coverage and reimbursement for our products by third party payers, our ability to market and sell our products would be adversely affected and our business would be harmed.

Due to the generally limited addressable market for our target orphan indications and the potential for our therapies to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates.

The relatively small market size for orphan indications and the potential for long-term therapeutic benefit from a single administration present challenges to pricing review and negotiation of our product candidates for which we may obtain marketing authorization. Most of our product candidates target rare diseases with relatively small patient populations. If we are unable to obtain adequate levels of reimbursement relative to these small markets, our ability to support our development and commercial infrastructure and to successfully market and sell our product candidates for which we may obtain marketing approval will be adversely affected.

We also anticipate that many or all of our gene therapy product candidates may provide long-term, and potentially curative benefit, with a single administration. This is a different paradigm than that of other pharmaceutical therapies, which often require an extended course of treatment or frequent administration. As a result, governments and other payers may be reluctant to provide the significant level of reimbursement that we seek at the time of administration of our gene therapies or may seek to tie reimbursement to clinical evidence of continuing therapeutic benefit over time. Although it is possible that our product candidates will need to be administered only once, there may be situations in which re-administration is required, which may further complicate the pricing and reimbursement for these treatments. In addition, considering the anticipated cost of these therapies, governments and other payers may be particularly restrictive in making coverage decisions. These factors could limit our commercial success and materially harm our business.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses to date, expect to incur losses over the next several years and may never achieve or maintain profitability.

We had a net loss of $59.2 million in the six months ended June 30, 2019, $83.3 million in the full year 2018 and $79.3 million in the full year 2017. As of June 30, 2019, we had an accumulated deficit of $594.7 million. To date, we have financed our operations primarily through the sale of equity securities and convertible debt, venture loans, through upfront payments from our collaboration partners and, to a lesser extent, subsidies and grants from governmental agencies and fees for services. We have devoted substantially all our financial resources and efforts to research and development, including preclinical studies and clinical trials. We expect to continue to incur significant expenses and losses over the next several years, and our net losses may fluctuate significantly from quarter to quarter and year to year.

We anticipate that our expenses will increase substantially as we:

- execute our pivotal study for AMT-061;
- initiate clinical studies related to our Huntington’s disease gene therapy program;
- advance multiple research programs related to gene therapy candidates targeting liver-directed and CNS diseases;
- continue to enhance and optimize our technology platform, including our manufacturing capabilities, next-generation viral vectors and promoters, and other enabling technologies;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- acquire or in-license rights to new therapeutic targets or product candidates; and
- maintain, expand and protect our intellectual property portfolio, including in-licensing additional intellectual property rights from third parties.

We may never succeed in these activities and, even if we do, may never generate revenues that are sufficient to achieve or sustain profitability. Our failure to become and remain profitable would depress the value of our company and could impair our ability to expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations.

We will likely need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations which could have a material adverse effect on our business, financial conditions, results of operations and cash flows.

We expect to incur significant expenses in connection with our on-going activities and that we will likely need to obtain substantial additional funding in connection with our continuing operations. In addition, we have based our estimate of our financing requirements on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Adequate capital may not be available to us when needed or may not be available on acceptable terms. Our ability to obtain debt financing may be limited by covenants we have made under our Loan and Security Agreement with Hercules Technology Growth Capital, Inc. ("Hercules") and our pledge to Hercules of substantially all our assets as collateral. If we raise additional capital through the sale of equity or convertible debt securities, our shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our ordinary shares.

If we raise additional funds through collaborations, strategic alliances, or marketing, distribution or licensing arrangements with third parties, we may have to issue additional equity, relinquish valuable rights to our technologies, future revenue streams, products or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts, which would have a negative impact on our financial condition, results of operations and cash flows.

Our existing and any future indebtedness could adversely affect our ability to operate our business.

As of June 30, 2019, we had $35.0 million of outstanding principal of borrowings under our Loan and Security Agreement with Hercules, which we are required to repay in monthly principal installments from January 2021 through June 2023. We could in the future incur additional debt obligations beyond our borrowings from Hercules. Our existing loan obligations, together with other similar obligations that we may incur in the future, could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, research and development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a disadvantage compared to our competitors that have less debt or better debt servicing options.

We may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under our existing loan obligations. Failure to make payments or comply with other covenants under our existing debt could result in an event of default and acceleration of amounts due. Under our agreement with Hercules, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets or condition is an event of default. If an event of default occurs and the lender accelerates the amounts due, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all our assets.

Risks Related to Other Legal Compliance Matters

Our relationships with customers and third-party payers will be subject to applicable anti-kickback, anti-bribery, fraud and abuse and other laws and regulations, which, if we are found in violation thereof, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payers will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third party payers and customers may expose us to broadly applicable anti-bribery laws, including the Foreign Corrupt Practices Act, as well as fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we would be able to market, sell and distribute any products for which we obtain marketing approval.

Efforts to ensure that our business arrangements with third parties will comply with applicable laws and regulations will involve substantial costs. If our operations, or the activities of our collaborators, distributors or other third-party agents are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs and the curtailment or restructuring of our operations. The cost associated with any of these actions could be substantial and could cause irreparable harm to our reputation or otherwise have a material adverse effect on our business, financial condition and results of operations.

We are subject to laws governing data protection in the different jurisdictions in which we operate. The implementation of such data protection regimes is complex, and should we fail to fully comply, we may be subject to penalties that they may have an adverse effect on our business, financial condition and results of operations.

Many national and state laws govern the privacy and security of health information and other personal and private information. They often differ from each other in significant ways. For instance, the EU has adopted a comprehensive data protection law called the General Data Protection Regulation (“GDPR”) that took effect in May 2018. The GDPR, together with the national legislation of the EU member states governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EU, security breach notifications, security and confidentiality of the personal data, and imposition of substantial potential fines for breaches of the data protection obligations. The GDPR imposes penalties for non-compliance of up to the greater of €20 million or 4% of worldwide revenue. Data protection authorities from the different EU member states may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the EU. Guidance on implementation and compliance practices are often updated or otherwise revised. The significant costs of compliance with, risk of regulatory enforcement actions under, and other burdens imposed by the GDPR as well as under other regulatory schemes throughout the world related to privacy and security of health information and other personal and private data could have an adverse impact on our business, financial condition and results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm 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 cannot eliminate the risk of contamination or injury from these materials. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

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

In addition, we may incur substantial costs 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. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions that could have a material adverse effect on our business, financial condition and results of operations.

Product liability lawsuits could cause us to incur substantial liabilities and to limit commercialization of our therapies.

We face an inherent risk of product liability related to the testing of our product candidates in human clinical trials and in connection with product sales. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we develop or sell;
- injury to our reputation and significant negative media attention;
- negative publicity or public opinion surrounding gene therapy;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to further develop or commercialize any products that we develop.

Dependent upon the country where the clinical trial is conducted, we currently hold a maximum of €6,000,000 and minimum of €2,000,000 in clinical trial insurance coverage in the aggregate, with a per incident limit of €450,000 to €1,000,000 with respect to the clinical studies we conduct. Such coverage may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials. In addition, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. In the event insurance coverage is insufficient to cover liabilities that we may incur, it could have a material adverse effect on our business, financial condition and results of operations.

Healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Our industry is highly regulated and changes in law may adversely impact our business, operations or financial results. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, is a sweeping measure intended to, among other things, expand healthcare coverage within the United States, primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program. Several provisions of the law may affect us and increase certain of our costs.

In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, following passage of the Bipartisan Budget Act of 2018, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations.

We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the reimbursement our customers may receive for our products. Further, there have been, and there may continue to be, judicial and Congressional challenges to certain aspects of the PPACA. For example, the U.S. Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additional legislative and regulatory changes to the PPACA, its implementing regulations and guidance and its policies, remain possible in the 116th U.S. Congress and under the Trump Administration. However, it remains unclear how any new legislation or regulation might affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

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

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. The size and complexity of our information technology systems, and those of our collaborators, contractors and consultants, and the large amounts of confidential information stored on those systems, make such systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced a system failure, accident, cyber-attack or security breach that has resulted in a material interruption in our operations to date, we have experienced and addressed recent system failures, cyber-attacks and security breaches. In the future, such events could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. Additionally, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, cause us not to comply with federal and/or state breach notification laws and foreign law equivalents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business and the further development and commercialization of our product and product candidates could be delayed.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and technical staff and to attract, retain and motivate qualified personnel.

We are highly dependent on hiring, training, retaining and motivating key personnel to lead our research and development, clinical operations and manufacturing efforts. Although we have entered into employment agreements with our key personnel, each of them may terminate their employment on short notice. We do not maintain key person insurance for any of our senior management or employees.

The loss of the services of our key employees could impede the achievement of our research and development objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing senior management and key employees may be difficult and may take an extended period because of the limited number of individuals in our industry with the breadth and depth of skills and experience required to successfully develop gene therapy products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms.

If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Risks Related to Our Ordinary Shares

The price of our ordinary shares has been and may in the future be volatile and fluctuate substantially.

Our share price has been and may in the future be volatile. From the start of trading of our ordinary shares on the NASDAQ Global Select Market on February 4, 2014 through July 25, 2019, the sale price of our ordinary shares ranged from a high of $82.49 to a low of $4.72. The closing price on July 25, 2019, was $66.97 per ordinary share. The stock market in general and the market for smaller biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our ordinary shares may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- public perception of gene therapy;
- regulatory delays and greater government regulation of potential products due to adverse events;
- regulatory or legal developments in the European Union, the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- mergers, acquisitions, licensing and collaboration activity among our peer companies in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions.

An active trading market for our ordinary shares may not be sustained.

Although our ordinary shares are listed on The NASDAQ Global Select Market, an active trading market for our shares may not be sustained. If an active market for our ordinary shares does not continue, it may be difficult for our shareholders to sell their shares without depressing the market price for the shares or sell their shares at all. Any inactive trading market for our ordinary shares may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Our directors, executive officers and major shareholders, if they choose to act together, will continue to have a significant degree of control with respect to matters submitted to shareholders for approval.

Our directors, executive officers and major shareholders holding more than 5% of our outstanding ordinary shares, in the aggregate, beneficially own approximately 39.8% of our issued shares (including such shares to be issued in relation to exercisable options to purchase ordinary shares) as at June 30, 2019. As a result, if these shareholders were to choose to act together, they may be able, as a practical matter, to control many matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could control the election of the board directors and the approval of any merger, consolidation or sale of all or substantially all our assets. These shareholders may have interests that differ from those of other of our shareholders and conflicts of interest may arise.

Provisions of our articles of association or Dutch corporate law might deter acquisition bids for us that might be considered favorable and prevent or frustrate any attempt to replace our board.

Certain provisions of our articles of association may make it more difficult for a third party to acquire control of us or effect a change in our board. These provisions include:

- staggered terms of our directors;
- a provision that our directors may only be removed at a general meeting of shareholders by a two-thirds majority of votes cast representing more than half of the issued share capital of the Company; and
- a requirement that certain matters, including an amendment of our articles of association, may only be brought to our shareholders for a vote upon a proposal by our board.

We do not expect to pay dividends in the foreseeable future.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that earnings, if any, will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. Accordingly, shareholders cannot rely on dividend income from our ordinary shares and any returns on an investment in our ordinary shares will likely depend entirely upon any future appreciation in the price of our ordinary shares.

We lost our status as an "emerging growth company" as of December 31, 2018 and are therefore subject to greater disclosure requirements.

We were an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 ("JOBS Act") through 2018. As of December 31, 2018, we are considered a large accelerated filer and as a consequence lost our status as an emerging growth company. We therefore no longer are permitted to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions included:

- reduced disclosure obligations surrounding executive compensation in our periodic reports and proxy statements;
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved; and
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the independent auditor's report providing additional information about the audit and the financial statements.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. We are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

Meeting these disclosure requirements as well as the auditor attestation of our internal control over financial reporting will require that our management and other personnel devote a substantial amount of time to these compliance incentives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities costlier and more time-consuming. In order to meet these additional reporting requirements, we may be required to divert resources away from research and development efforts, which could have a material adverse effect on our business, financial condition and results of operations.

If we fail to maintain an effective system of internal controls, we may be unable to accurately report our results of operations or prevent fraud or fail to meet our reporting obligations, and investor confidence and the market price of our ordinary shares may be materially and adversely affected.

If we fail to maintain the adequacy of our internal control over financial reporting, we may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting. If we fail to maintain effective internal control over financial reporting, we could experience material misstatements in our financial statements and fail to meet our reporting obligations, which would likely cause investors to lose confidence in our reported financial information. This could in turn limit our access to capital markets, harm our results of operations, and lead to a decline in the trading price of our ordinary shares. Additionally, ineffective internal control over financial reporting could expose us to increased risk of fraud or misuse of corporate assets and subject us to potential delisting from The NASDAQ Global Select Market, regulatory investigations and civil or criminal sanctions. Our reporting and compliance obligations may place a significant strain on our management, operational and financial resources and systems for the foreseeable future.

Unfavorable global economic conditions, including those caused by political instability in the United States or by the U.K.'s pending departure from the European Union ("Brexit"), could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Political instability in the United States and surrounding Brexit has the potential to disrupt global economic conditions and supply changes. While we do not believe that our operations will be directly adversely affected materially by Brexit, we may not be able to anticipate the effects Brexit will have on our suppliers and any collaborators. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a

variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payers or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Risks for U.S. Holders

We have in the past qualified and in the future may qualify as a passive foreign investment company, which may result in adverse U.S. federal income tax consequence to U.S. holders.

Based on our average value of our gross assets, our cash and cash equivalents as well as the price of our shares we qualified as a passive foreign investment company ("PFIC") for U.S. federal income tax for 2016 but not in 2017 or 2018. A corporation organized outside the United States generally will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which at least 75% of its gross income is passive income or on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held to produce passive income. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions. Our status in any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will continue to qualify as a PFIC in future taxable years. The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate, and may fluctuate considerably given that market prices of biotechnology companies have been especially volatile. If we were considered a PFIC for the current taxable year or any future taxable year, a U.S. holder would be required to file annual information returns for such year, whether the U.S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year. In certain circumstances a U.S. holder may be able to make certain tax elections that would lessen the adverse impact of PFIC status; however, in order to make such elections the U.S. holder will usually have to have been provided information about the company by us, and we do not intend to provide such information.

The U.S. federal income tax rules relating to PFICs are complex. U.S. holders are urged to consult their tax advisors with respect to the purchase, ownership and disposition of our shares, the possible implications to them of us being treated as a PFIC (including the availability of applicable election, whether making any such election would be advisable in their particular circumstances) as well as the federal, state, local and foreign tax considerations applicable to such holders in connection with the purchase, ownership and disposition of our shares.

Any U.S. or other foreign judgments may be difficult to enforce against us in the Netherlands.

Although we now report as a U.S. domestic filer for SEC reporting purposes, we are incorporated under the laws of the Netherlands. Some of the members of our board and senior management reside outside the United States. As a result, it may not be possible for shareholders to effect service of process within the United States upon such persons or to enforce judgments against them or us in U.S. courts, including judgments predicated upon the civil liability provisions of the federal securities laws of the United States. In addition, it is not clear whether a Dutch court would impose civil liability on us or any of our Board members in an original action based solely upon the federal securities laws of the United States brought in a court of competent jurisdiction in the Netherlands.

The United States and the Netherlands currently do not have a treaty providing for the reciprocal recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in the Netherlands. To obtain a judgment which is enforceable in the Netherlands, the party in whose favor a final and conclusive judgment of the U.S. court has been rendered will be required to file its claim with a court of competent jurisdiction in the Netherlands. Such party may submit to the Dutch court the final judgment rendered by the U.S. court. If and to the extent that the Dutch court finds that the jurisdiction of the U.S. court has been based on grounds which are internationally acceptable and that proper legal procedures have been observed, the Dutch court will, in principle, give binding effect to the judgment of the U.S. court, unless such judgment contravenes principles of public policy of the Netherlands. Dutch courts may deny the recognition and enforcement of punitive damages or other awards. Moreover, a Dutch court may reduce the amount of damages granted by a U.S. court and recognize damages only to the extent that they are necessary to compensate actual losses or damages. Enforcement and recognition of judgments of U.S. courts in the Netherlands are solely governed by the provisions of the Dutch Civil Procedure Code.

Therefore U.S. shareholders may not be able to enforce against us or our board members or senior management who are residents of the Netherlands or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

The rights and responsibilities of our shareholders and directors are governed by Dutch law and differ in some important respects from the rights and responsibilities of shareholders under U.S. law.

Although we now report as a U.S. domestic filer for SEC purposes, our corporate affairs are governed by our articles of association and by the laws governing companies incorporated in the Netherlands. The rights of our shareholders and the responsibilities of members of our board under Dutch law are different than under the laws of some U.S. jurisdictions. In the performance of their duties, our board members are required by Dutch law to consider the interests of uniQure, its shareholders, its employees and other stakeholders and not only those of our shareholders (as would be required under the law of most U.S. jurisdictions). As a result of these considerations our directors may take action that would be different than those that would be taken by a company organized under the law of some U.S. jurisdictions.

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

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

See the Exhibit Index immediately preceding the signature page to this Quarterly Report on Form 10-Q for a list of exhibits filed or furnished with this report, which Exhibit Index is incorporated herein by reference.

EXHIBIT INDEX

3.1 Amended Articles of Association (incorporated by reference to Exhibit 3.1 of the Company's annual report on Form 10-K for the year ended December 31, 2018 (file no. 0001-36294) filed with the Securities and Exchange Commission).

10.42* Second Amendment Lease relating to 113 Hartwell Avenue, Lexington Massachusetts, dated as of June 17, 2019, by and between the Company and King 113 Hartwell LLC

10.43* Form of Share Option Agreement, effective June 18, 2019, under the 2014 Share Incentive Plan

31.1* Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer

31.2* Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer

32.1± Section 1350 Certification

101* The following financial information from our Quarterly Report on Form 10-Q for the period ended June 30, 2019, filed with the Securities and Exchange Commission on July 29, 2019 is formatted in Inline Extensible Business Reporting Language ("iXBRL"): (i) Consolidated Balance Sheets; (ii) Consolidated Statements of Operations and Comprehensive Loss; (iii) Consolidated Statements of Shareholders' Equity; (iv) Consolidated Statements of Cash Flows; and (v) Notes to Consolidated Financial Statements (tagged as blocks of text)

* Filed herewith.

± Furnished herewith

SIGNATURE

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

UNIQURE, N.V.

By: /s/ Matthew Kapusta
Matthew Kapusta
Chief Executive Officer
(Principal Executive and Financial Officer)

By: /s/ Christian Klemt
Christian Klemt
Chief Accounting Officer

Dated July 29, 2019

113 Hartwell Avenue
Lexington, Massachusetts
(the "Building")

SECOND AMENDMENT
June 17, 2019

LANDLORD:	King 113 Hartwell LLC, a Massachusetts limited liability company
TENANT:	uniQure, Inc., a Delaware corporation
EXISTING PREMISES:	Approximately 83,998 rentable square feet of space in the Building, as more particularly shown as hatched, highlighted or outlined on the plan attached to the Lease as Exhibit 1A and as shown on Exhibit A, First Amendment
DATE OF LEASE:	July 24, 2013
EXTENDED EXPIRATION DATE:	As defined in Section 1 of the First Amendment
PRIOR LEASE AMENDMENTS:	First Amendment dated as of November 9, 2018 ("First Amendment")

WHEREAS, due to a scrivener's error, the parties desire to revise Section 3.A and Section 3.B (Base Rent) of the First Amendment, on the terms and conditions hereinafter set forth;

NOW THEREFORE, the above described lease, as previously amended (collectively, the "Lease"), is hereby further amended as follows:

1. BASE RENT

Section 3.A and Section 3.B of the First Amendment are deleted in their entirety and the following are substituted in their place:

A. Existing Premises. The Base Rent payable with respect to the Existing Premises commencing as of the Expansion Premises Rent Commencement Date and continuing thereafter throughout the Term of the Lease shall be as follows:

Time Period	Annual Base Rent	Monthly Payment
Expansion Premises Rent Commencement Date – 4/30/20:	$1,920,348.00	$160,029.00
5/1/20-4/30/21:	$1,973,691.00	$164,474.25
5/1/21-4/30/22:	$2,027,034.00	$168,919.50
5/1/22-4/30/23:	$2,080,377.00	$173,364.75
5/1/23-4/30/24:	$2,133,720.00	$177,810.00
5/1/24-4/30/25:	$2,782,762.06	$231,896.83
5/1/25-4/30/26:	$2,866,244.92	$238,853.74
5/1/26-4/30/27:	$2,952,232.27	$246,019.35
5/1/27-4/30/28:	$3,040,799.24	$253,399.93
5/1/28-4/30/29:	$3,132,023.22	$261,001.93
5/1/29-Extended Expiration Date	$3,225,983.88*	$268,831.99

*annualized

B. Expansion Premises: Base Rent with respect to the Expansion Premises shall be as follows:

Rent Year	Annual Base Rent	Monthly Payment
1	$1,379,475.00	$114,956.25
2	$1,420,859.25	$118,404.93
3	$1,463,485.03	$121,957.08
4	$1,507,389.58	$125,615.79
5	$1,552,611.27	$129,384.27
6	$1,599,189.60	$133,265.80
7	$1,647,165.29	$137,263.76
8	$1,696,580.25	$141,381.68
9	$1,747,477.66	$145,623.13
10	$1,799,901.99	$149,991.82

2. CONFLICT

In the event that any of the provisions of the Lease are inconsistent with this Second Amendment or the state of facts contemplated hereby, the provisions of this Second Amendment shall control.

3. RATIFICATION

As hereby amended, the Lease is ratified, confirmed and approved in all respects.

[remainder of page blank; signature page to follow]

EXECUTED under seal as of the date first above written.

LANDLORD:
KING 113 HARTWELL LLC,
a Massachusetts limited liability company

By: King Dickey LLC, its manager

By: King Street Properties Investments LLC,
its manager

By: _____
Name: _____
Title: _____

TENANT:
UNIQURE, INC.,
a Delaware corporation

By: _____
Name: _____
Title: _____

CONFIRMATION OF GUARANTY

The undersigned, as Guarantor of the above-referenced Lease pursuant to a Guaranty dated as of July 24, 2013, hereby consents to the foregoing Second Amendment and confirms and agrees that said Guaranty shall remain in full force and effect in accordance with the terms thereof with respect to the Lease as amended by the foregoing Second Amendment.

EXECUTED UNDER SEAL as of the date first above written.

GUARANTOR:
UNIQURE N.V., a public limited liability company
organized under the laws of the Netherlands

By: _____
Name: Matt Kapusta
Title: Chief Executive Officer

By: _____
Name: Christian Klemt
Title: Chief Accounting Officer

uniQure N.V.

Share Option Agreement
Granted Under 2014 Share Incentive Plan, Amended and Restated effective as of June 13, 2018

Name

[Date]

1. Grant of Option.

This agreement evidences the grant by uniQure N.V., a public limited company incorporated under the laws of the Netherlands (the "**Company**"), on [ ] (the "**Grant Date**") to: [name] (the "Participant"), of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2014 Share Incentive Plan, as amended and restated (the "**Plan**"), a total of:

[amount] ordinary shares, €0.05 par value per share, of the Company ("**Ordinary Shares**") at:

USD$ [ ] per share. Unless earlier terminated, this option shall expire at 17:00, Central European time, on date, [ ] (the "**Final Exercise Date**").

2. Vesting Schedule.

(a) This option will become exercisable ("**vest**") as to 25% of the original number of Ordinary Shares on the first anniversary of the Grant Date and as to an additional 6.25% of the original number of Ordinary Shares at the end of each successive three-month period following the first anniversary of the Grant Date until the fourth anniversary of the Grant Date, in each case, subject to continued employment as an Eligible Participant (as defined below in Section 3(b)).

(b) The right of exercise shall be cumulative (but shall not exceed 100% of the Ordinary Shares subject to the Option) so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Ordinary Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan. If the foregoing schedule would produce fractional Ordinary Shares, the number of Ordinary Shares for which the option vests shall be rounded down to the nearest whole Ordinary Share.

(c) Notwithstanding the provisions of paragraph (a) above, the option shall automatically accelerate and become fully vested if a Reorganization Event (as defined in the Plan) occurs before the option is fully vested and while the Participant is an Eligible Participant, the option shall automatically accelerate and become fully vested immediately prior to the date of the Reorganization Event.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be in writing, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or by such other method as shall be approved by the Company, in each case together with payment in full in

the manner provided in the Plan. The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, officer or a director of, or consultant or advisor (as such terms are defined for purposes of Form S-8 under the Securities Act of 1933, as amended) to, the Company or any parent or subsidiary of the Company (an "Eligible Participant").

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate six months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Employer, the right to exercise this option shall terminate immediately upon written notice to the Participant from the Employer describing such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Employer has not terminated such relationship for Cause as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability (including as provided in Section 2(c)), and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment is terminated by the Employer for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If, prior to the Final Exercise Date, the Participant is given notice by the Employer of the termination of his or her employment by the Employer for Cause, and the effective date of such employment or other termination is subsequent to the date of delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's employment shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment (or other relationship) (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate upon the effective date of such termination of employment). If the Participant is party to an employment, consulting or severance agreement with the Employer that contains a definition of "cause" for termination of employment, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Employer (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Employer), as determined by the Employer, which determination shall be conclusive. The Participant's employment (or other

relationship) shall be considered to have been terminated for Cause if the Employer determines, within 30 days after the Participant's resignation, that termination for Cause was warranted.

4. Tax Matters.

(a) Withholding. No Ordinary Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Employer, or makes provision satisfactory to the Employer for payment of, any national, federal, state and local or other income, national insurance, social and employment taxes required by law to be withheld in respect of this option.

5. Transfer Restrictions.

This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

6. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

7. Nature of the Grant.

In accepting the option, the Participant acknowledges that:

(a) the Plan is established voluntarily by the Company, it provides for certain criteria in order to be eligible to receive an award, it is restricted in time, it is discretionary in nature and it may be modified, amended, suspended or terminated by the Company at any time, unless otherwise provided in the Plan and this agreement;

(b) the grant of the option is voluntary and occasional and does not create any contractual or other right to receive future grants of options, or benefits in lieu of options, even if options have been granted repeatedly in the past;

(c) all decisions with respect to future option grants, if any, will be at the sole discretion of the Management Board;

(d) the Participant is voluntarily participating in the Plan;

(e) the options are an extraordinary item that does not constitute compensation of any kind for services of any kind rendered to the Company or the Employer and which is outside the scope of the Participant's employment or consultancy agreement of his or her corporate mandate, if any;

(f) the options are not part of normal or expected compensation or salary for any purposes, including, but not limited to, calculation of any severance, resignation, termination, redundancy, end of service payments, bonuses, long-service awards, pension, retirement or welfare benefits or similar payments and in no event should be considered as compensation for, or relating in any way, to past services for the Company or the Employer;

(g) in the event that the Participant is not an employee of uniQure N.V., the options and the Participant's participation in the Plan will not be interpreted to form an employment or service contract or relationship with the Company;

(h) the future value of the underlying Ordinary Shares is unknown and cannot be predicted with certainty; if the Participant's options never vest, the Participant will not be able to exercise the options; and

(i) in consideration of the options, no claim or entitlement to compensation or damages shall arise from termination of the options or from any decrease in value of the options or Ordinary Shares acquired upon exercise of the options resulting from termination of the Participant's employment, consultancy or corporate mandate by or with the Company or the Employer (for any reason whatsoever and whether or not in breach of contract or local laws) and the Participant irrevocably releases the Company and the Employer from any such claim that may arise.

8. Data Privacy.

The Participant hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of his or her personal data as described in this agreement by and among, as applicable, his or her Employer or contracting party and the Company for the exclusive purpose of implementing, administering and managing his or her participation in the Plan.

The Participant understands that the Company holds certain personal information about him or her, including, but not limited to, his or her name, home address and telephone number, work location and phone number, date of birth, hire date, details of all options or any other entitlement to Ordinary Shares awarded, cancelled, exercised, vested, unvested or outstanding in the Participant's favor, for the purpose of implementing, administering and managing the Plan ("Personal Data"). The Participant understands that Personal Data may be transferred to any third parties assisting in the implementation, administration and management of the Plan, that these recipients may be located in the Participant's country or elsewhere, and that the recipient's country may have different data privacy laws and protections than the Participant's country. The Participant understands that he or she may request a list with the names and addresses of any potential recipients of the Personal Data by contacting his or her local human resources representative. The Participant authorizes the recipients to receive, possess, use, retain and transfer the Personal Data, in electronic or other form, for the purposes of implementing, administering and managing his or her participation in the Plan, including any requisite transfer of such Personal Data as may be required to a broker or other third party with whom the Participant may elect to deposit any Ordinary Shares acquired upon exercise of the options. The Participant understands that Personal Data will be held only as long as is necessary to implement, administer and manage his or her participation in the Plan. The Participant understands that he or she may, at any time, view Personal Data, request additional information about the storage and processing of Personal Data, require any necessary amendments to Personal Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing his or her local human resources representative. The Participant understands, however, that refusing or withdrawing his or her consent may affect his or her ability to participate in the Plan. For more information on the consequences of Participant's refusal to consent or withdrawal of consent, the Participant understands that he or she may contact his or her local human resources representative.

The Company has caused this option to be executed by its duly authorized officer.

UNIQURE N.V.

By:

Name:
Title:

PARTICIPANT'S ACCEPTANCE

The undersigned hereby accepts the foregoing option and agrees to the terms and conditions thereof. The undersigned hereby acknowledges receipt of a copy of the Company's 2014 Share Incentive Plan, Amended and Restated effective as of June 13, 2018.

PARTICIPANT

_____

Name:

Exhibit 31.1

Certification of Chief Executive Officer

I, Matthew Kapusta, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of uniQure N.V.;

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 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;

(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;

5. The registrant's other certifying officer 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.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Chief Executive Officer
July 29, 2019

Exhibit 31.2

Certification of Chief Financial Officer

I, Matthew Kapusta, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of uniQure N.V.;

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 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;

(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;

5. The registrant's other certifying officer 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.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Principal Financial Officer
July 29, 2019

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 this Quarterly Report of uniQure N.V. (the "Company") on Form 10-Q for the period ended June 30, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Matthew Kapusta, Chief Executive Officer and Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 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 results of operations of the Company.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Chief Executive Officer and
Chief Financial Officer
July 29, 2019

A signed original of this written statement required by Section 906 has been provided to uniQure N.V. and will be retained by uniQure N.V. and furnished to the SEC or its staff upon request.