Concord Medical Services Holdings Ltd
Form 20-F
April 28, 2014
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 20-F

(Mark One)

¨ **Registration statement pursuant to Section 12(b) or 12(g) of the Securities Exchange Act of 1934**
or

x **Annual report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
For the fiscal year ended December 31, 2013

or

¨ **Transition report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
For the transition period from to

or

¨ **Shell company report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
Date of event requiring this shell company report

Commission file number 001-34563

Concord Medical Services Holdings Limited

(Exact Name of Registrant as Specified in Its Charter)

Cayman Islands

(Jurisdiction of Incorporation or Organization)

18/F, Tower A, Global Trade Center

36 North Third Ring Road, Dongcheng District

Beijing 100013

People s Republic of China

(Address of Principal Executive Offices)

Mr. Adam Jigang Sun

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18/F, Tower A, Global Trade Center

36 North Third Ring Road, Dongcheng District

Beijing 100013

People s Republic of China

(Name, Telephone, E-mail and/or Facsimile Number and Address of Company Contact Person)

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

Title of Each Class	Name of Each Exchange on Which Registered
Ordinary shares, par value US$0.0001 per share*	**New York Stock Exchange***

*

Not for trading, but only in connection with the listing of the American depositary shares, or ADSs, on the New York Stock Exchange. Each ADS represents the right to receive three ordinary shares. The ADSs are registered under the Securities Act of 1933, as amended, pursuant to a registration statement on Form F-6. Accordingly, the ADSs are exempt from registration under Section 12(b) of the Securities Exchange Act of 1934, as amended, pursuant to Rule 12a-8 thereunder.

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Securities registered or to be registered pursuant to Section 12(g) of the Act:

None

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

Indicate the number of outstanding shares of each of the Issuer s classes of capital or common stock as of the close of the period covered by the annual report.

134,836,300 Ordinary Shares Issued and Outstanding

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

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ¨ No x

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 x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes x No ¨

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

Large accelerated filer ¨ Accelerated filer x Non-accelerated filer ¨

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

International Financial Reporting Standards as issued

U.S. GAAP x by the International Accounting Standards Board ¨ Other ¨

If Other has been checked in response to the previous question, indicate by check mark which consolidated financial statement item the registrant has elected to follow.

Item 17 ¨ Item 18 ¨

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ¨ No x

(APPLICABLE ONLY TO ISSUERS INVOLVED IN BANKRUPTCY PROCEEDINGS DURING THE PAST FIVE YEARS)

Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court. Yes ¨ No ¨

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CONVENTIONS THAT APPLY TO THIS ANNUAL REPORT ON FORM 20-F

Unless otherwise indicated, references in this annual report on Form 20-F to:

ADRs are to the American depositary receipts, which, if issued, evidence our ADSs;

ADSs are to our American depositary shares, each of which represents three ordinary shares;

China and the PRC are to the People s Republic of China, excluding, for the purposes of this annual report only, Taiwan and the special administrative regions of Hong Kong and Macau;

Concord Medical, we, us, our company and our are to Concord Medical Services Holdings Limited, its predecessor entities and its consolidated subsidiaries;

ordinary shares are to our ordinary shares, par value US$0.0001 per share;

PRC subsidiaries are to our subsidiaries incorporated in the People s Republic of China, including CMS Hospital Management Co., Ltd., Beijing Yundu Internet Technology Co., Ltd., Shenzhen Aohua Medical Technology & Services Ltd., Shenzhen Lingdun Medical Investment & Management Co., Ltd., Tianjin Kangmeng Radiology Equipment Management Co., Ltd., Medstar (Shanghai) Leasing Co., Ltd., Guangzhou Concord Medical Cancer Hospital Co., Ltd., Xi An Wanjiehuaxiang Medical Technology Development Co., Ltd., Beijing Jinweiyikang Technology Co., Ltd., Guangzhou Jinkangshenyou Investment Co., Ltd. and Chang an Hospital Co., Ltd.

RMB and Renminbi are to the legal currency of China;

US$ and U.S. dollars are to the legal currency of the United States; and

£ is to the legal currency of the United Kingdom of Great Britain and Northern Ireland.

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PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not Applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not Applicable.

ITEM 3. KEY INFORMATION

A. Selected Financial Data

The following selected consolidated statements of comprehensive income and other consolidated financial data for the years ended December 31, 2011, December 31, 2012 and December 31, 2013 (other than the income (loss) per ADS data) and the selected consolidated balance sheets data as of December 31, 2012 and 2013 have been derived from our audited consolidated financial statements, which is included elsewhere in this annual report on Form 20-F. The selected consolidated balance sheets data as of December 31, 2009, 2010 and 2011 have been derived from our audited consolidated financial statements, which are not included in this annual report on Form 20-F. You should read the selected consolidated financial data in conjunction with those financial statements and the related notes and Item 5. Operating and Financial Review and Prospects included elsewhere in this annual report on Form 20-F. Our consolidated financial statements are prepared and presented in accordance with generally accepted accounting principles in the United States, or U.S. GAAP. Our historical results are not necessarily indicative of our results expected for any future periods.

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	Concord Medical Year Ended December, 31					
	2009 RMB	2010 RMB	2011 RMB	2012 RMB	2013 RMB	US$
	(in thousands, except share, per share and per ADS data)					
Selected Consolidated Statements of Comprehensive Income Data						
Revenues, net of business tax, value-added tax and related surcharges:						
Network	292,436	389,524	450,125	465,040	563,124	93,021
Hospital-medicine income				89,813	180,130	29,755
Hospital-medical service income				107,496	237,381	39,213
Total net revenues	**292,436**	**389,524**	**450,125**	**662,349**	**980,635**	**161,989**
Cost of revenues:						
Network	(87,561)	(122,700)	(159,416)	(169,905)	(224,062)	(37,012)
Hospital-medicine cost				(76,590)	(151,920)	(25,095)
Hospital-medical service cost				(90,709)	(210,967)	(34,849)
Total cost of revenues	**(87,561)**	**(122,700)**	**(159,416)**	**(337,204)**	**(586,949)**	**(96,956)**
Gross profit	**204,875**	**266,824**	**290,709**	**325,145**	**393,686**	**65,033**
Operating expenses:						
Selling expenses [(1)]	(7,675)	(17,150)	(37,453)	(53,911)	(107,842)	(17,814)
General and administrative expenses [(2)]	(29,821)	(66,789)	(80,628)	(71,754)	(105,114)	(17,364)
Asset impairment		(3,219)	(333,934)	(3,360)		
Other operating income				10,433		
Total operating expenses	(37,496)	(87,518)	(452,015)	(118,592)	(212,956)	(35,178)
Operating income (loss)	**167,379**	**179,666**	**(161,306)**	**206,553**	**180,730**	**29,855**
Interest expense	(6,891)	(7,448)	(6,454)	(16,255)	(47,027)	(7,768)
Foreign exchange (losses) gains, net	(213)	(5,436)	(10,975)	(101)	767	127
Gain (loss) from disposal of equipment		543		(1,072)	(1,235)	(204)
Interest income	948	7,865	13,357	5,895	17,712	2,926
Share of net profit of equity investee				1,790	15,521	2,564
Other (expense) income, net		(399)	346	(144)	608	100
Income (loss) before income taxes	**161,223**	**174,791**	**(165,032)**	**196,666**	**167,076**	**27,600**
Income tax expenses	(36,396)	(43,873)	(46,320)	(62,186)	(75,880)	(12,534)
Net income (loss)	**124,827**	**130,918**	**(211,352)**	**134,480**	**91,196**	**15,066**
Net income attributable to non-controlling interests		**1,518**	**3,651**	**3,649**	**5,303**	**876**
Net income (loss) attributable to Concord Medical Services Holdings Limited s shareholders	**46,418**	**129,400**	**(215,003)**	**130,831**	**85,893**	**14,190**

Earning (loss) per share	basic / diluted[3]	0.62	0.89	(1.51)	0.95	0.64	0.11
Earning (loss) per ADS	basic / diluted	1.86	2.66	(4.53)	2.84	1.92	0.32

(1) Our selling expenses included share-based compensation of RMB0.3 million in 2009, RMB2.5 million in 2010, RMB2.4 million in 2011; RMB2.3 million in 2012; and RMB2.3 million (US$0.4 million) in 2013.

(2) Our general and administrative expenses included share-based compensation expenses related to certain share options granted in 2009, 2010, 2011, 2012 and 2013 of RMB0.7 million, RMB7.0 million, RMB6.9 million, RMB6.8 million and RMB6.5 million (US$1.1 million) respectively.

(3) On November 17, 2009, we effected a share split whereby all of our issued and outstanding 704,281 ordinary shares of a par value of US$0.01 per share were split into 70,428,100 ordinary shares of US$0.0001 par value per share and the number of our authorized ordinary shares was increased from 4,500,000 to 450,000,000. The share split has been retroactively reflected in this annual report so that share numbers, per share price and par value data are presented as if the share split had occurred from our inception.

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	Concord Medical					
	As of December 31,					
	2009 RMB	2010 RMB	2011 RMB	2012 RMB	2013 RMB	2013 US$
	(in thousands)					
Selected Consolidated Balance Sheets Data						
Cash	1,037,239	535,783	219,078	75,382	283,033	46,754
Total current assets	1,252,512	904,416	733,657	853,133	1,300,010	214,748
Property, plant and equipment, net	573,042	907,336	1,068,703	1,522,920	1,492,573	246,555
Goodwill	300,163	300,163		292,885	292,885	48,381
Intangible assets, net	155,345	146,113	129,018	146,512	116,843	19,301
Total assets	2,443,865	2,663,044	2,393,446	3,665,220	4,093,557	676,209
Long-term bank borrowings, current portion	57,487	60,906	77,479	191,473	273,310	45,148
Total equity	2,153,748	2,301,835	2,038,096	2,339,910	2,433,717	402,023
Total liabilities and equity	2,443,865	2,663,044	2,393,446	3,665,220	4,093,557	676,209

	Concord Medical					
	Year Ended December 31,					
	2009 RMB	2010 RMB	2011 RMB	2012 RMB	2013 RMB	2013 US$
	(in thousands)					
Selected Consolidated Statements of Cash Flow Data						
Net cash generated from operating activities	135,883	190,972	137,102	259,515	259,033	42,788
Net cash used in investing activities [(1)]	(272,269)	(529,468)	(494,867)	(659,290)	(133,540)	(22,059)
Net cash generated from (used in) financing activities	819,846	(154,933)	41,785	255,932	77,722	12,839
Exchange rate effect on cash	(212)	(8,027)	(725)	147	4,436	734
Net increase (decrease) in cash	683,248	(501,456)	(316,705)	(143,696)	207,651	34,302

(1) Net cash used in investing activities in 2009, 2010, 2011, 2012 and 2013 includes acquisitions, net of cash acquired, of RMB32.2 million, RMB45.0 million, RMB20.3 million, RMB223.4 million and nil respectively.

	Concord Medical					
	Year Ended December 31,					
	2009 RMB	2010 RMB	2011 RMB	2012 RMB	2013 RMB	2013 US$
	(in thousands)					
Total net revenues generated by our primary medical equipment under lease and management services arrangements:						

Linear accelerators	90,278	108,974	114,250	115,009	135,268	22,345
Head gamma knife systems	67,406	80,909	77,035	76,239	68,553	11,324
Body gamma knife systems	25,241	38,599	42,512	31,365	42,016	6,941
PET-CT scanners	24,196	41,036	59,054	71,895	107,536	11,170
MRI scanners	33,880	51,738	65,031	79,220	83,619	13,813
Others [1]	19,161	27,992	22,576	38,602	61,564	16,763
Total net revenues lease and management services	260,162	349,248	380,457	412,330	498,556	82,356

(1) Other primary medical equipment used includes CT scanners and ECT scanners for diagnostic imaging, electroencephalography for the diagnosis of epilepsy, thermotherapy to increase the efficacy of and for pain relief after radiotherapy and chemotherapy, high intensity focused ultrasound therapy for the treatment of cancer, stereotactic radiofrequency ablation for the treatment of Parkinson s Disease and refraction and tonometry for the diagnosis of ophthalmic conditions.

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Exchange Rate Information

Our business is primarily conducted in China and all of our revenues are denominated in Renminbi. Periodic reports made to shareholders will be expressed in Renminbi with translations of Renminbi amounts into U.S. dollars at the then current exchange rate solely for the convenience of the reader. Conversions of Renminbi into U.S. dollars in this annual report are based on, for all dates through December 31, 2009, at the noon buying rate in the City of New York for cable transfers in Renminbi per U.S. dollar as certified for customs purposes by the Federal Reserve Bank of New York, or the noon buying rate, and for January 1, 2010 and all later dates and periods, the noon buying rate as set forth in the H.10 statistical release of the Federal Reserve Board. Unless otherwise noted, all translations from Renminbi to U.S. dollars and from U.S. dollars to Renminbi in this annual report were made at a rate of RMB6.0537 to US$1.00, the noon buying rate in effect as of December 31, 2013. We make no representation that any Renminbi or U.S. dollar amounts could have been, or could be, converted into U.S. dollars or Renminbi, as the case may be, at any particular rate, the rates stated below, or at all. The PRC government imposes control over its foreign currency reserves in part through direct regulation of the conversion of Renminbi into foreign exchange and through restrictions on foreign trade. On April 18, 2014, the noon buying rate was RMB6.2240 to US$1.00.

The following table sets forth information concerning exchange rates between the Renminbi and the U.S. dollar for the periods indicated.

	Exchange Rate (Renminbi per US Dollar)[1]			
	Period End	Average[2]	High	Low
Period	(RMB per US$1.00)			
2009	6.8259	6.8295	6.8470	6.8176
2010	6.6000	6.7603	6.8330	6.6000
2011	6.2939	6.4475	6.6364	6.2939
2012	6.2301	6.2990	6.3879	6.2221
2013	6.0537	6.1412	6.2438	6.0537
October	6.0943	6.1032	6.1209	6.0815
November	6.0922	6.0929	6.0993	6.0903
December	6.0537	6.0738	6.0927	6.0537
2014				
January	6.0590	6.0509	6.0600	6.0402
February	6.1448	6.0816	6.1488	6.0591
March	6.2164	6.1729	6.2273	6.1183
April (through April 18)	6.2240	6.2121	6.2240	6.2064

(1) The source of the exchange rate is: (i) with respect to any period ending on or prior to December 31, 2009, the Federal Reserve Bank of New York, and (ii) with respect to any period ending on or after January 1, 2010, the H.10 statistical release of the Federal Reserve Board.

(2) Annual averages are calculated from month-end rates. Monthly averages are calculated using the average of the daily rates during the relevant period.

B. Capitalization and Indebtedness

Not Applicable.

C. Reasons for the Offer and Use of Proceeds

Not Applicable.

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D. Risk Factors

Risks Related to Our Company

We may encounter difficulties in successfully opening new centers or renewing agreements for existing centers due to the limited number of suitable hospital partners and their potential ability to finance the purchase of medical equipment directly.

Our growth was driven by our ability to expand our network of radiotherapy and diagnostic imaging centers by primarily entering into new agreements with top-tier hospitals in China, which are 3A hospitals, the highest ranked hospitals by quality and size in China as determined in accordance with the standards of the Ministry of Health. The agreements that hospitals enter into with us and our competitors are typically long-term in nature with terms of up to 20 years. As a result, in any locality or at any given time, there may only be a limited number of top-tier hospitals that have not yet entered into long-term agreements with us or our competitors and with which we are able to enter into new agreements. In addition, quotas imposed by government authorities as to the number and type of certain medical equipment that can be purchased, such as head gamma knife systems or PET-CT scanners, will further limit the number of top-tier hospitals that we or our competitors can enter into agreements within a given period. See Risks Related to Our Industry Healthcare administrative authorities in China currently set procurement quotas for certain types of medical equipment. Due to the limited supply of suitable top-tier hospitals and increasing competition, we may not be able to enter into agreements with new hospital partners or renew agreements with existing hospital partners on terms as favorable as those that we have been able to obtain in the past, or at all. Some of our competitors may have greater financial resources than us, which may provide them with an advantage in negotiating new agreements with hospitals, including our existing hospital partners. In addition, if adequate funding becomes available for hospitals to purchase medical equipment directly, hospitals may choose to purchase and manage radiotherapy and diagnostic imaging equipment on their own instead of entering into or renewing agreements with us or our competitors. If we are unable to compete effectively in entering into agreements with new hospital partners or to renew existing agreements on favorable terms, or at all, or if hospitals choose to purchase and manage their own medical equipment, our growth prospects could be materially and adversely affected. Finally, the development of new centers generally involves a ramp-up period during which time the operating efficiency of such centers may be lower than our established centers, which may negatively affect our profitability.

We have historically derived a significant portion of our revenues from centers located at a limited number of our hospital partners and regions in which we operate and our accounts receivable are also concentrated with a few hospital partners.

We have historically derived a large portion of our total net revenues from a limited number of our partner hospitals. In 2011, 2012 and 2013, net revenues derived from our top five hospital partners amounted to approximately 33.0%, 22.9% and 24.2% of our total net revenues, respectively. Our largest hospital partner accounted for 14.3%, 6.9% and 5.6% of our total net revenues during those periods, respectively. In addition, centers located in Beijing, Shaanxi province and Liaoning province accounted for 19.0%, 15.9% and 8.5% of our total net revenues in 2011, respectively, centers located in Beijing, Henan province and Shandong province accounted for 18.3%, 10.0% and 8.1% of our total net revenues in 2012, respectively, and centers located in Beijing, Heinan province and Sichuan Province accounted for 17.1%, 9.4% and 8.5% of our total net revenues in 2013, respectively. We may continue to experience such revenue concentration in the future. Due to the concentration of our revenues and dependence on a limited number of hospital partners, any one or more of the following events, among others, may cause material fluctuations or declines in our revenues and could have a material adverse effect on our financial condition, results of operations and prospects:

reduction in the number of patient cases at the centers located at these partner hospitals;

loss of key experienced medical professionals;

decrease in the profitability of such centers;

failure to maintain or renew our agreements with these hospital partners;

any failure of these hospital partners to pay us our contracted percentage of any such center s revenue net of specified operating expenses;

any regulatory changes in the geographic areas where our hospital partners are located; or

any other disputes with these hospital partners.

In addition, ten of our hospital partners in terms of revenue contribution, accounted for 43.2% of our total network accounts receivable as of December 31, 2013. Any significant delay in the payment of such accounts receivable could have a material impact on our financial condition and results of operations.

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We conduct our business in a heavily regulated industry.

The operation of our network of centers is subject to various laws and regulations issued by a number of government agencies at the national and local levels. Such rules and regulations relate mainly to the procurement of large medical equipment, the pricing of medical services, the operation of radiotherapy and diagnostic imaging equipment, the licensing and operation of medical institutions, the licensing of medical staff and the prohibition on non-profit civilian medical institutions from entering into cooperation agreements with third parties to set up for-profit centers that are not independent legal entities. Our growth prospects may be constrained by such rules and regulations, particularly those relating to the procurement of large medical equipment. If we or our hospital partners fail to comply with such applicable laws and regulations, we could be required to make significant changes to our business and operations or suffer fines or penalties, including the potential loss of our business licenses, the suspension from use of our medical equipment, and the suspension or cessation of operations at centers in our network. In addition, many of the agreements we have entered into with our hospital partners provide for termination in the event of major government policy changes that cause the agreements to become inexecutable. Our hospital partners may invoke such termination right to our disadvantage.

We depend on our hospital partners to recruit and retain qualified doctors and other medical professionals to ensure the high quality of treatment services provided in our network of centers.

Our success is dependent in part upon our hospital partners ability to recruit and retain doctors and other medical professionals and on our and our hospital partners ability to train and manage these medical professionals. Although we may help our hospital partners to identify and recruit suitable, qualified doctors and other medical professionals, almost all of these medical professionals are employed by our partner hospitals rather than by us. As a result, we may have little control over whether such medical professionals will continue to work in the centers in our network. In addition, there is a limited pool of qualified medical professionals with expertise and experience in radiotherapy and diagnostic imaging in China, and our hospital partners face competition for such qualified medical professionals from other public hospitals, private healthcare providers, research and academic institutions and other organizations. In the event that our hospital partners fail to recruit and retain a sufficient number of these medical professionals, the resulting shortage could adversely affect the operation of centers in our network and our growth prospects.

Any failure by our hospital partners to make contracted payments to us or any disputes over, or significant delays in receiving, such payments could have a material adverse effect on our business and financial condition.

Most of the centers in our network are established through long-term lease and management services arrangements entered into with our hospital partners. We also provide management services to certain radiotherapy and diagnostic imaging centers through service-only agreements. Payments for treatment and diagnostic imaging services provided in the centers in our network are typically collected by our hospital partners who then pass on to us our contracted percentage of such revenue net of specific operating expenses on a periodic basis. Our total outstanding accounts receivable from our hospital partners were RMB244.2 million, RMB210.3 million and RMB272.3 million (US$45.0 million) as of December 31, 2011, 2012 and 2013, respectively. As of December 31, 2013, approximately 12.3% of our network accounts receivable reported on our consolidated balance sheets as of December 31, 2012 were still outstanding. The average turnover days of our network accounts receivable in 2013 were 145 days. Any failure by our hospital partners to pay us our contracted percentage, or any disputes over or significant delays in receiving such payments from our hospital partners, for any reason, could negatively impact our financial condition. Accordingly, any failure by us to maintain good working relationships with our hospital partners, or any dissatisfaction on the part of our hospital partners with our services, could negatively affect the operation of the centers and our ability to collect revenue, reduce the likelihood that our agreements with hospital partners will be renewed, damage our reputation and otherwise have a material adverse effect on our business, financial condition and results of operation.

We may not be able to effectively manage the expansion of our operations through new acquisitions or joint ventures or to successfully realize the anticipated benefits of any such acquisition or joint venture.

We have historically complemented our organic development of new centers through the selective acquisition of complementary businesses or assets or the formation of joint ventures, and we may continue to do so in the future. For example, in June 2012, we acquired 52% of the equity interest in Chang an Hospital, a licensed full-service private hospital. In December 2012, we acquired 19.98% of equity interest in The University of Texas MD Anderson Cancer Center Proton Therapy Center, a leading proton treatment center in the world. The identification of suitable acquisition targets or joint venture candidates can be difficult, time consuming and costly, and we may not be able to successfully capitalize on identified opportunities. We may not be able to continue to grow our business as anticipated if we are unable to successfully identify and complete potential acquisitions in the future. Even if we successfully complete an acquisition or establish a joint venture, we may not be able to successfully integrate the acquired businesses or assets or cooperate successfully with the joint venture partner. Integration of the acquired business or assets or cooperation with the joint venture partners can be expensive, time consuming and may strain our resources. Such integration or cooperation could also require significant attention from our management team, which may prevent key members of our management from focusing on other important aspects of our business.

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In addition, we may be unable to successfully integrate or retain employees or management of the acquired businesses or assets or retain the acquired entity s patients, suppliers or other partners. Consequently, we may not achieve the anticipated benefits of any acquisitions or joint ventures. For example, we plan to transform Chang an Hospital into a full-service hospital with a special focus on cancer diagnosis and treatment services. In addition, we plan to merge Xi An Wanjiehuaxiang Medical Technology Development Co. Ltd. (CCICC) into Chang an Hospital after which CCICC will become part of Chang an Hospital. We cannot assure such transformation and integration would be implemented successfully, or without incurring significant cost. Furthermore, future acquisitions or joint ventures could result in potentially dilutive issuances of equity or equity-linked securities or the incurrence of debt, contingent liabilities or expenses, or other charges, any of which could have a material adverse effect on our business, financial condition and results of operations.

We had net current liabilities as of December 31, 2012 and we cannot assure you that we will not experience net current liabilities in the future.

We had net current liabilities of RMB6.4 million as of December 31, 2012 primarily due to cost incurred in connection with the acquisition of equity interests in Chang an Hospital and Texas MD Anderson Cancer Center Proton Therapy Center in 2012. The total consideration we paid for the acquisition was RMB248.8 million for Chang an Hospital and US$32.3 million for Texas MD Anderson Cancer Center Proton Therapy Center, respectively. We had net current assets of RMB125.4 million (US$20.7 million) as of December 31, 2013. We believe that our current cash and anticipated cash flow from operations will be sufficient to meet our anticipated cash needs, including our cash needs for working capital and capital expenditures, for at least the next 12 months. However, we cannot assure you that we will not have net current liabilities in the future. If we fail to generate current assets to the extent that the aggregate amount of our current assets on any given day exceeds the aggregate current liabilities on the same day, we will continue to record net current liabilities. If we have significant net current liabilities for an extended period of time, our working capital for purposes of our operations may be subject to constraints, which may have a material adverse effect on our business, financial condition and results of operations.

We may not be successful in negotiating the conversion of a few of our cooperation agreements with our partner hospitals into lease and management agreements due to regulatory changes.

Since the effectiveness in September 2000 of the Implementation Opinions on the Classified Management of Urban Medical Institutions, which was promulgated by the Ministry of Health, the State Administration of Traditional Chinese Medicine, the Ministry of Finance and the National Development Reform Committee, or NDRC, non-profit civilian medical institutions are no longer permitted to enter into cooperation agreements or to continue to operate under existing cooperation agreements with third parties pursuant to which the parties jointly invest in or cooperate to set up for-profit centers or units that are not independent legal entities. However, according to the Opinions on Certain Issues Regarding Classified Management of Urban Medical Institutions issued in July 2001 by the same authorities, a non-profit civilian medical institution may, if lacking sufficient funds to purchase medical equipment outright, enter into a leasing agreement pursuant to which the medical institution leases medical equipment from its partner at market rates. To comply with these regulatory changes, we have transitioned most of our cooperation agreements with non-profit civilian hospitals to lease and management agreements. However, we are still negotiating the transition of our cooperation agreements relating to 1 of our centers located at one of our partner hospitals, which center s revenue in 2013 was immaterial. Although neither we nor any of our hospital partners have incurred any penalties to date for continuing to operate under cooperation agreements at these centers, there can be no assurance that we will not incur penalties in the future or that we will be able to successfully negotiate the conversion of these agreements. If we are unable to successfully negotiate the conversion of our cooperation agreements with these hospitals or if government authorities decide to assess penalties against either us or our hospital partners or to suspend the operation of these centers before we are able to complete the transition, our business, financial condition and results of operation could

be materially and adversely affected.

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We are not aware of any similar restriction imposed by military healthcare administrative authorities on the cooperation agreements that we have entered into with military hospitals, which are hospitals regulated by the military but most of which are otherwise the same as other government-owned civilian hospitals open to the public. Accordingly, we have maintained our cooperation agreements with 41 military hospitals as of December 31, 2013. However, as military hospitals are also government-owned, if military hospitals are required by military healthcare administrative authorities to transition away from cooperation agreements in the future, we will have to negotiate a similar conversion of the agreements with our military hospital partners. If we are unable to successfully negotiate lease and management or other alternative agreements with our existing military hospital partners on terms not less favorable than those under our cooperation agreements, our business, financial condition and results of operation may be adversely affected.

We cannot assure you that government authorities will not interpret regulations differently from us to find that our lease and management agreements are still not in compliance with relevant regulations.

We believe that our lease and management agreements with civilian public hospital partners, which terms continue to provide that our revenues from hospital-based centers are to be calculated based on contracted percentages of each center s revenue net of specified operating expenses, are in compliance with the Implementation Opinions on the Classified Management of Urban Medical Institutions and the Opinions on Certain Issues Regarding Classified Management of Urban Medical Institutions. However, we cannot assure you that the Ministry of Health or other competent authorities will not interpret these regulations differently to find that our lease and management agreements are still not in compliance with such regulations, in which instance, such authorities could, among other things, declare our lease and management agreements to be void, order our civilian hospital partners to terminate such agreements with us, order our civilian hospitals partners to suspend or cease operation of the centers governed by such agreements, suspend the use of our medical equipment, or confiscate revenues generated under the noncompliant agreements. Furthermore, we may have to change our business model which may not be successful. If any of the above were to occur, our business, financial condition and results of operation could be materially and adversely affected.

There may be corrupt practices in the healthcare industry in China, which may place us at a competitive disadvantage if our competitors engage in such practices and may harm our reputation if our hospital partners and the medical personnel who work in our centers, over whom we have limited control, engage in such practices.

There may be corrupt practices in the healthcare industry in China. For example, in order to secure agreements with hospital partners or to increase direct sales of medical equipment or patient referrals, our competitors, other service providers or their personnel or equipment manufacturers may engage in corrupt practices in order to influence hospital personnel or other decision-makers in violation of the anti-corruption laws of China and the U.S. Foreign Corrupt Practices Act, or the FCPA. We have adopted a policy regarding compliance with the anti-corruption laws of China and the FCPA to prevent, detect and correct such corrupt practice. However, as competition persists and intensifies in our industry, we may lose potential hospital partners, patient referrals and other opportunities to the extent that our competitors engage in such practices or other illegal activities. In addition, our partner hospitals or the doctors or other medical personnel who work in our network of centers may engage in corrupt practices without our knowledge to procure the referral of patients to centers in our network. Although our policies prohibit such practices, we have limited control over the actions of our hospital partners or over the actions of the doctors and other medical personnel who work in our network of centers since they are not employed by us. If any of them were to engage in such illegal practices with respect to patient referrals or other matters, we or the centers in our network may be subject to sanctions or fines and our reputation could be adversely affected by any negative publicity stemming from such incidents.

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We could also face increased exposure to liability claims at our specialty cancer hospitals, including claims for medical malpractice. We may need to obtain medical malpractice insurance and other types of insurance that we do not currently carry, each of which could increase our expenses and decrease our profitability. In addition, there can be no assurance that such insurance will be available at a reasonable price or that we will be able to maintain adequate levels of liability insurance coverage, if at all. In addition, our specialty cancer hospitals will also be required to obtain various quotas, permits and authorizations, which are currently the responsibility of our hospital partners under our existing agreements. See Risks Related to Our Industry Healthcare administrative authorities in China currently set procurement quotas for certain types of medical equipment and Risks Related to Our Industry We or our hospital partners may be unable to obtain various permits and authorizations from regulatory authorities in China relating to our medical equipment, which could delay the installation or interrupt the operation of our equipment.

Finally, if our plans change for any reason or the anticipated timetable or costs of development change for our specialty cancer hospitals, our business and future prospects may be negatively impacted. There can be no assurance that the planned specialty cancer hospitals will be completed or that, if completed, they will achieve sufficient patient cases to generate positive operating margins. In addition, as our currently planned specialty cancer hospitals are to be established through joint ventures with other parties, we also may not be successful in cooperating with such joint venture partners in operating our specialty cancer hospitals. See Risk Factors Related to Our Business We may not be able to effectively manage the expansion of our operations through any new acquisitions or joint ventures, which we may not be able to successfully execute.

We rely on the doctors and other medical professionals providing services in our network of centers to make proper clinical decisions and we rely on our hospital partners to maintain proper control over the clinical aspects of the operation of our network of centers.

We rely on the doctors and other medical professionals who work in our network to make proper clinical decisions regarding the diagnosis and treatment of their patients. Although we develop treatment protocols for doctors, provide periodic training for medical professionals in our network of centers on proper treatment procedures and techniques and host seminars and conferences to facilitate consultation among doctors providing services in our network of centers, we ultimately rely on our hospital partners to maintain proper control over the clinical activities of each center and over the doctors and other medical professionals who work in such centers. Any incorrect clinical decisions on the part of doctors and other medical professionals or any failure by our hospital partners to properly manage the clinical activities of each center may result in unsatisfactory treatment outcomes, patient injury or possibly death. Although part of the liability for any such incidents may rest with our partner hospitals and the doctors and other medical professionals they employ, we may be made a party to any such liability claim which, regardless of its merit or eventual outcome, could result in significant legal defense costs for us, harm our reputation, and otherwise have a material adverse effect on our business, financial condition and results of operations. The centers in our network have experienced claims as to a limited number of medical disputes since they commenced operations. As of December 31, 2013, 3 centers in our network have agreed to pay an aggregate amount of approximately RMB0.1 million (US$22.3 thousand) to settle such claims. Any expenses resulting from such liability claims are generally required to be accounted for as expenses of the relevant center, which could reduce our revenue derived from such center. We do not carry malpractice or other liability insurance at many of the centers in our network, and at those centers that do carry such insurance, it may not be sufficient to cover any potential liability that may result from such claims. For our specialty cancer hospitals that are currently under development, we will likely face direct liability claims for any such incidents.

Any failures or defects of the medical equipment in our network of centers or any failure of the medical personnel who work at the centers in our network to properly operate our medical equipment could subject us to liability claims and we may not have sufficient insurance to cover any potential liability.

Our business exposes us to liability risks that are inherent in the operation of complex medical equipment, which may contain defects or experience failures. We rely to a large degree on equipment manufacturers to provide technical training to the medical technicians who work in our network of centers on the proper operation of our complex medical systems. If such medical technicians are not properly and adequately trained by the equipment manufacturers or by us, they may misuse or ineffectively use the complex medical equipment in our network of centers. These medical technicians may also make errors in the operation of the complex medical equipment even if they are properly trained. Any medical equipment defects or failures or any failure of the medical personnel who work in the centers to properly operate the medical equipment could result in unsatisfactory treatment outcomes, patient injury or possibly death. Although the liability for any such incidents rests with the equipment manufacturers or the medical technicians, we may be made a party to any such liability claim which, regardless of its merit or eventual outcome, could result in significant legal defense costs for us, harm our reputation, and otherwise have a material adverse effect on our business, financial condition and results of operations. In addition, any expenses resulting from such liability claims may be accounted for as expenses of the center, which could reduce our revenue derived from such center. We do not carry product liability insurance at any of the centers in our network.

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Any downtime for maintenance and repair of our medical equipment could lead to business interruptions that could be expensive and harmful to our reputation and to our business.

Significant downtime associated with the maintenance and repair of medical equipment used in our network of centers would result in the inability of the centers to provide radiotherapy treatment or diagnostic imaging services to patients in a timely manner. We primarily rely on equipment manufacturers or third party service companies for maintenance and repair services. The failure of manufacturers or third party service companies to provide timely repairs on our equipment could interrupt the operation of centers in our network for extended periods of time. Such extended downtime could result in lost revenues for us and our partner hospitals, dissatisfaction on the part of patients and our partner hospitals and damage to the reputation of the centers in our network, our partner hospitals and our company.

We rely on a limited number of equipment manufacturers.

Much of the medical equipment used in our network of centers is highly complex and is produced by a limited number of equipment manufacturers. These equipment manufacturers provide training on the proper operation of our medical equipment to the medical personnel who work in the centers in our network as well as maintenance and repair services for such equipment. Any disruption in the supply of the medical equipment or services from these manufacturers, including as a result of failure by any such manufacturers to obtain the requisite third-party consents and licenses for the intellectual property used in the equipment they manufacture, may delay the development of new centers or negatively affect the operation of existing centers and could have a material adverse effect on our business, financial condition and results of operations.

We may fail to protect our intellectual property rights or we may be exposed to misappropriation and infringement claims by third parties, either of which may have a material adverse effect as to our business.

We have applied for and obtained the registration of our trademark Medstar in China to protect our corporate name. As of December 31, 2013, we also owned the rights to 87 domain names that we use in connection with the operation of our business. We believe that such domain names provide us with the opportunity to enhance our marketing efforts for the treatments and services provided in our network and enhance patients knowledge as to cancers, the benefits of radiotherapy and the various treatment options that are available. Our failure to protect our trademark or such domain names may undermine our marketing efforts and result in harm to our reputation and the growth of our business.

Furthermore, we cannot be certain that the equipment manufacturers from whom we purchase equipment have all requisite third-party consents and licenses for the intellectual property used in the equipment they manufacture. As a result, those equipment manufacturers may be exposed to risks associated with intellectual property infringement and misappropriation claims by third parties which, in turn, may subject us to claims that the equipment we have purchased infringes the intellectual property rights of third parties. We have in the past been subject to, and may in the future continue to be subject to, such claims by third parties. As a result, we may be named as a defendant in, or joined as a party to, any intellectual property infringement proceedings against equipment manufacturers relating to any equipment we have purchased. If a court determines that any equipment we have purchased from our equipment manufacturers infringes the intellectual property rights of any third party, we may be required to pay damages to such third party and the centers in our network may be prohibited from using such equipment, either of which could damage our reputation and have a material adverse effect on our business prospects, financial condition and results of operations. In addition, any such proceeding may also be costly to defend and may divert our management s attention and other resources away from our business. Furthermore, the standard equipment purchase agreements that we enter into with our equipment manufacturers typically do not contain indemnification provisions for intellectual property claims. Although we have obtained specific indemnity from one equipment manufacturer for a patent infringement claim, there can be no assurance that we would be able to recover any damages, lost profits or litigation costs resulting

from any intellectual property infringement claims or proceedings in which we are named as a party.

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Our reported earnings could decline if we recognize impairment losses on intangible assets and goodwill relating to the Chang an Hospital and other acquisitions.

We acquired 52% equity interest in Chang an Hospital in 2012 and recorded goodwill in the amount of RMB292.9 million as well as certain acquired intangibles. We quantitatively assessed the goodwill for impairment as of December 31, 2013. The fair value of the reporting unit exceeded its carrying amount and therefore goodwill was not impaired and we were not required to perform further testing. If there are any significant adverse changes in the operating results of Chang an Hospital in the future, the impairment losses on goodwill may be resulted. The headroom of the goodwill impairment test as of December 31, 2013 was 10%. We may continue to selectively acquire complementary businesses in the future, which may result in recorded goodwill and additional acquired intangibles. Any future goodwill we record will be tested for impairment by us annually or more frequently if an event occurs or a circumstance develops that would require more frequent assessments. Examples of such events or circumstances include, but are not limited to, a significant adverse change in the legal or business climate, an adverse regulatory action or unanticipated competition. In the future, we could recognize additional impairment losses on the intangible assets and goodwill, which could result in a charge to our reported results of operations and cause our reported earnings to decline.

We do not have insurance coverage for some of our medical equipment and do not carry any business interruption insurance.

We do not have insurance for nine units of electroencephalography and thermotherapy equipment at centers from which we derived less than 0.11% of our total revenues in each of 2011, 2012 and 2013. Damage to, or the loss of, such uninsured equipment due to natural disasters, such as fires, floods or earthquakes, could have an adverse effect on our financial condition and results of operation. In addition, the operations in our network of centers may be particularly vulnerable to natural disasters that disrupt transportation since many patients travel long distances to reach such centers. Also, we do not have any business interruption insurance. Any business disruption could result in substantial expenses and diversion of resources and could have a material adverse effect on our business, financial condition and results of operations. For example, the strong earthquake that struck Sichuan Province in May 2008 resulted in the suspension of operations at three of our centers in Chengdu, the provincial capital of Sichuan Province, for approximately one month due to the diversion of hospital resources toward the treatment of earthquake victims.

Most of our radiotherapy and diagnostic imaging equipment contains radioactive materials or emits radiation during operation.

Most of the radiotherapy and diagnostic imaging equipment in our network of centers, including gamma knife systems, proton beam therapy systems, linear accelerators and PET-CT systems, contain radioactive materials or emit radiation during operation. Radiation and radioactive materials are extremely hazardous unless properly managed and contained. Any accident or malfunction that results in radiation contamination could cause significant harm to human beings and could subject us to significant legal expenses and result in harm to our reputation. Although equipment manufacturers and our hospital partners and their staff may bear some or all of the liability and costs associated with any accidents or malfunctions, if we are found to be liable in any way we may also face severe fines, legal reparations and possible suspension of our operating permits, all of which could have a material and adverse effect on our business, results of operations and financial condition. Also, certain of our medical equipment require the periodic replacement of their radioactive source materials. We do not directly oversee the handling of radioactive materials during the replacement or reloading process or during the disposal process, and any failure on the part of our hospital partners to handle or dispose of such radioactive materials in accordance with PRC laws and regulations may have an adverse effect on the operation of such centers.

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Any change in the regulations governing the use of medical data in China, which are still in development, could adversely affect our ability to use our medical data and could potentially subject us to liability for our past use of such medical data.

The centers in our network collect and store medical data from radiotherapy treatments for purposes of analysis, use in training doctors providing services in our network and improving the effectiveness of the treatments provided in our network of centers. In addition, doctors in our network utilize such medical data to conduct clinical research. We do not make any such medical data public and only keep such medical data for our internal use and for research purposes by doctors upon the approval of our medical affairs department and our hospital partners. Chinese regulations governing the use of such medical data are still in development but currently do not impose any restrictions on the internal use of such data by us as long as we have the permission of our hospital partners who have ownership of such data. Any change in the regulations governing the use of such medical data could adversely affect our ability to use such medical data and could subject us to liability for past use of such data, either of which could have a material adverse effect on our business, operations and financial results.

We plan to establish and operate additional specialty cancer hospitals that will be majority owned by us and are subject to significant risks.

As part of our growth strategy we plan to establish specialty cancer hospitals that will focus on providing radiotherapy services as well as diagnostic imaging services, chemotherapy and surgery. For example, in June 2012, we acquired, through our subsidiaries, Cyber Medical Network Limited, or Cyber Medical, and Medstar (Shanghai) Leasing Co., Ltd., or Shanghai Medstar, 52% of the equity interest in Chang an Hospital or a total consideration of approximately RMB248.8 million. In addition, at the Beijing Proton Medical Center, one of our planned specialty cancer hospitals, we plan to offer proton beam therapy treatment services with which we have had no prior experience. Since we have limited experience in operating our own specialty cancer hospital, or in providing many of the services that we plan to offer in our specialty cancer hospitals, such as chemotherapy treatments, surgical procedures or proton beam therapy, we may not be able to provide as high a level of service quality for those treatment options as compared to the other treatments that are currently offered at our network of centers, which may result in damage to our reputation and our future growth prospects. In addition, we may not be successful in recruiting qualified medical professionals to effectively provide the services that we intend to offer in our specialty cancer hospitals. Furthermore, although our brand name is well known among referring doctors, patients are not currently familiar with our brand as we do not carry our own brand name in our network of centers under our existing agreements with our hospital partners. Therefore, when we establish our own specialty cancer hospitals under our brand name, we may not be able to immediately gain wide acceptance among patients and, thus, may be unable to attract a sufficient number of patients to our new hospitals.

We plan to carry out a number of large-scale hospital construction projects in the near future, which requires substantial increase in capital expenditures. Our operation and financial conditions and results will be adversely affected if we could not effectively manage capital expenditures.

We plan to build three premium cancer hospitals in major cities in China, namely Beijing, Shanghai and Guangzhou. All these cities are considered top-tier cities in China, with large and nationally-renowned government hospitals. To attract patients, our planned premium hospitals need to train our staff members properly, provide services and treatment environment superior to local hospitals as well as install high-end equipment, including CyberKnife, IMRT (Intensity-Modulated Radiation Therapy) and proton beam therapy. The required capital expenditure will be substantial. The process of capital expenditure planning, designing and construction of the premium hospitals will be time consuming and complex which requires a dedicated team in our company. We do not have prior experience and existing team in managing projects of the planned size. If we cannot manage the process properly, our operating and

financial results will be affected adversely.

Our growth plan includes the construction of premium cancer hospitals, free-standing radiotherapy and diagnostic centers. If we cannot identify and seize the growth opportunities in the fast-changing market, our future growth will face uncertainties.

We plan to apply for approvals to build free-standing radiotherapy and diagnostic centers in multiple regions in China. These free-standing centers will not be affiliated with local government hospitals like our current centers. While the current healthcare reform policies encourage the establishment of private medical institutions, the implementation process will be complex and time-consuming and subject to uncertainty. We are in the process of identifying suitable regions for such free-standing centers by taking into consideration a number of factors including the regional market size, existing competition and potential strategic partners. There are uncertainties about how successful we can identify the suitable market, acquire the required government approvals timely and control the planned investments. In addition, we may face competition from the existing centers.

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With the rising conflicts between doctors and patients, if we cannot properly handle disputes in a timely manner with the patients, we will face the increasing risk of litigation.

Recently, there were more incidents of patient / doctor conflicts and litigations in China. Patients in China are demanding more higher-service quality of the medical services and treatments they receive from the hospitals. In our Chang an Hospital and our network centers, we also deal with patient disputes and litigations due to real or perceived medical incidents and practices. While we offer periodic training to all medical staff in our centers and hospitals, our patients may still raise issues with the treatment procedures, especially with cancer patients who experience higher than expected side-effects, sometimes resulting in unexpected deaths. While all of our centers and Chang an Hospital are covered by medical malpractice insurance and we also purchased body-injury insurance for our medical staff, the process to reach a settlement, usually financial settlement under the medical malpractice insurance, is time-consuming and our management team needs to divert their attention from the normal operation of the centers and hospital. If we cannot properly handle the medical disputes in our centers and Chang an Hospital, we may face increasing risks of litigation and our reputation among patients may be affected adversely. As of December 31, 2013, Chang an Hospital has agreed to pay an aggregate amount of approximately RMB1.09 million (US$0.18 million) to settle such claims.

The proper implementation of our strategy requires that we recruit, train and retain the doctors, specialists and other medical staff. If we cannot achieve the proper level of doctor recruitment and retention, our current and future hospitals business may be affected adversely.

The financial and operational performance of our planned premium cancer hospitals and Chang an Hospital depend significantly on our ability to attract and retain quality doctors, nurses, hospital administrators and managers. Under the current regulatory environment of China, doctors and nurses are affiliated with various hospitals, whose professional registration and accreditation need the approval of hospitals they serve. The government policy is relaxing on the mobility of doctors and other medical professionals, such as the policy to allow multiple-location practice for doctors. However, the full enactment and implementation may take time and vary from region to region. In order to attract, train and retain a qualified team of doctors, nurses and hospital managers, we may need to offer compensation packages superior to those of government hospitals, provide more professional training opportunities, including overseas training and exchange, and include the medical team into our ESOP. All these measures may result in higher compensation and administrative expenses and therefore have an adverse effect on our financial and operational results.

Our business is subject to seasonality.

Both our network centers and hospital business are subjected to seasonality. During a fiscal year, the first quarter usually sees fewest patient visits, both inpatient and outpatient, mainly due to the Chinese New Year. The fourth quarter is usually the busiest quarter during the year, as most patients, especially patients from the rural areas, will have more free time to visit hospitals. Since our network centers are located within the government hospitals, they are subjected to seasonality of the patient traffic as well. Our planned premium cancer hospitals will also be affected by seasonality, although to a lesser degree, as cancer patients need to receive treatment and diagnosis immediately. If we cannot manage and mitigate the seasonality effectively, our financial and operational results will be adversely affected.

Our future high-end cancer Hospitals will provide patients high-end medical services and medicines that are covered by the national basic medical insurance, and as a result we may need to cooperate with commercial insurance companies and face risks in respect of charge fees and patients ability of payment.

Currently, the majority of patients in our network centers and Chang an Hospital are covered under the national basic medical insurance. We settle the payment with the local medical insurance agencies on regular basis. However, our planned premium cancer hospitals will offer high-end radiotherapy and other services that will not be covered under the national basic medical insurance program. Our patients will be self-pay or covered under various commercial insurances. We need to negotiate with various insurance companies, both domestic and international, which would enroll our hospitals into their coverage. We cannot assure you that we can establish and manage the business relationship with insurance companies properly and effectively. Without the insurance coverage, our future revenue may not meet our forecasts and profitability will be adversely affected. We may also face collection risks as insurance companies may decide not to pay for certain clinical procedures or refuse to pay accordingly to our requests.

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Our business depends substantially on the continuing efforts of our executive officers and other key personnel, and our business may be severely disrupted if we lose their services.

We depend on key members of our management team, which includes Mr. Jianyu Yang, chairman and our chief executive officer, Dr. Zheng Cheng, a director and our chief operating officer, Mr. Adam Jigang Sun, our chief financial officer, Mr. Jing Zhang, our chief administrative officer, Mr. Yaw Kong Yap, senior vice president, as well as other key personnel for the continued growth of our business. The loss of any of these members of our management team or other key employees could delay the implementation of our business strategy and adversely affect our operations. Our future success will also depend in large part on our continued ability to attract and retain highly qualified management personnel. The process of hiring suitable, qualified personnel is often lengthy and such talented and highly qualified management personnel is often in short supply in China. If our recruitment and retention efforts are unsuccessful in the future, it may be more difficult for us to execute our business strategy. We cannot assure we can always make similar smooth transition if any executive officers or key personnel were to leave our company in the future. Although none of the key members of our management team is nearing retirement age in the near future and we are not aware of any current key members of our management team or other key personnel planning to retire or leave us, if one or more of such personnel are unable or unwilling to continue in their present positions, we may not be able to replace them readily, if at all. Consequently, our business may be severely disrupted, and we may incur additional expenses to recruit and retain new officers. In addition, we do not maintain key employee insurance. We have entered into employment agreements and confidentiality agreements with all of the key members of our management team and other key personnel. However, if any disputes arise between any of our key members of our management team or other key personnel and us, we cannot assure you, in light of uncertainties associated with the PRC legal system, the extent to which any of these agreements could be enforced in China, where all key members of our management team and other key personnel reside and hold some of their assets. See Risks Related to Doing Business in China Uncertainties with respect to the PRC legal system could have a material adverse effect on us.

Our directors, executive officers and significant shareholders have substantial influence over our company and their interests may not be aligned with the interests of our other shareholders.

As of the date of this annual report, our directors, executive officers and significant shareholders beneficially owned approximately 46.4% of our outstanding share capital. As such, they have substantial influence over our business, including decisions regarding mergers, consolidations and the sale of all or substantially all of our assets, election of directors and other significant corporate actions. This concentration of ownership may discourage, delay or prevent a change in control of our company, which could deprive our shareholders of an opportunity to receive a premium for their shares as part of a sale of our company and might reduce the price of our ADSs. These actions may be taken even if they are opposed by our other shareholders.

Our articles of association contain anti-takeover provisions that could adversely affect the rights of holders of our ordinary shares and ADSs.

Our third amended and restated articles of association limit the ability of others to acquire control of our company or cause us to engage in change-of-control transactions. These provisions could have the effect of depriving our shareholders of an opportunity to sell their shares at a premium over prevailing market prices by discouraging third parties from seeking to obtain control of our company in a tender offer or similar transaction. For example, our board of directors has the authority, without further action by our shareholders, to issue preferred shares in one or more series and to fix their designations, powers, preferences, privileges, and relative participating, optional or special rights and the qualifications, limitations or restrictions, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, any or all of which may be greater than the rights associated with our ordinary shares, in the form of ADS or otherwise. Preferred shares could be issued quickly with terms calculated to

delay or prevent a change in control of our company or to make removal of management more difficult. If our board of directors issues preferred shares, the price of our ADSs may fall and the voting and other rights of the holders of our ordinary shares and ADSs may be adversely affected.

We may require additional funding to finance our operations, which financing may not be available on terms acceptable to us or at all, and if we are able to raise funds, the value of your investment in us may be negatively impacted.

Our business operations may require expenditures that exceed our available capital resources. To the extent that our funding requirements exceed our financial resources, we will be required to seek additional financing or to defer planned expenditures. There can be no assurance that we can obtain these bank loans or additional funds on terms acceptable to us, or at all. In addition, our ability to raise additional funds in the future is subject to a variety of uncertainties, including, but not limited to:

our future financial condition, results of operations and cash flows;

general market conditions for capital raising and debt financing activities; and

economic, political and other conditions in China and elsewhere.

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Furthermore, if we raise additional funds through equity or equity-linked financings, your equity interest in our company may be diluted. Alternatively, if we raise additional funds by incurring debt obligations, we may be subject to various covenants under the relevant debt instruments that may, among other things, restrict our ability to pay dividends or obtain additional financing. Servicing such debt obligations could also be burdensome to our operations. If we fail to service such debt obligations or are unable to comply with any of these covenants, we could be in default under such debt obligations and our liquidity and financial condition could be materially and adversely affected.

If we fail to comply with financial covenants under our loan agreements, our financial condition, results of operations and business prospects may be materially and adversely affected.

We have entered into and may in the future enter into loan agreements containing financial covenants that require us to maintain certain financial ratios. We may not be able to comply with some of those financial covenants from time to time. For example, as of December 31, 2013, we were not in compliance with certain financial covenants as provided in a loan agreement which would give the lender the right to demand immediate repayment of the outstanding loan amount. In March 2014, we obtained from the relevant lender a waiver on the right to demand immediate repayment of the outstanding loan amount based on the non-compliance of the financial covenants as of December 31, 2013. However, if we need to obtain waivers from lenders again in the future with respect to prepayment or to amend financial covenants or other relevant provisions under such loan agreements to address potential breaches, we cannot assure you that we would be able to reach agreements with the lenders to avoid a breach. In addition, Chang an Hospital might be deemed not in incompliance with certain terms of the loan agreement for a loan which Chang an Hospital took from Chang an Bank. For more details, see Item 7B. Related Party Transactions. If we are required to repay a significant portion or all of our existing indebtedness prior to their maturity, we may lack sufficient financial resources to do so. Furthermore, a breach of those financial covenants will also restrict our ability to pay dividends. Any of those events could have a material adverse effect on our financial condition, results of operations and business prospects.

We have granted security interests over certain of our medical equipment in order to secure bank borrowings. Any failure to satisfy our obligations under such borrowings could lead to the forced sale of such equipment.

In order to secure bank loans in an aggregate amount of RMB201.2 million, RMB875.5 million and RMB1,086.2 million (US$179.4 million) as of December 31, 2011, 2012 and 2013, respectively, we have granted security interests in equipment with a net carrying value of RMB171.3 million, RMB205.3 million and RMB502.6 million (US$83.0 million), respectively, representing 16.0%, 13.5% and 33.7% of the net value of our net property, plant and equipment of RMB1,068.7 million, RMB1,522.9 million and RMB1,492.6 million (US$246.6 million) as of December 31, 2011, 2012 and 2013, respectively. Any failure on our part to satisfy our obligations under these loans could lead to the forced sale of our medical equipment that secure these loans, the suspension of the operation of the centers in which such medical equipment is used, or otherwise damage our relationship with our hospital partners and our reputation in the medical community, all of which could have a material adverse effect on our business, financial condition and results of operation. We may grant additional security interests in our equipment in order to secure future bank borrowings.

If we fail to establish or maintain an effective system of internal controls over our financial reporting, we may be unable to accurately report our financial results or prevent fraud, and investor confidence and the market price of our ADSs may, therefore, be adversely impacted.

In connection with management s assessment of the effectiveness of our internal control over financial reporting for the year ended December 31, 2010, we and our current independent registered public accounting firm identified a material weakness in our internal controls over financial reporting related to our lack of adequate resources with the

requisite U.S. GAAP and SEC financial accounting and reporting expertise to support the accurate and timely assembly and presentation of our consolidated financial statements and related disclosures. As of December 31, 2011, this material weakness has been remediated. We have successfully completed our Section 404 assessment for the year ended December 31, 2013 and received the auditor s attestation. However, in the future, if we fail to maintain effective internal controls over financial reporting or to obtain an unqualified auditors attestation, our ability to accurately report our financial results may be impaired, which could adversely impact investor confidence and the market price of our ADSs.

Our business may be adversely affected by fluctuations in the value of the Renminbi as a significant portion of our capital expenditures relates to the purchase of medical equipment priced in U.S. dollars.

A significant portion of our capital expenditures relates to the purchase of radiotherapy and diagnostic imaging equipment from manufacturers outside of China. As the price of such equipment is denominated almost exclusively in U.S. dollars, any depreciation in the value of the Renminbi against the U.S. dollar could cause a significant increase our capital expenditures, reduce the profitability of our network of centers and have a material and adverse effect on our business, results of operations and financial condition.

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If we grant employee share options, restricted shares or other equity incentives in the future, our net income could be adversely affected.

We adopted our 2008 share incentive plan on October 16, 2008, which was subsequently amended on November 17, 2009. We are required to account for share-based compensation in accordance with ASC 718, *Compensation-Stock Compensation*, which requires a company to recognize, as an expense, the fair value of share options and other equity incentives to employees based on the fair value of equity awards on the date of the grant, with the compensation expense recognized over the period in which the recipient is required to provide service in exchange for the equity award. On November 27, 2009 and September 30, 2011, we granted options to purchase 4,765,800 ordinary shares at an exercise price of US$3.67 and US$2.17 per share, respectively, under our 2008 share incentive plan to our directors and employees. We did not grant any option under our 2008 share incentive plan in 2012 and 2013. We granted share options in 2007, before adopting our 2008 share incentive plan, to certain executive officers that were subsequently exercised in 2008. As a result, we have incurred share-based compensation expenses of RMB9.2 million in 2011, RMB9.1 million in 2012 and RMB8.8 million (US$1.5 million) in 2013 related to such options. If we grant more options, restricted shares or other equity incentives in the future, we could incur significant compensation charges and our results of operations could be adversely affected.

We are a Cayman Islands company and, because judicial precedent regarding the rights of shareholders is more limited under Cayman Islands law than that under U.S. law, you may have less protection for your shareholder rights than you would under U.S. law.

Our corporate affairs are governed by our memorandum and articles of association, as amended and restated from time to time, the Companies Law (as amended) of the Cayman Islands and the common law of the Cayman Islands. The rights of shareholders to take action against the directors, actions by minority shareholders and the fiduciary responsibilities of our directors to us under Cayman Islands law are to a large extent governed by the common law of the Cayman Islands. The common law of the Cayman Islands is derived in part from comparatively limited judicial precedent in the Cayman Islands as well as from English common law, which has persuasive, but not binding, authority on a court in the Cayman Islands. The rights of our shareholders and the fiduciary responsibilities of our directors under Cayman Islands law are not as clearly established as they would be under statutes or judicial precedent in some jurisdictions in the United States. In particular, the Cayman Islands has a less developed body of securities laws than the United States. In addition, some U.S. states, such as Delaware, have more fully developed and judicially interpreted bodies of corporate law than the Cayman Islands.

As a result of all of the above, public shareholders may have more difficulty in protecting their interests in the face of actions taken by management, members of the board of directors or controlling shareholders than they would as shareholders of a company headquartered in the U.S.

You may have difficulty enforcing judgments obtained against us.

We are a Cayman Islands company and substantially all of our assets are located outside of the United States. Substantially all of our current operations are conducted in the PRC. In addition, most of our directors and officers are nationals and residents of countries other than the United States. As a result, it may be difficult for you to effect service of process within the United States upon these persons. It may also be difficult for you to enforce judgments obtained in U.S. courts based on the civil liability provisions of the U.S. federal securities laws against us and our officers and directors, most of whom are not residents in the United States and the substantial majority of whose assets are located outside of the United States. In addition, there is uncertainty as to whether the courts of the Cayman Islands or the PRC would recognize or enforce judgments of U.S. courts against us or such persons predicated upon the civil liability provisions of the securities laws of the United States or any state and it is uncertain whether such

Cayman Islands or PRC courts would be competent to hear original actions brought in the Cayman Islands or the PRC against us or such persons predicated upon the securities laws of the United States or any state.

We are exempt from certain corporate governance requirements of the New York Stock Exchange.

We are exempt from certain corporate governance requirements of the New York Stock Exchange, or the NYSE, by virtue of being a foreign private issuer. We are required to provide a brief description of the significant differences between our corporate governance practices and the corporate governance practices required to be followed by U.S. domestic companies under the NYSE rules. The standards applicable to us are considerably different than the standards applied to U.S. domestic issuers. The significantly different standards applicable to us do not require us to:

- have a majority of the board be independent (other than due to the requirements for the audit committee under the United States Securities Exchange Act of 1934, as amended, or the Exchange Act);

- have a minimum of three members in our audit committee;

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have a compensation committee, a nominating or corporate governance committee;

provide annual certification by our chief executive officer that he or she is not aware of any non-compliance with any corporate governance rules of the NYSE;

have regularly scheduled executive sessions with only non-management directors;

have at least one executive session of solely independent directors each year;

seek shareholder approval for (i) the implementation and material revisions of the terms of share incentive plans, (ii) the issuance of more than 1% of our outstanding ordinary shares or 1% of the voting power outstanding to a related party, (iii) the issuance of more than 20% of our outstanding ordinary shares, and (iv) an issuance that would result in a change of control;

adopt and disclose corporate governance guidelines; or

adopt and disclose a code of business conduct and ethics for directors, officers and employees.

We intend to rely on all such exemptions provided by the NYSE to a foreign private issuer, except that we have established a compensation committee and have three members of the audit committee, will seek shareholder approval for the implementation of share incentive plans and for the increase in the number of shares available to be granted under share incentive plans and have adopted and disclosed corporate governance guidelines and a code of business conduct and ethics for directors, officers and employees. As a result, you may not be provided with the benefits of certain corporate governance requirements of the NYSE.

We may be classified as a passive foreign investment company, which could result in adverse United States federal income tax consequences to United States Holders.

We believe we were not a passive foreign investment company, or a PFIC, for our taxable year ended on December 31, 2013, and we do not expect to become one for our current taxable year or in the future, although there can be no assurance in this regard. The determination of whether or not we are a PFIC is made on an annual basis and depends on the composition of our income and assets. A non-U.S. corporation will be considered a PFIC for any taxable year if either (i) at least 75% of its gross income is passive income or (ii) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income (which includes cash). The market value of our assets may be determined in large part by the market price of our ADSs and ordinary shares, which is likely to fluctuate. In addition, the composition of our income and assets will be affected by how, and how quickly, we spend our cash. If we are treated as a PFIC for any taxable year during which United States Holders (as defined in Item 10. Additional Information E. Taxation United States Federal Income Taxation) hold ADSs or ordinary shares, certain adverse United States federal income tax consequences could apply to such United States Holders. See Item 10. Additional Information E. Taxation United States Federal Income Taxation Passive Foreign Investment Company.

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Risks Related to Our Industry

Healthcare administrative authorities in China currently set procurement quotas for certain types of medical equipment.

The procurement, installation and operation of large medical equipment in China are regulated by the Rules on Procurement and Use of Large Medical Equipment issued on December 31, 2004 by the Ministry of Health, the NDRC, and the Ministry of Finance. Pursuant to these rules, quotas for large medical equipment are set by the NDRC and the Ministry of Health or the relevant provincial healthcare administrative authorities, and hospitals must obtain a large medical equipment procurement license prior to the procurement of any such equipment. For medical equipment classified as Class A large medical equipment, which includes gamma knife systems, proton beam therapy systems and PET-CT scanners, procurement planning and approval are conducted by the Ministry of Health and the NDRC and large medical equipment procurement licenses are issued by the Ministry of Health. For medical equipment classified as Class B large medical equipment, which includes linear accelerators and MRI and CT scanners, procurement planning and approval are conducted by the relevant provincial healthcare administrative authorities with ratification by the Ministry of Health and the large medical equipment procurement licenses are issued by the relevant provincial healthcare administrative authorities. These rules apply to all public and private civilian medical institutions, whether non-profit or for-profit. Although these rules do not directly apply to military hospitals in China, which are hospitals regulated by the military but most of which are otherwise the same as other government-owned civilian hospitals open to the public, they are used as a reference by the healthcare administrative authority of the general logistics department of the PRC People s Liberation Army, or the PLA, in approving the procurement of such medical equipment. The procurement regulations issued by the Ministry of Health stipulate that from 2011 to 2015, the total number of PET-CT large medical equipment procurement licenses issued in China cannot exceed 160 and by the end of 2015, the total number of PET-CT systems in China cannot exceed 270. There is currently no guidance as to the total number of Class A large medical equipment procurement licenses that may be issued for other types of Class A large medical equipment that the centers in our network operate. In addition, many provincial administrative authorities do not provide the general public with information on their procurement planning and quotas for Class B large medical equipment procurement licenses, if any. Although the current number of procurement licenses available did not have a significant impact on our existing expansion plan in 2013, the limitation on the number of procurement licenses available and any adverse change to such procurement licenses available in the future as a result of any change in government policy, increases in competition and the number of applicants for the procurement licenses or other factors, or any failure of our hospital partners to obtain such licenses as expected, may affect our expansion plan after 2013, which could have a material adverse effect on our future prospects.

In addition, for most of the medical equipment that we intend to install and operate in our specialty cancer hospitals, we will need to obtain large medical equipment procurement licenses from the Ministry of Health or provincial level healthcare administrative authorities. Such licenses might not be obtained in a timely manner or at all, which could delay or prevent the opening of our specialty cancer hospitals, and could have a material adverse effect on our growth strategy and results of operations. See Risks Related to Our Business We plan to establish and operate additional specialty cancer hospitals that will be majority owned by us and are subject to significant risks.

Certain of our hospital partners have not received large medical equipment procurement licenses or interim procurement permits for some of the medical equipment in our network of centers which could result in fines or the suspension from use of such medical equipment.

The quota requirement for large medical equipment procurement became effective in March 2005. A medical institution that houses equipment purchased prior to that time is required to retroactively apply for and obtain a large medical equipment procurement license. If a medical institution is unable to obtain a procurement license as a result of

a lack of procurement quotas for such medical equipment allocated to the region in which the medical institution is located, an interim procurement permit for large medical equipment must be obtained instead. As of December 31, 2013, of the 138 units of medical equipment in the centers in our network that are subject to large medical equipment procurement quota requirements, 116 were issued with a procurement license, 3 were issued with an interim procurement permit subsequent to the implementation of the quota requirement, 15 were issued with procurement permits or authorizations by competent regulatory authorities prior to the implementation of the quota requirement but have not received new procurement licenses or interim procurement permits under the quota requirements that became effective in 2005, and 6, which accounted for approximately 4.2%, 3.2% and 1.5% of our total net revenues in 2011, 2012 and 2013 respectively, have not yet been issued with any procurement license or permit. Although our hospital partners have applied to the competent regulatory authorities for procurement licenses for these last six centers, we cannot assure you that they will be successful. If our hospital partners fail to receive either a procurement license or an interim procurement permit, the centers in our network operating such medical equipment may be required to discontinue operations and may be deprived of the revenue derived from the operation of such equipment or assessed a fine, any of which could have a material adverse effect on our business, financial condition and results of operation.

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3.96

Outstanding at June 30, 2011

3,389 $4.01

8. Subsequent Events
Cowen Royalty Financing Agreement

On July 18, 2011, the Company closed the royalty financing agreement (the Financing Agreement) with Cowen Royalty. Under the terms of the Financing Agreement, the Company borrowed $30,000,000 from Cowen Royalty (the Borrowed Amount) and the Company agreed to repay such Borrowed Amount together with a return to Cowen Royalty, as described below, out of the Company s direct product sales, co-promotion revenues and out-license revenues (collectively, Revenue Interest) that the Company may record or receive as a result of worldwide commercialization of the Company s products including Sumavel DosePro, Zohydro (formerly ZX002) and other future products.

In addition, upon the closing of and in connection with the Financing Agreement, the Company issued and sold to Cowen Royalty $1,500,000 of the Company s common stock, or 388,601 shares, at a price of $3.86 per share. The Company also issued to Cowen Royalty a warrant exercisable into 225,000 share of the Company s common stock. The warrant is exercisable at $9 per share and has a term of 10 years.

Under the Financing Agreement, the Company is obligated to pay to Cowen Royalty:

5% of the first $75 million of Revenue Interest recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year (or 5.75% if the co-promotion agreement with Astellas is terminated prior to June 30, 2013, with a reversion back to 5% possible if certain net sales of Sumavel DosePro are achieved or if Zohydro is commercialized in the four calendar quarters immediately following the effective date of termination);

2.5% of the next $75 million of Revenue Interest recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year; and

0.5% of Revenue Interest over and above $150 million recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year.

Net sales of Sumavel DosePro outside the United States are only included in the Revenue Interest if such net sales exceed $10 million. Once the aggregate payments, including the fixed payments described below, made by the Company to Cowen Royalty equal $75 million, the percentage of Revenue Interest owed to Cowen Royalty is reduced to 0.5% for the remainder of the term of the financing agreement, with only Sumavel DosePro and Zohydro subject to the Revenue Interest payments thereafter. The Company is also obligated to make three fixed payments of $10 million on (or before at the option of the Company) each of January 31, 2015, January 31, 2016 and January 31, 2017. Prepayment requires the consent of the lenders under the Amended Oxford/SVB Agreement while balances remain outstanding under that facility.

The obligation of the Company to make the Revenue Interest payments during the term of the Financing Agreement are secured under a security agreement by a second priority security interest (junior to the security interest of Oxford and SVB under the Amended Oxford /SVB Agreement) in all assets of the Company, including intellectual property and other rights of the Company to the extent necessary or used to commercialize the Company products. The security interest will be extinguished at the end of the term or once the aggregate payments made by the Company to Cowen Royalty equal $75 million, whichever is sooner. Cowen Royalty, Oxford and SVB entered into an intercreditor agreement which governs their respective rights as secured creditors. The Company has agreed to specified positive and negative covenants in connection with the Financing Agreement.

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The Company has the option to terminate the Financing Agreement at the Company s election in connection with a change of control of the Company, upon the payment of a base amount of $52.5 million, or, if higher, an amount that generates a 19% internal rate of return on the Borrowed Amount as of the date of prepayment, in each case reduced by the Revenue Interest and principal payments received by Cowen Royalty up to the date of prepayment.

Cowen Royalty has the option to terminate the Financing Agreement at its election in connection with a change of control of the Company (which includes the sale, transfer, assignment or licensing of the Company s rights in the United States to either Sumavel DosePro or Zohydro), a bankruptcy event with respect to the Company or an event of default under the financing agreement. Upon such a termination by Cowen Royalty, the Company is obligated to make a payment of a base amount of $45 million, or, if higher, an amount that generates a 17% internal rate of return on the Borrowed Amount as of the date of prepayment, in each case reduced by the Revenue Interest and principal payments received by Cowen Royalty up to the date of prepayment.

Unless terminated earlier as discussed above, the financing agreement terminates on March 31, 2018.

Durect Development and License Agreement

On July 11, 2011, the Company entered into a development and license agreement with Durect Corporation (the License Agreement). Under the License Agreement, the Company will be responsible for the clinical development and commercialization of Relday, a proprietary, long-acting injectable formulation of risperidone using Durect s SABER controlled-release formulation technology in combination with the Company s DosePro® needle-free, subcutaneous drug delivery system. Durect will be responsible for non-clinical, formulation and CMC development responsibilities. Durect will be reimbursed by the Company for its research and development efforts on the product.

The Company paid a non-refundable upfront fee to Durect of $2,250,000. The Company is obligated to pay Durect up to $103,000,000 in total future milestone payments with respect to the product subject to and upon the achievement of various development, regulatory and sales milestones. The Company is also required to pay a mid single-digit to low double-digit percentage patent royalty on annual net sales of the product determined on a jurisdiction-by-jurisdiction basis. The patent royalty term is equal to the later of the expiration of all Durect technology patents or joint patent rights in a particular jurisdiction, the expiration of marketing exclusivity rights in such jurisdiction, or 15 years from first commercial sale in such jurisdiction. After the patent royalty term, the Company will continue to pay royalties on annual net sales of the product at a reduced rate for so long as the Company continues to sell the product in the jurisdiction. The Company is also required to pay to Durect a tiered percentage of fees received in connection with any sublicense of the licensed rights.

Durect granted to the Company an exclusive worldwide license, with sub-license rights, to Durect intellectual property rights related to Durect s proprietary polymeric and non-polymeric controlled-release formulation technology to make and have made, use, offer for sale, sell and import risperidone products, where risperidone is the sole active agent, for administration by injection in the treatment of schizophrenia, bipolar disorder or other psychiatric related disorders in humans. Durect retains the right to supply the Company s Phase 3 clinical trial and commercial product requirements on the terms set forth in the License Agreement.

Durect retains the right to terminate the License Agreement with respect to specific countries if the Company fails to advance the development of the product in such country, either directly or through a sublicensee. In addition, either party may terminate the License Agreement upon insolvency or bankruptcy of the other party, upon written notice of a material uncured breach or if the other party takes any act impairing such other party s relevant intellectual property rights. The Company may terminate the License Agreement upon written notice if during the development or commercialization of the product, the product becomes subject to one or more serious adverse drug experiences or if either party receives notice from a regulatory authority, independent review committee, data safety monitory board or other similar body alleging significant concern regarding a patient safety issue. The Company may also terminate the License Agreement with or without cause, at any time upon prior written notice.

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

Forward-Looking Statements

This Quarterly Report on Form 10-Q and the information incorporated herein by reference contain forward-looking statements that involve substantial risks and uncertainties, including statements regarding the future sales potential for Sumavel DosePro, the progress and timing of clinical trials, the safety and efficacy of our product candidates, the goals of our development activities, estimates of the potential markets for our product candidates, estimates of the capacity of manufacturing and other facilities to support our products, projected cash needs and our expected future revenues, operations and expenditures. The forward-looking statements are contained principally in the sections entitled Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business. In some cases, you can identify forward-looking statements by the following words: may, will, could, would, should, expect, intend, plan, anticipate, believe, project, potential, continue, ongoing or the negative of these terms or other comparable terminology, although not all forward-looking statemen contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. We discuss many of these risks, uncertainties and other factors in this Quarterly Report on Form 10-Q in greater detail under the heading Item 1A Risk Factors.

Given these risks, uncertainties and other factors, we urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. You should read this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. For all 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. We undertake no obligation to revise or update publicly any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

Sumavel®, DosePro®, Zohydro , Intraject® and Zogenix are our trademarks. All other trademarks, trade names and service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective owners.

Unless the context requires otherwise, references in this Quarterly Report on Form 10-Q to Zogenix, we, us and our refer to Zogenix, Inc., including, as of June 7, 2010, its consolidated subsidiary.

The interim financial statements and this Management s Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with the financial statements and notes thereto for the year ended December 31, 2010 and the related Management s Discussion and Analysis of Financial Condition and Results of Operations, both of which are contained in our Annual Report on Form 10-K for the year ended December 31, 2010.

Overview

Background

We are a pharmaceutical company commercializing and developing products for the treatment of central nervous system disorders and pain. Our first commercial product, Sumavel DosePro (*sumatriptan* injection) Needle-free Delivery System, offers fast-acting, easy-to-use, needle-free subcutaneous administration of *sumatriptan* for the acute treatment of migraine and cluster headache in a pre-filled, single-use delivery system. We launched the commercial sale of Sumavel DosePro in the United States in January 2010 with our co-promotion partner, Astellas Pharma US, Inc., or Astellas. Our sales and marketing organization is comprised of approximately 100 professionals. Our field sales force of approximately 80 representatives is promoting Sumavel DosePro primarily to neurologists and other key prescribers of migraine medications, including headache clinics and headache specialists. Given our success in growing Sumavel DosePro prescriptions with these key prescribers, we have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. Our promotional efforts are complemented by our collaboration with Astellas and approximately 400 of its sales representatives, who are promoting Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists in the United States, or the Astellas Segment. Our lead product candidate, Zohydro (formerly ZX002), is a novel, oral, single-entity extended-release formulation of *hydrocodone* currently in Phase 3 clinical trials for the treatment of moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. We initiated the Phase 3 clinical development program for Zohydro in March 2010 and, if successful, expect to submit a New Drug Application, or NDA, with the U.S. Food and Drug Administration, or FDA, by early 2012. We in-licensed exclusive U.S. rights to Zohydro from Elan Pharma International Limited, or Elan, in 2007.

In July 2011, we entered into a development and license agreement with Durect Corporation, or the Relday license agreement, pursuant to which, we will be responsible for the clinical development and commercialization of Relday, a proprietary, long-acting

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injectable formulation of risperidone using Durect s SABER® controlled-release formulation technology in combination with our DosePro needle-free, subcutaneous drug delivery system. Risperidone is used to treat the symptoms of schizophrenia and bipolar I disorder in adults and teenagers 13 years of age and older. Relday will be developed to address unmet clinical needs in this patient population and is being developed to be a once-monthly, subcutaneous antipsychotic product. We expect to initiate clinical studies for the new product candidate in patients with schizophrenia in early 2012 following filing of an Investigational New Drug application.

We have experienced net losses and negative cash flow from operating activities since inception, and as of June 30, 2011, had an accumulated deficit of $236.3 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next several years primarily as a result of the development expenses in connection with clinical trials and pre-clinical studies for Zohydro and the cost of the sales and marketing expenses associated with Sumavel DosePro. As of June 30, 2011, we had cash and cash equivalents of $7.7 million. On June 30, 2011, we amended certain terms of our loan agreement with Oxford and SVB including the deferral of principal repayment to commence on February 1, 2012 and in July 2011, we entered into equity and royalty financing agreements with Cowen Healthcare Royalty Partners II, L.P., or Cowen Royalty, resulting in net proceeds of $29.5 million to us. Although it is difficult to predict future liquidity requirements, based on our current operating plan we believe that our cash and cash equivalents as of June 30, 2011, together with future product revenue and borrowings available under our $10.0 million revolving credit facility and the net proceeds from the recently completed equity and royalty financing with Cowen Royalty and amendment to the loan agreement with Oxford and SVB, will be sufficient to fund our operations through the fourth quarter of 2011. We will need to obtain additional capital to finance our operations beyond that point. We intend to raise additional capital through debt or equity financings or through collaborations or partnerships with other companies. If we are not be able to raise additional capital on terms acceptable to us, or at all, as and when needed, we may be required to reduce or curtail our operations and costs, and we may be unable to continue as a going concern. In its report on our consolidated financial statements for the year ended December 31, 2010, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern.

Co-Promotion Agreement

Under our co-promotion agreement with Astellas that we entered into in July 2009, or the co-promotion agreement, Astellas primarily promotes Sumavel DosePro to the Astellas Segment in the United States. Our sales force promotes Sumavel DosePro primarily to neurologists and other key prescribers of migraine medications, including headache clinics and headache specialists in the United States. We jointly share in the cost of advertising, marketing and other promotional activities related to the Sumavel DosePro brand and are required to provide minimum levels of sales effort to promote Sumavel DosePro. Under the co-promotion agreement, we are responsible for the manufacture, supply and distribution of all Sumavel DosePro commercial product and are principally responsible for entering into any contracts and other arrangements with third parties regarding the sale of Sumavel DosePro.

At the inception of the co-promotion agreement and in exchange for the right to promote Sumavel DosePro, Astellas made a non-refundable up-front payment of $2.0 million to us and agreed to make an additional $18.0 million of payments to us upon the achievement of a series of milestones. As of June 30, 2011, we had received a total of $20.0 million from Astellas. These proceeds are reflected as deferred revenues on our consolidated balance sheets at June 30, 2011 and December 31, 2010. Beginning with the launch of Sumavel DosePro in January 2010, we began recognizing these proceeds as contract revenues on a ratable basis over the remaining term of the agreement, which remains in effect through June 30, 2013, subject to extension by one year at Astellas option, contingent upon payment of a predetermined option fee.

In consideration for Astellas performance of its commercial efforts, we are required to pay Astellas a service fee on a quarterly basis that represents a fixed percentage of between 45% and 55% of Sumavel DosePro net sales to the Astellas Segment. In addition, upon completion of the co-promotion term, Astellas generally will be eligible to receive two additional annual tail payments calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion. Astellas pays us the lesser of our direct out-of-pocket costs or a fixed fee for all sample units they order for distribution to their sales force. Amounts received from Astellas for shared marketing costs and sample product are reflected as a reduction of selling, general and administrative expenses, and amounts payable to Astellas for shared marketing expenses and service fees are reflected as selling, general and administrative expenses. For the three months ended June 30, 2011 and 2010, we incurred $1.7 million and $0.8 million, respectively, and for the six months ended June 30, 2011 and 2010, we incurred $3.2 million and $1.1 million, respectively, in service fee expenses.

We record the revenues related to all products sales, including sales generated by the Astellas sales force. Consequently, we record cost of sales for all product sales.

We rely on Astellas and its sales force to promote Sumavel DosePro to the Astellas Segment and any inability of its sales force to effectively sell the product or any termination, amendment or restructuring of the co-promotion agreement could adversely affect our consolidated results of operations and financial condition. For the three and six months ended June 30, 2011, the Astellas

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Segment represented approximately 40% of our net product revenue before consideration of the cost of the service fee payable to Astellas for its sales efforts as described above.

Under the terms of the co-promotion agreement, Astellas could terminate the agreement for any or no reason upon 180-days written notice. The co-promotion agreement may also be terminated by Astellas or us for a number of other specified reasons, some of which are beyond our control. In the event Astellas terminates the agreement for specified reasons or a material uncured breach by us of our minimum sales effort obligations, we would be required to pay Astellas only the first of the two annual tail payments described above.

In addition, either party may terminate the agreement based upon a failure of the Sumavel DosePro brand to achieve certain minimum sales levels in 2011 as defined in the co-promotion agreement. Based on our net product revenue through June 30, 2011, we do not expect to meet these 2011 minimum sales levels for Sumavel DosePro, and therefore expect that both we and Astellas will have the right to terminate the agreement on this basis. If either party were to exercise this termination right, it must provide 90 days written notice to the other party after the actual net sales of Sumavel DosePro through December 31, 2011 have been ascertained. In the event of such a termination relating to sales levels of Sumavel DosePro, we would be required to make the two annual tail payments described above.

In the event of a termination by us or Astellas, we would expect to either expand our sales force to promote Sumavel DosePro to certain physicians within the Astellas Segment, and/or seek another co-promotion partner in order to support the future sales and marketing of Sumavel DosePro.

Durect License Agreement

In June 2011, we paid a non-refundable upfront fee to Durect of $2.25 million under the Relday license agreement. We are obligated to pay Durect up to $103.0 million in total future milestone payments with respect to Relday subject to and upon the achievement of various development, regulatory and sales milestones. We are also required to pay a mid single-digit to low double-digit percentage patent royalty on annual net sales of the product determined on a jurisdiction-by-jurisdiction basis. The patent royalty term is equal to the later of the expiration of all Durect technology patents or joint patent rights in a particular jurisdiction, the expiration of marketing exclusivity rights in such jurisdiction, or 15 years from first commercial sale in such jurisdiction. After the patent royalty term, we will continue to pay royalties on annual net sales of the product at a reduced rate for so long as we continue to sell the product in the jurisdiction. We are also required to pay to Durect a tiered percentage of fees received in connection with any sublicense of the licensed rights.

Revenues

During the year ended December 31, 2010, we began recognizing product revenues from sales of Sumavel DosePro made by us and Astellas under our co-promotion agreement and through sales by us to Desitin Arzneimittel GmbH, or Desitin, under our licensing and distribution agreement. During this same period, we began recognizing contract revenues from license and milestone payments received under the Astellas co-promotion agreement. For the six months ended June 30, 2011 and 2010 we recognized $16.2 million and $6.1 million, respectively, in net product revenues. For the six months ended June 30, 2011 and 2010 we recognized $3.1 million and $1.5 million, respectively, in contract revenues associated with license and milestone payments made to us by Astellas under the co-promotion agreement.

We sell Sumavel DosePro product in a package of six pre-filled, single-dose units to wholesale pharmaceutical distributors, and on a limited basis to retail pharmacies, or, collectively, our customers, at a wholesale acquisition cost, or gross sales price, of $522 per package as of June 30, 2011. Sales to our customers are subject to specified rights of return. We currently defer recognition of revenue on product shipments of Sumavel DosePro to our customers until the right of return no longer exists, which occurs at the earlier of the time Sumavel DosePro units are dispensed through patient prescriptions or expiration of the right of return. We do not have significant history estimating the number of patient prescriptions dispensed. If we underestimate or overestimate patient prescriptions dispensed for a given period, adjustments to net product revenue may be necessary in future periods.

As a result of this policy, we had a deferred revenue balance of $0.7 million at June 30, 2011 for Sumavel DosePro product shipments, which is net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs. We will continue to recognize revenue upon the earlier to occur of prescription units dispensed or expiration of the right of return until we can reliably estimate product returns, at which time we will record a one-time increase in net revenue related to the recognition of revenue previously deferred.

In November 2010, Desitin received regulatory approval to market Sumavel DosePro in Denmark and subsequently received approvals in Germany, Sweden, Norway and the United Kingdom. As a result, we started to sell Sumavel DosePro to Desitin under our licensing and distribution agreement in December 2010. We sell our product to Desitin at a specified transfer price with the right

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of return available for damaged goods upon receipt by Desitin or in the event of a recall. Desitin maintains all risk for retail and wholesaler fees and discounts, collectability of customer receivables, customer returns and expiration of the product. We will also receive a low single-digit royalty from Desitin on net sales of Sumavel DosePro in Europe and other licensed territories, as a pass through of royalties payable to Aradigm. As such, we recognize revenues for product sales to Desitin upon acceptance of product by Desitin (generally at point of shipment). For the six months ended June 30, 2011 and 2010 we recognized no revenue for sales to Desitin. We recognized an immaterial amount of royalty revenues related to the Desitin agreement for the six months ended June 30, 2011.

Cost of Sales

Cost of sales consist primarily of materials, third-party manufacturing costs, freight and indirect personnel and other overhead costs associated with sales of Sumavel DosePro based on units dispensed through patient prescriptions, as well as reserves for excess, dated or obsolete commercial inventories and production manufacturing variances. Our cost of sales for the three months ended June 30, 2011 and 2010, was $4.0 million and $3.2 million, respectively and for the six months ended June 30, 2011 and 2010, our cost of sales was $8.9 million and $5.3 million, respectively. Our product gross margin for the three months ended June 30, 2011 and 2010 was 54% and 24%, respectively and for the six months ended June 30, 2011 and 2010, our product gross margin was 45% and 13%, respectively. The cost of sales associated with the deferred product revenues are recorded as deferred costs, which are included in inventory, until such time the deferred revenue is recognized. Deferred cost of sales totaled $0.2 million and $1.1 million at June 30, 2011 and December 31, 2010, respectively.

Royalty Expense

Royalty expense consists of the amortization of the $4.0 million milestone payment paid by us to Aradigm Corporation upon the first commercial sale of Sumavel DosePro in the United States (which occurred in January 2010) and royalties payable to Aradigm based on net sales of Sumavel DosePro by us or one of our licensees. We are not required to make any further milestone payments to Aradigm. Our ongoing royalty obligation payable to Aradigm is set forth in the asset purchase agreement we entered into with Aradigm in August 2006 pursuant to which we acquired the rights to the DosePro technology. We incurred $0.3 million in royalty expense to Aradigm during each of the three months ended June 30, 2011 and 2010, and during the six months ended June 30, 2011 and 2010, we incurred $0.6 million and $0.4 million, respectively, in royalty expense to Aradigm.

Research and Development Expenses

Our research and development expenses consist of expenses incurred in developing, testing and seeking marketing approval of our product candidates, including:

- payments made to third-party contract research organizations, or CROs, and investigational sites, which conduct our trials on our behalf, and consultants;
- expenses associated with regulatory submissions, preclinical development and clinical trials;
- payments to third-party manufacturers, which produce our active pharmaceutical ingredient and finished product;
- payments made to third-party CROs, laboratories and consultants in connection with preclinical studies;
- personnel related expenses, such as salaries, benefits, travel and other related expenses, including stock-based compensation; and
- facility, maintenance, depreciation and other related expenses.

We expense all research and development costs as incurred.

In March 2010, we initiated our Phase 3 clinical development program for Zohydro. We utilize CROs, contract laboratories and independent contractors for the conduct of pre-clinical studies and clinical trials. In 2010, we began tracking third party costs by type of study being conducted. We recognize the expenses associated with the services provided by CROs based on the percentage of each study completed at the end of each reporting period. We coordinate clinical trials through a number of contracted investigational sites and recognize the associated expense based on a number of factors, including actual and estimated subject enrollment and visits, direct pass-through costs and other clinical site fees. For the three and six months ended June 30, 2011, we incurred $6.4 million and $12.9 million, respectively, in third party research and development costs related to Zohydro.

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We use our employee and infrastructure resources across our product and product candidate development programs. Therefore, we have not tracked salaries, other personnel related expenses, facilities or other related costs to our product development activities on a program-by-program basis. However, we estimate that the majority of our research and development expenses incurred to date are attributable to our Zohydro program.

We expect our research and development costs for 2011 to increase over amounts incurred in 2010 as we progress through the Phase 3 clinical program of Zohydro and with the addition of our Relday program. We expect third party research and development costs for Zohydro remaining through NDA filing to range from $17 million to $19 million. These expenditures are subject to numerous uncertainties regarding timing and cost to completion. Completion of our Phase 3 clinical trials may take longer than currently estimated. The cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others:

- the number of sites included in the trials;
- the length of time required to enroll suitable subjects;
- the duration of subject follow-ups;
- the length of time required to collect, analyze and report trial results;
- the cost, timing and outcome of regulatory review; and
- potential changes by the FDA in clinical trial and NDA filing requirements for a specific therapeutic area.

In addition, we may be obligated to pay Elan, from whom we in-licensed exclusive rights to Zohydro in November 2007, up to $4.5 million in total future milestone payments with respect to Zohydro depending upon the achievement of various development and regulatory events. If Zohydro is approved, we are also required to pay a mid single-digit percentage royalty on its net sales for a specified period of time and continue to pay royalties on net sales of the product thereafter at a reduced low single-digit percentage rate in accordance with the terms of the license agreement.

If our Phase 3 clinical trials are successful, we expect to submit an NDA for Zohydro with the FDA by early 2012. However, the successful development and commercialization of Zohydro is highly uncertain. We also expect to incur customary regulatory costs associated with the NDA, if and when submitted, which will be significant. If Zohydro is approved, we also expect to incur significant expenses related to manufacturing and marketing activities. However, at this time, we cannot reasonably estimate or know the nature, specific timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of Zohydro after submission of our NDA filing, if or when Zohydro will receive regulatory approval and, if approved, if and when material net cash inflows may commence from Zohydro or the amount of any such inflows. This is due to the numerous risks and uncertainties associated with developing and commercializing drugs, including the uncertainty of:

- the costs, timing and outcome of our clinical trials and pre-clinical studies of Zohydro;
- the costs, timing and outcome of regulatory review of Zohydro;
- the costs of commercialization activities, including product marketing, sales and distribution;

- the potential for future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development and commercialization plans and capital requirements;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the emergence of competing technologies and products and other adverse marketing developments;
- the effect on our product development activities of actions taken by the FDA or other regulatory authorities; and
- our degree of success in commercializing Zohydro, if approved.

A change in the outcome of any of these variables with respect to the development of Zohydro could mean a significant change in the costs and timing associated with these efforts.

We also expect to incur costs associated with pre-clinical studies and formulation work for our early-stage product candidates. However, at this time, due to the inherently unpredictable nature of pre-clinical development and given the early stage of such product candidates, we are unable to estimate with any certainty the costs we will incur for such pre-clinical work.

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Selling, General and Administrative Expenses

Our selling expenses, which include sales and marketing costs, consisted primarily of salaries, benefits, consulting fees, costs of obtaining prescription and market data and market research studies related to Sumavel DosePro and Zohydro, including shared marketing and advertising costs under our co-promotion agreement with Astellas, service fees to Astellas and sample costs.

Our general and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, accounting, business development and internal support functions. In addition, general and administrative expenses include facility costs and professional fees for legal, consulting and accounting services. We expect general and administrative expense to increase as a result of the costs we incur operating as a public company. These increases likely will include salaries and related expenses, legal and consultant fees, accounting fees, director fees, increased directors and officers insurance premiums, fees for investor relations services and enhanced business and accounting systems.

Interest Income

Interest income consists of interest earned on our cash and cash equivalents.

Interest Expense

Interest expense consists of interest incurred in connection with the $4.5 million borrowed under our loan and security agreement with General Electric Capital Corporation, or GE Capital, our $25.0 million loan and security agreement and revolving credit facility with Oxford Finance LLC, as successor in interest to Oxford Finance Corporation, or Oxford, and Silicon Valley Bank, or SVB, and non-cash interest expense associated with amortization of debt discount and debt issuance costs.

On June 30, 2011, we amended and restated the existing loan and security agreement with Oxford and SVB, or the amended Oxford/SVB loan agreement to provide for, among other things, the addition of intellectual property to the collateral securing the Oxford/SVB loan and deferral of principal repayment to commence on February 1, 2012. In connection with entering into the amended Oxford/SVB loan agreement, we issued to Oxford and SVB warrants exercisable into an aggregate of 26,455 shares of our common stock. The warrants are exercisable at $3.78 per share of common stock and have a term of 7 years. The amended Oxford/SVB loan agreement consists of a $25.0 million term loan and a $10.0 million revolving credit facility. As of June 30, 2011, we had borrowed $3.7 million under the revolving credit facility. Concurrently with the amended Oxford/SVB loan agreement in 2010, we issued $15.0 million in new convertible promissory notes, or the 2010 Notes, to current investors. The 2010 Notes were subsequently converted into 3,873,756 shares of common stock in connection with our initial public offering in November 2010. As a result of additional borrowings under the amended Oxford loan agreement, and the deferral of principal payments resulting from the amended Oxford/SVB loan agreement in June 2011 and the $30.0 million royalty financing entered into in July 2011, interest expense related to debt service will increase over 2010 levels.

Change in Fair Value of Warrant Liability

Change in fair value of warrant liability for the six months ended June 30, 2010 represents non-cash (expense) income associated with changes in the fair value of the warrants to purchase preferred stock.

In connection with our initial public offering in November 2010, the liability reflected on our consolidated balance sheet for convertible preferred stock warrants was reclassified to stockholders equity (deficit) and we will no longer recognize the change in fair value of these warrants in the consolidated statement of operations.

Other Income (Expense)

Other income (expense) consists of foreign currency transaction gains and losses. All of our revenues are currently generated in U.S. dollars while a majority of our manufacturing expenses are payable in foreign currencies, primarily U.K. pounds sterling and the Euro.

Provision for Income Taxes

We incurred $13,000 and $0 in income tax expense for the six months ended June 30, 2011 and 2010, respectively, related to taxable income generated by our wholly-owned subsidiary, Zogenix Europe Limited.

Internal Control Over Financial Reporting

Assessing our staffing and training procedures to improve our internal control over financial reporting is an ongoing process. We are not currently required to comply with Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and are therefore not required to make an assessment of the effectiveness of our internal control over financial reporting. Further, our

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independent registered public accounting firm has not been engaged to express, nor have they expressed, an opinion on the effectiveness of our internal control over financial reporting.

For the year ending December 31, 2011, pursuant to Section 404 of the Sarbanes-Oxley Act, management will be required to deliver a report that assesses the effectiveness of our internal control over financial reporting. Pursuant to Section 404(c) of the Sarbanes-Oxley Act, our independent registered public accounting firm will not be required to deliver an attestation report on the effectiveness of our internal control over financial reporting for the year ending December 31, 2011.

Critical Accounting Policies and Estimates

There have been no significant changes in critical accounting policies during the six months ended June 30, 2011, as compared to the critical accounting policies described in *Item 7-Management s Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies and Significant Judgments and Estimates* in our Annual Report on Form 10-K for the year ended December 31, 2010.

Results of Operations

Comparison of the three months ended June 30, 2011 and 2010

Revenue. Revenue for the three months ended June 30, 2011 was $10.2 million and $5.1 million for the three months ended June 30, 2010. Product revenue for the three months ended June 30, 2011 and 2010 consists of $8.7 million and $4.2 million, respectively, of Sumavel DosePro dispensed to patients, which is net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs. The $4.5 million increase in product revenue is primarily due to an increase in prescription volume from the initial launch of Sumavel DosePro in late January 2010. Contract revenue for the three months ended June 30, 2011 and 2010 consists of $1.6 million and $0.9 million, respectively. Contract revenue represents amortization of license fee payments and milestone payments we received in connection with the co-promotion agreement we entered into with Astellas in July 2009 and which we began recognizing upon the commencement of sales of Sumavel DosePro in January 2010. The contract revenue in the second quarter of 2010 reflects a pro-rata amount of amortization of license fees and milestones that did not have recourse provisions as compared to the contract revenues in the second quarter of 2011which reflects the full amortization of all license fees and milestone payments.

Cost of Sales. Cost of sales for the three months ended June 30, 2011 was $4.0 million and $3.2 million for the three months ended June 30, 2010. Product gross margin was 54% for the three months ended June 30, 2011 compared to 24% for the three months ended June 30, 2010. Cost of sales, for the three months ended June 30, 2011and 2010 represents the cost of Sumavel DosePro units dispensed to patients and the impact of underutilized production capacity and other manufacturing variances. We developed production capacity to support higher levels of Sumavel DosePro production than initial sample and prescription demand was required to ensure adequate safety stock levels and to maintain the ability to support increased demand, as necessary. Until our prescription and sample demands are at a level where we can fully utilize the capacity committed to our contract manufacturing facilities, we will continue to experience underutilization of our production capacity. In addition, as we adjust production levels in certain periods to manage our inventory levels, we may incur additional charges for excess capacity which will negatively impact our gross margins.

Royalty Expense. Royalty expense for each of the three months ended June 30, 2011 and 2010,was $0.3 million. Royalty expense represents the amortization of a $4.0 million milestone payment we made in connection with the asset purchase agreement with Aradigm payable on the first commercial sale of Sumavel DosePro, which occurred in January 2010, as well as royalties payable to Aradigm from net sales of Sumavel DosePro during the period.

Research and Development Expenses. Research and development expenses increased to $8.9 million for the three months ended June 30, 2011 compared to $7.7 million for the three months ended June 30, 2010. This increase of $1.2 million primarily was due to:

an increase of $1.7 million in research and development costs as a result of the ongoing Phase 3 clinical trials for Zohydro, which were initiated in March 2010; offset by

a decrease of $0.5 million in research and development costs incurred for the Phase 4 study conducted for Sumavel DosePro as it was completed in the second quarter of 2010 and other costs related to product development.

Selling, General and Administrative Expenses. Selling, general and administrative expenses increased to $15.0 million for the three months ended June 30, 2011 compared to $12.3 million for the three months ended June 30, 2010. Selling expenses were $11.5 million for the three months ended June 30, 2011 compared to $10.6 million for the three months ended June 30, 2010. General and administrative expenses were $3.5 million for the three months ended June 30, 2011 compared to $1.7 million for the three months ended June 30, 2010. The increase of $2.7 million in selling, general and administrative expenses primarily was due to:

an increase of $1.8 million of general and administrative expenses as a result of the costs we incurred for operating as a public company. These costs include salaries and related expenses, stock-based compensation charges, legal and

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consultant fees, accounting fees, director fees, increased directors and officers insurance premiums and fees for investor relations services.; and

an increase of $0.9 million in sales and marketing expense primarily as a result of higher services fees payable to our co-promotion partner from higher net product revenues over the prior quarter and increased spending in marketing activities related to Zohydro.

Interest Income. Interest income increased to $3,000 for the three months ended June 30, 2011 compared to $2,000 for the three months ended June 30, 2010. This increase of $1,000 was due primarily to the increase in average cash and cash equivalent balances.

Interest Expense. Interest expense increased to $1.3 million for the three months ended June 30, 2011 compared to $0.9 million for the three months ended June 30, 2010. This increase of $0.4 million was primarily due to:

an increase of $0.5 million in interest expense due to higher debt balances in connection with the amended Oxford loan agreement; and

an decrease of $0.1 million in the amortization of debt issuance and debt discount costs in connection with the $25.0 million amended Oxford/SVB loan agreement.

Change in Fair value of Warrant Liability. During the three months ended June 30, 2011 there was no warrant liability outstanding due to the termination or conversion of the preferred stock warrants to warrants of common stock in connection with the initial public offering in November 2010. The change in fair value of warrant liability during the three months ended June 30, 2010 of $8.6 million is due to the increase in fair value of convertible preferred stock during the period.

Other Income (Expense). Other income was $0.1 million of expense for each of the three months ended June 30, 2011 and 2010. Any changes in other income are primarily related to foreign currency transaction gains and losses which primarily related to the settlement of our liabilities payable in Euro and U.K pounds sterling.

Comparison of the six months ended June 30, 2011 and 2010

Revenue. Revenue for the six months ended June 30, 2011 was $19.3 million and $7.6 million for the six months ended June 30, 2010. Product revenue for the six months ended June 30, 2011 and 2010 consists of $16.2 million and $6.1 million, respectively, of Sumavel DosePro dispensed to patients, which is net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs. The $10.1 million increase in product revenue is primarily due to an increase in prescription volume from the initial launch of the Sumavel DosePro in late January 2010. Contract revenue for the six months ended June 30, 2011 and 2010 consists of $3.1 million and $1.5 million, respectively. Contract revenue represents amortization of license fee payments and milestone payments we received in connection with the co-promotion agreement we entered into with Astellas in July 2009 and which we began recognizing upon the commencement of sales of Sumavel DosePro in January 2010. The contract revenue in the first six months of 2010 reflects a pro-rata amount of amortization of license fees and milestones that did not have recourse provisions as compared to the contract revenues in the first six months of 2011,which reflects the full amortization of all license fees and milestone payments.

Cost of Sales. Cost of sales for the six months ended June 30, 2011 was $8.9 million and $5.3 million for the six months ended June 30, 2010. Product gross margin for the six months ended June 30, 2011 was 45% compared to 13% for the six months ended June 30, 2010. Cost of sales, for the six months ended June 30, 2011 represents the cost of Sumavel DosePro units dispensed to patients and the impact of underutilized production capacity and other manufacturing variances. We developed production capacity to support higher levels of Sumavel DosePro production than initial sample and prescription demand was required to ensure adequate safety stock levels and to maintain the ability to support increased demand, as necessary. Until our prescription and sample demands are at a level where we can fully utilize the capacity committed to our contract manufacturing facilities, we will continue to experience underutilization of our production capacity. In addition, as we adjust production levels in certain periods to manage our inventory levels, we may incur additional charges for excess capacity which will negatively impact our gross margins.

Royalty Expense. Royalty expense increased to $0.6 million for the six months ended June 30, 2011 from $0.4 million for the six months ended June 30, 2010. Royalty expense represents the amortization of a $4.0 million milestone payment we made in connection with the asset purchase agreement with Aradigm payable on the first commercial sale of Sumavel DosePro, which occurred in January 2010, as well as royalties payable to Aradigm from net sales of Sumavel DosePro during the period. The $0.2 million increase in royalty expense is primarily due to the increase in

sales.

Research and Development Expenses. Research and development expenses increased to $17.4 million for the six months ended June 30, 2011 compared to $11.4 million for the six months ended June 30, 2010. This increase of $6.0 million primarily was due to:

- an increase of $7.1 million in research and development costs as a result of the ongoing Phase 3 clinical trials for Zohydro, which were initiated in March 2010; offset by

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- a decrease of $1.1 million in research and development costs incurred for the Phase 4 study conducted for Sumavel DosePro as it was completed in the second quarter of 2010 and other costs related to product development.

Selling, General and Administrative Expenses. Selling, general and administrative expenses increased to $28.0 million for the six months ended June 30, 2011 compared to $25.4 million for the six months ended June 30, 2010. Selling expenses were $21.4 million for the six months ended June 30, 2011 compared to $21.6 million for the six months ended June 30, 2010. General and administrative expenses were $6.5 million for the six months ended June 30, 2011 compared to $3.8 million for the six months ended June 30, 2010. The increase of $2.6 million in selling, general and administrative expenses primarily was due to:

- an increase of $2.7 million of general and administrative expenses as a result of the costs we incurred for operating as a public company. These costs include salaries and related expenses, stock-based compensation charges, legal and consultant fees, accounting fees, director fees, increased directors and officers insurance premiums and fees for investor relations services; offset by

- a decrease of $0.1 million in sales and marketing expense primarily as a result of a decrease in sampling efforts and other advertising and promotion activities relative to the levels of activity during the initial launch in the first half of 2010 of Sumavel DosePro, partially offset by increased services fees payable to our co-promotion partner from higher net product revenues over the prior quarter

Interest Income. Interest income increased to $19,000 for the six months ended June 30, 2011 compared to $3,000 for the six months ended June 30, 2010. This increase of $16,000 was due primarily to the increase in average cash and cash equivalent balances.

Interest Expense. Interest expense increased to $2.5 million for the six months ended June 30, 2011 compared to $1.5 million for the six months ended June 30, 2010. This increase of $1.0 million was primarily due to higher debt balances in connection with the amended Oxford/SVB loan agreement.

Change in Fair Value of Warrant Liability. During the six months ended June 30, 2011 there was no warrant liability outstanding due to the termination or conversion of the preferred stock warrants to warrants of common stock in connection with the initial public offering in November 2010. The change in fair value of warrant liability during the six months ended June 30, 2010 of $13.0 million is due to the increase in fair value of convertible preferred stock during the period.

Other Income (Expense). Other income (expense) decreased to $0.1 million of expense for the six months ended June 30, 2011 compared to $0.1 million of income for the six months ended June 30, 2010. This decrease was due to foreign currency transaction losses which primarily related to the settlement of our liabilities payable in Euro and U.K. pounds sterling.

Liquidity and Capital Resources

We have experienced net losses and negative cash flow from operations since inception, and as of June 30, 2011, had an accumulated deficit of $236.3 million, and expect to continue to incur net losses and negative cash flow from operations for at least the next several years primarily as a result of, among other things, the development expenses in connection with our clinical trials and pre-clinical studies for Zohydro and the cost of the sales and marketing expenses associated with Sumavel DosePro.

As of June 30, 2011, we had cash and cash equivalents of $7.7 million. On June 30, 2011, we amended certain terms of our loan agreement with Oxford and SVB including the deferral of principal repayment to commence on February 1, 2012 and in July 2011, we entered into equity and royalty financing agreements with Cowen Royalty, pursuant to which we borrowed $30.0 million from Cowen Royalty and sold $1.5 million of our common stock to Cowen Royalty resulting in $29.5 million in net proceeds to us. Although it is difficult to predict future liquidity requirements, based on our current operating plan we believe that our cash and cash equivalents as of June 30, 2011, together with future revenues, the proceeds from the recently completed equity and royalty financing with Cowen Royalty and the deferment of principal payments under the amended Oxford/SVB loan agreement, and borrowings available under our $10.0 million revolving credit facility, will be sufficient to fund our operations through the fourth quarter of 2011. We will need to obtain additional capital to finance our operations beyond that point. We intend to raise additional capital through debt or equity financings or through collaborations or partnerships with other companies. If we are not be able to raise additional capital on terms acceptable to us, or at all, as and when needed, we may be required to reduce or curtail our operations and costs, and we may be unable to continue as a going concern.

In its report on our consolidated financial statements for the year ended December 31, 2010, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern. A going concern opinion

means, in general, that our independent registered public accounting firm has substantial doubt about our ability to continue our operations without continuing infusions of capital from external sources and this opinion could impair our ability to finance our operations through the sale of debt or equity securities or commercial bank loans.

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Since inception, our operations have been financed primarily through equity and debt financings, the issuance of convertible notes and payments received from Astellas under our co-promotion agreement. Through June 30, 2011, we received aggregate net cash proceeds of approximately $215.1 million from the sale of shares of our preferred and common stock, including the following recent financing transactions:

- in July 2010, we issued unsecured convertible promissory notes in an aggregate amount of $15.0 million under which all the outstanding principal and interest automatically converted to 3,873,756 shares of common stock upon the completion of our initial public offering; and

- in November 2010 and December 2010, we issued and sold a total of 14,436,493 shares of common stock in our initial public offering, including shares issued upon the exercise of the underwriters overallotment option, for aggregate net proceeds of $51.7 million.

On June 30, 2011, we amended the existing loan agreement with Oxford and SVB to provide for, among other things, the addition of intellectual property to the collateral securing the Oxford/SVB loan and deferral of principal repayment to commence on February 1, 2012. In connection with entering into the amended Oxford/SVB loan agreement, we issued to Oxford and SVB warrants exercisable into an aggregate of 26,455 shares of our common stock. The warrants are exercisable at $3.78 per share of common stock and have a term of 7 years. In addition, in July 2011 we issued and sold $388,601 shares of our common stock to Cowen Royalty in connection with the equity and royalty financing for net proceeds of $1.5 million to us. The Amended Oxford/SVB Agreement consists of a $25.0 million term loan and a $10.0 million revolving credit facility. The obligations under the amended Oxford/SVB loan agreement are collateralized by our intellectual property (including among other things, copyrights, patents, patent applications, trademarks, service marks and trade secret rights) and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash).

The amended Oxford/SVB loan agreement includes financial covenants requiring that we achieve, as of the last day of each month measured on a trailing three-month basis, actual revenue of at least a specified percentage of our projected revenue as provided to Oxford and SVB in the event we fail to maintain a liquidity ratio (defined, in general, as the ratio of (a) cash and cash equivalents deposited with SVB plus unused borrowing capacity under that agreement to (b) all debt, capital lease obligations and contingent obligations owed to the lenders) of 1.25 to 1.00. The agreement also includes a covenant that the audit report accompanying our year-end consolidated financial statements for fiscal year 2010 and thereafter not include a going concern qualification. In March 2011, we obtained a waiver from Oxford and SVB for the breach caused by the receipt of the 2010 audit report from our independent registered public accounting firm, which includes a modification of their standard report for the going concern uncertainty. In addition, the amended Oxford/SVB loan agreement prohibits us from (1) incurring any debt other than, among other things, debt under the amended Oxford/SVB loan agreement, and (2) entering into mergers with, or acquisitions of all or substantially all the assets of, another entity with a value in excess of $100,000, and also prohibits the occurrence of a change in control of our company as defined in the amended Oxford/SVB loan agreement. The agreement provides that an event of default will occur if, among other customary events of default, (1) there is a material adverse change in our business, operations or condition (financial or otherwise) or material impairment in the prospects of us repaying any portion of our obligations under the agreement, (2) there is a material impairment in the value of the collateral pledged to secure our obligations under the agreement, (3) we default in the payment of any amount payable under the agreement when due, or (4) we breach any covenant in the agreement (subject to a grace period in some cases). The $25.0 million term loan bears an interest rate of 12.06% per annum. Payments consist of monthly interest only payments for the first 12 months followed by principal and interest payments for the subsequent 30 months. The term loan requires a final payment of $1.2 million, in addition to the repayment of unpaid principal, at the loan maturity date, which is January 1, 2014. We have the option to prepay the outstanding balance of the term loan in full subject to a prepayment fee of either 2% or 3% of the principal amount being prepaid depending upon when the prepayment occurs as well as the $1.2 million final payment. Under the terms of the revolving credit facility, we may borrow up to $10.0 million, but not more than a specified percentage of our eligible accounts receivable and inventory balances (as defined in the agreement). Amounts outstanding under the revolving credit facility accrue interest payable monthly at a floating rate per annum equal to the greater of 3.29% above SVB s prime rate or 7.29%. In addition, we pay a monthly fee equal to 0.5% per annum of the average unused portion of the revolving credit facility. If the revolving credit facility is terminated, a final payment is required in the amount of $0.1 million, $0.2 million or $0.3 million depending upon when the termination occurs. The amended Oxford/SVB loan agreement matures on the earliest of January 1, 2014, the occurrence of an event of default resulting in our obligations becoming due and payable in accordance with the amended Oxford/SVB loan agreement or the date of any prepayment of all outstanding obligations under the Amended Oxford/SVB loan agreement, at which time a final payment of $0.1 million, plus all unpaid principal, must be paid in full. As of June 30, 2011, we had borrowed $3.7 million under the revolving credit facility.

On July 18, 2011, we closed the royalty financing agreement with Cowen Royalty, or the financing agreement. Under the terms of the financing agreement, we borrowed $30.0 million and we are obligated to repay such borrowed amount together with a specified return to Cowen Royalty, through the payment of tiered royalties ranging from .5% to 5% of our direct product sales, co-promotion

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revenues and out-license revenues, or collectively, revenue interest that we may record or receive as a result of worldwide commercialization of our products including Sumavel DosePro, Zohydro and other future products.

We are also obligated to make three fixed payments of $10 million on (or before at our option) each of January 31, 2015, January 31, 2016 and January 31, 2017. Prepayment requires the consent of the lenders under the amended Oxford/SVB loan agreement while balances remain outstanding under that facility.

We have the option to terminate the financing agreement at our election in connection with a change of control of our company, upon the payment of a base amount of $52.5 million, or, if higher, an amount that generates a 19% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the revenue interest and principal payments received by Cowen Royalty up to the date of prepayment.

Cowen Royalty has the option to terminate the financing agreement at its election in connection with a change of control of our company (which includes the sale, transfer, assignment or licensing of our rights in the United States to either Sumavel DosePro or Zohydro), a bankruptcy event with respect to our company or an event of default under the financing agreement. Upon such a termination by Cowen Royalty, we are obligated to make a payment of a base amount of $45 million, or, if higher, an amount that generates a 17% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the Revenue Interest and principal payments received by Cowen Royalty up to the date of prepayment.

Unless terminated earlier as discussed above, the financing agreement terminates on March 31, 2018.

We depend in part upon borrowings available under the revolving credit facility provided under the amended Oxford/SVB loan agreement, the term loan obtained under the Oxford/SVB loan agreement and the borrowed amount under the Cowen Royalty financing agreement to finance our ongoing operations. Accordingly, any termination of those agreements, or any requirement that we repay any of our outstanding term loans or the borrowed amount under the financing agreement, whether as the result of our default under the applicable agreement or otherwise, could have a material adverse effect on our business, results of operations and financial condition.

Cash and Cash Equivalents. Cash and cash equivalents totaled $7.7 million and $49.2 million at June 30, 2011 and December 31, 2010, respectively.

The following table summarizes our cash flows used in operating, investing and financing activities for the six months ended June 30, 2011 and 2010:

	Six Months Ended June 30,	
	2011	2010
	(In Thousands)	
Statement of Cash Flows Data:		
Total cash provided by (used in):		
Operating activities	$ (40,507)	$ (35,821)
Investing activities	(366)	(1,162)
Financing activities	(627)	(3,435)
Decrease in cash and cash equivalents	$ (41,500)	$ (40,418)

Operating Activities. Net cash used in operating activities was $40.5 million and $35.8 million for the six months ended June 30, 2011 and 2010, respectively. Net cash used for the six months ended June 30, 2011and 2010 primarily reflects the use of $34.4 million and $34.0 million, respectively for operations (excluding non-cash items), investments of $0.3 million and $2.2 million, respectively, in commercial inventory of Sumavel DosePro, and cash used of $5.8 million and cash provided of $0.4 million, respectively, for other working capital uses.

Investing Activities. Net cash used in investing activities was $0.4 million and $1.2 million for the six months ended June 30, 2011 and 2010, respectively. These amounts are the result of the purchase of property and equipment primarily for use in manufacturing Sumavel DosePro.

We expect to incur capital expenditures of approximately $0.4 million to $0.9 million in the last six months of 2011. These planned capital expenditures primarily relate to further investments in our manufacturing operations toward enhancing our existing manufacturing technology and equipment.

Financing Activities. Net cash used in financing activities was $0.6 million and $3.4 million for six months ended June 30, 2011 and 2010, respectively. Net cash used in financing activities for the six months ended June 30, 2011 relates to the repayment of

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the GE Capital equipment financing of $0.6 million, payment of fees to Oxford in connection with the amended Oxford/SVB loan agreement of $0.1 million and net proceeds from our revolving credit facility of $0.1 million. Net cash used in financing activities for the six months ended June 30, 2010 relates to payments on borrowings of debt.

Our sources of liquidity include our cash balances, cash receipts from the sale of Sumavel DosePro, our debt facilities, and the proceeds from the recently completed equity and royalty financing with Cowen Royalty. As of June 30, 2011, we had $7.7 million in cash and cash equivalents and in July 2011, we received an additional $29.5 million in cash under our equity and royalty financing with Cowen Royalty. Other potential sources of near-term liquidity include (i) entering into a commercialization agreement for Zohydro or a licensing arrangement on our DosePro technology, (ii) equity, debt or other financing or (iii) leveraging our sales force capacity to promote a new product.

Since inception, our operations have been financed primarily through equity and debt financings, the issuance of convertible notes and payments received from Astellas under our co-promotion agreement. Through June 30, 2011, we received aggregate net cash proceeds of approximately $263.9 million from the sale of shares of our preferred and common stock, the issuance of a notes and payments from collaborators. Although we will continue to be opportunistic in our efforts to obtain cash, there is no guarantee that additional funding will be available or that, if available, such funding will be adequate or available on terms that we or our stockholders view as favorable. In addition, as a result of our outstanding loan with Oxford and SVB, our ability to engage in debt financing transactions is subject to certain limitations and certain debt financing transactions, if consummated, may accelerate our repayment obligations to Oxford and SVB.

Successful transition to profitability is dependent upon achieving a level of product revenues adequate to support our cost structure. We will continue to monitor and evaluate our sales progress, the level of our research, development, manufacturing, sales and marketing and general and administrative expenditures and may adjust such expenditures based upon a variety of factors, such as our available cash, our ability to obtain additional cash, the results and progress of our Sumavel DosePro commercialization efforts, results and progress in our clinical program, the time and costs related to clinical trials and regulatory decisions, as well as the U.S. economic environment.

As described above, under our amended Oxford/SVB loan agreement, we are subject to financial covenants that require us to achieve certain revenue targets in the event we fail to maintain a liquidity ratio (defined, in general, as the ratio of (a) cash and cash equivalents deposited with SVB plus unused borrowing capacity under that agreement to (b) all debt, capital lease obligations and contingent obligations owed to the lenders) of 1.25 to 1.00 and we are also subject to other covenants and obligations under that agreement. Likewise, the amended Oxford/SVB loan agreement permits the lenders to demand the immediate repayment of all borrowings and other amounts outstanding thereunder if, among other customary events of default, the lender determines, in its sole discretion that a material adverse change with respect to us has occurred. As noted above, we have agreed to specified positive and negative covenants under the financing agreement with Cowen Royalty and upon a termination by Cowen Royalty, we are obligated to make a payment of a base amount of $45.0 million, or, if higher, an amount that generates a 17% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the payments received by Cowen Royalty up to the date of prepayment. If we were required to accelerate the payment of these amounts upon a default, we would be required to find an alternate source of capital from which to draw funds and there can be no assurances that we would be able to do so on terms acceptable to us, or at all.

If we fail to pay amounts owing under either our loan or financing agreements when due, if we breach our other covenants or obligations under either of these agreements, or if other events of default under either of these agreements occur, the applicable lenders would be entitled to demand immediate repayment of all borrowings and other obligations thereunder and to seize and sell the collateral pledged as security under the agreements to satisfy those obligations. If we were to breach our covenants and obligations and we were unable to obtain a waiver or amendment from the lender, we would be required to seek additional equity or debt financing to refinance our obligations under the agreement. Additional debt or equity financing may not be available to us in amounts or on terms we consider acceptable, or at all. In that regard, we have from time to time been required to obtain waivers and amendments under our debt instruments in order to avoid breaches or other defaults. For example, in each of 2009, 2010 and 2011 we were required to obtain amendments or waivers under our credit facilities.

We cannot be certain if, when and to what extent we will generate positive cash flow from operations from the commercialization of our product and, if approved, product candidates. We expect our development and commercialization expenses to be substantial and to increase over the next few years as we continue to grow the Sumavel DosePro brand and continue to advance our Zohydro product through Phase 3 clinical trials and potentially through commercialization.

Although it is difficult to predict future liquidity requirements, based on our current operating plan we believe that our cash and cash equivalents as of June 30, 2011, together with future product revenue, our recently completed equity and royalty financing with Cowen Royalty , and borrowings available under our $10.0 million revolving credit facility, will be sufficient to fund our operations through the fourth quarter of 2011. We will need to obtain additional capital to finance our operations beyond that point through

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public or private equity or debt financings. Although we are currently not a party to any agreement or letter of intent with respect to potential investments in, or acquisitions of, businesses, services or technologies, we may enter into these types of arrangements in the future, which could also require us to seek additional equity or debt financing. There can be no assurance that we will be able to raise additional funds from any of these sources on terms we deem acceptable, or at all. In addition, future issuance of equity, convertible or other equity-linked securities could materially dilute the ownership interests of holders of our common stock and additional debt financing could result in a material increase in the amount of cash necessary to fund debt service payments and also could require that we comply with financial and other covenants that limit our flexibility and operations. In addition, the fact that we have pledged substantially all of our assets to secure our existing loan facilities will likely increase the cost, perhaps substantially, of any additional debt financing we may obtain or prevent us from obtaining additional debt financing altogether.

Recent Accounting Pronouncements

In October 2009, the Financial Accounting Standards Board (the FASB) issued an Accounting Standard Update which replaced the concept of allocating revenue consideration amongst deliverables in a multiple-element revenue arrangement according to fair value with an allocation based on selling price. The amended guidance also establishes a hierarchy for determining the selling price of revenue deliverables sold in multiple element revenue arrangements. The selling price used for each deliverable will be based on vendor-specific objective evidence (VSOE) if available, third-party evidence if VSOE is not available, or management s estimate of an element s stand-alone selling price if neither VSOE nor third-party evidence is available. The amendments in this update also require an allocation of selling price amongst deliverables be performed based upon each deliverable s relative selling price to total revenue consideration, rather than on the residual method previously permitted. The updated guidance is effective for the first annual reporting period beginning on or after June 15, 2010, and may be applied retrospectively for all periods presented or prospectively to arrangements entered into or materially modified after the adoption date. We prospectively adopted the updated guidance on January 1, 2011 and will apply the amended guidance to revenue arrangements containing multiple deliverables that are entered into or significantly modified on or after January 1, 2011. We will now allocate revenue consideration, excluding contingent consideration, based on the relative selling prices of the separate units of accounting contained within an arrangement containing multiple deliverables. Selling prices are determined using fair value, when available, or our estimate of selling price when fair value is not available for a given unit of accounting. As we did not enter into any new collaborations or materially modify any existing collaborations, adoption of this guidance had no impact on our results of operations for the six months ended June 30, 2011.

In March 2010, the FASB Emerging Issues Task Force (EITF) ratified a new accounting standard which amends guidance on the milestone method of revenue recognition. The EITF concluded that the milestone method is a valid application of the proportional performance model when applied to research or development arrangements. Milestones, as defined per the revised guidance, are (1) events that can only be achieved in whole or in part on either the entity s performance or on the occurrence of a specific outcome resulting in the entity s performance (2) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and (3) that would result in additional payments being due to us, we evaluate events under this guidance at the inception of an arrangement to determine the existence of milestones and if they are substantive. This standard allows an entity to make an accounting policy election to recognize a payment that is contingent upon the achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. This standard is effective for fiscal years beginning on or after June 15, 2010 with early adoption permitted. The guidance may be applied prospectively for milestones achieved after the adoption date or retrospectively for all periods presented. We adopted this guidance on January 1, 2011 on a prospective basis. Adoption of this guidance did not have a material impact on our results of operations.

In June 2011, the FASB issued an Accounting Standards Update which requires entities to present reclassification adjustments included in other comprehensive income on the face of the financial statements and allows entities to present the total of comprehensive income, the components of net income and the components of other comprehensive income either in a single continuous statement of comprehensive income or in two separate consecutive statements. It also eliminates the option for entities to present components of other comprehensive income as part of the statement of changes to stockholders equity. The updated guidance is effective for fiscal and interim periods beginning after December 15, 2011, with early adoption permitted. The adoption of this updated standard is not expected to have a material effect on our results of operations.

Off-Balance Sheet Arrangements

We have not engaged in any off-balance sheet activities.

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Item 3. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our cash and cash equivalents as of June 30, 2011 consisted primarily of cash and money market funds. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. Instruments that meet this objective include commercial paper, money market funds and government and non-government debt securities. Some of the investment securities available-for-sale that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment securities available-for-sale to fluctuate. To minimize this risk, we intend to continue to maintain our portfolio of cash and money market funds. Due to the short-term nature of our investments and our ability to hold them to maturity, we believe that there is no material exposure to interest rate risk.

Our $10.0 million revolving credit facility with Oxford and SVB bears interest at the greater of 3.29% above SVB s prime rate or 7.29%. As of June 30, 2011, we had $3.6 million outstanding on this revolving credit facility.

Foreign Exchange Risk

All of the revenues we have generated to date have been paid in U.S. dollars and we expect that our revenues will continue to be generated primarily in U.S. dollars for at least the next several years. Payments to our material suppliers and contract manufactures are denominated in the Euro and U.K. pounds sterling, thereby increasing our exposure to exchange rate gains and losses on non-U.S. currency transactions. Foreign currency gains and losses associated with these expenditures have not been significant to date. However, fluctuations in the rate of exchange between the U.S. dollar and these or other foreign currencies could adversely affect our financial results in the future, particularly to the extent we increase production to support Sumavel DosePro sales demands. For the six months ended June 30, 2011, approximately $5.3 million (based on exchange rates as of June 30, 2011) of our materials and contract manufacturing costs were denominated in foreign currencies. We do not currently hedge our foreign currency exchange rate risk. We intend to evaluate various options to mitigate the risk of financial exposure from transacting in foreign currencies in the future.

Item 4. Controls and Procedures

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the timelines specified in the Securities and Exchange Commission s rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Securities and Exchange Commission Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of June 30, 2011 at the reasonable assurance level.

This Quarterly Report on Form 10-Q does not include a report of management s assessment regarding internal control over financial reporting or an attestation report of the Company s registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Disclosure Controls and Procedures

There were no changes in our internal controls over financial reporting during the fiscal quarter ended June 30, 2011 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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PART II OTHER INFORMATION

Item 1. Legal Proceedings

We are not currently a party to any legal proceedings.

Item 1A. Risk Factors

We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business prospects, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Quarterly Report on Form 10-Qand our other public filings with the SEC. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

We have marked with an asterisk (*) those risk factors that reflect substantive changes from the risk factors included in our previously filed Annual Report on Form 10-K for the year ended December 31, 2010.

Risks Related to Our Business and Industry

We will require additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts. *

Our operations have consumed substantial amounts of cash since inception. To date, our operations have been primarily financed through the proceeds from the issuance of our common and preferred stock, including the proceeds from our initial public offering completed in November 2010, and borrowings under our loan agreements with Cowen Healthcare Royalty Partners II, L.P, or Cowen Royalty, Oxford Finance LLC, as successor in interest to Oxford Finance Corporation, or Oxford, Silicon Valley Bank, or SVB, and General Electric Capital Corporation, or GE Capital. We believe, based on our current operating plan, that our cash and cash equivalents, future revenues, availability under our debt facilities as of June 30, 2011 and the recently completed royalty financing with Cowen Royalty and amended loan agreement with Oxford and SVB to defer principal payments to February 2012, will be sufficient to fund our operations through the fourth quarter of 2011. We will need to obtain additional funds to finance our operations beyond that point in order to:

- maintain and continue to increase our sales and marketing activities for Sumavel DosePro;
- qualify secondary sources for the manufacturing of Sumavel DosePro;
- fund our operations, continue to conduct clinical trials of Zohydro, initiate clinical trials for Relday and fund development of any other product candidate to support potential regulatory approval of marketing applications; and
- commercialize any of our product candidates or any products or product candidates that we may develop, in-license or otherwise acquire, if any of these product candidates receive regulatory approval.

In addition, our estimates of the amount of cash necessary to fund our business and development and commercialization activities may prove to be wrong, and we could spend our available financial resources much faster than we currently expect. Our future funding requirements will depend on many factors, including, but not limited to:

the commercial success of Sumavel DosePro;

the timing of regulatory approval, if granted, of Zohydro or any other product candidates;

the rate of progress and cost of our clinical trials and other product development programs for Zohydro, Relday and our other product candidates and any other product candidates that we may develop, in-license or acquire;

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with Sumavel DosePro, Zohydro, Relday and any of our other product candidates;

the costs and timing of completion of outsourced commercial manufacturing supply arrangements for any product candidate;

the costs of maintaining and expanding our sales and marketing infrastructure or establishing distribution capabilities, should we elect to do so;

the effect of competing technological and market developments; and

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the terms and timing of any additional collaborative, licensing, co-promotion or other arrangements that we may establish.

Until we can generate a sufficient amount of product revenue and cash flow from operations and achieve profitability, we expect to finance future cash needs through public or private equity offerings, debt financings, receivables financings or corporate collaboration and licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unsuccessful in raising additional required funds, we may be required to significantly delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts, or cease operating as a going concern. We also may be required to relinquish, license or otherwise dispose of rights to product candidates or products that we would otherwise seek to develop or commercialize ourselves on terms that are less favorable than might otherwise be available. If we raise additional funds by issuing equity securities, substantial dilution to existing stockholders would result. If we raise additional funds by incurring debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business. If we are unable to maintain sufficient financial resources, including by raising additional funds when needed, our business, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our consolidated financial statements, and it is likely that investors will lose all or a part of their investment.

We are largely dependent on the commercial success of Sumavel DosePro and although we have generated revenue from sales of Sumavel DosePro, we may never become profitable. *

We anticipate that, for at least the next several years, our ability to generate revenues and become profitable will depend in large part on the commercial success of our only marketed product, Sumavel DosePro, which in turn, will depend on several factors, including our ability to:

successfully maintain and increase market demand for, and sales of, Sumavel DosePro through our sales and marketing efforts and those of Astellas Pharma US, Inc., or Astellas, our co-promotion partner;

obtain greater acceptance of Sumavel DosePro by physicians and patients;

maintain adequate levels of coverage and reimbursement for Sumavel DosePro from commercial health plans and government health programs, which we refer to collectively as third-party payors, particularly in light of the availability of other branded and generic competitive products;

maintain compliance with regulatory requirements;

establish and maintain agreements with wholesalers and distributors on commercially reasonable terms;

maintain commercial manufacturing arrangements with third-party manufacturers as necessary to meet commercial demand for Sumavel DosePro and continue to manufacture commercial quantities at acceptable cost levels; and

successfully maintain intellectual property protection for Sumavel DosePro.

We cannot be certain that our continued marketing of Sumavel DosePro will result in increased demand for, and sales of, the product. For example, while we have generally experienced monthly growth in total prescriptions from the launch of Sumavel DosePro in January 2010 through June 30, 2011, we have at certain times experienced a reduction in total and new prescriptions month over month. If we fail to successfully increase sales of Sumavel DosePro, we may be unable to generate sufficient revenues to grow or sustain our business and we may never become profitable, and our business, financial condition and results of operations will be materially adversely affected.

We are at an early stage of commercialization and have a history of net losses and negative cash flow from operations. We cannot predict if or when we will become profitable and anticipate that our net losses and negative cash flow from operations will continue for at least the

next several years. *

We were organized in 2006, have a limited operating history and there is little historical basis upon which to assess how we will respond to competitive, economic or technological challenges. Our business and prospects must be considered in light of the risks and uncertainties frequently encountered by pharmaceutical companies in the early stages of commercialization.

We have generated substantial net losses and negative cash flow from operations since our inception in 2006. For example, for 2009, 2010 and the six months ended June 30, 2011, we incurred net losses of $45.9 million, $73.6 million and $38.2 million, respectively, our net cash used in operating activities was $32.4 million, $72.0 million, and $40.5 million, respectively, and, at June 30, 2011, our accumulated deficit was $236.3 million. We expect our losses and negative cash flow to continue for at least the next several years as a result of the development expenses in connection with our ongoing clinical development for Zohydro, the initiation of clinical development for Relday and the cost of the sales and marketing expense associated with Sumavel DosePro. Our ability to generate revenues from Sumavel DosePro or any of our product candidates will depend on a number of factors, including, in the case

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of Sumavel DosePro, the factors described in the following two risk factors and, in the case of our product candidates, our ability to successfully complete clinical trials, obtain necessary regulatory approvals and negotiate arrangements with third parties to help finance the development of, and market and distribute, any product candidates that receive regulatory approval. In addition, we will be subject to the risk that the marketplace will not accept our products.

Because of the numerous risks and uncertainties associated with our product development and commercialization efforts, we are unable to predict the extent of our future losses or when or if we will become profitable and it is possible we will never become profitable. Our failure to increase sales of Sumavel DosePro or to successfully commercialize any of our product candidates that may receive regulatory approval would likely have a material adverse effect on our business, results of operations, financial condition and prospects and could result in our inability to continue operations.

We may not be successful in executing our sales and marketing strategy for the commercialization of Sumavel DosePro and, as part of this strategy, we are dependent on our collaboration with Astellas to promote Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists. If we are unable to successfully execute such strategy, we may not be able to generate significant revenue.

Prior to the launch of Sumavel DosePro in January 2010, we built a commercial sales and marketing organization including sales, marketing, communications, managed markets, trade and distribution functions, which is now focused exclusively on marketing and selling Sumavel DosePro primarily to physicians, nurses and other healthcare professionals in the United States. Our field sales force includes approximately 80 sales representatives who are promoting Sumavel DosePro primarily to neurologists and other key prescribers of migraine medications, including headache clinics and headache specialists in the United States. We have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. Although we believe we have adequately sized our sales force in order to reach this targeted audience, we may either increase or decrease the size of our sales force in the future based upon market conditions and actual sales performance. In addition, we could lose sales personnel or the performance of our sales personnel as measured by actual sales may be disappointing. Many of our competitors have significantly larger sales and marketing organizations, and significantly greater experience than we do in selling, marketing and distributing pharmaceuticals, and we may not be able to compete successfully with them with the commercial infrastructure we have developed.

To complement our sales force, we entered into an exclusive co-promotion agreement with Astellas in July 2009 under which Sumavel DosePro is also being promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists, or collectively the Astellas Segment, in the United States by approximately 400 Astellas sales representatives. Although the agreement stipulates annual minimum levels of sales effort, we have limited control over the amount and timing of resources that Astellas dedicates to the promotion of Sumavel DosePro, and we do not hire, train or manage such resources. For example, Astellas could reduce the number of its sales representatives promoting Sumavel DosePro while still complying with these minimum requirements. The ability to generate revenue from our arrangement with Astellas depends on Astellas efforts in promoting Sumavel DosePro and its ability to achieve broad market acceptance and prescribing of Sumavel DosePro in the Astellas Segment.

We are subject to a number of additional risks associated with our dependence on our co-promotion arrangement with Astellas, including:

- Astellas could fail to devote sufficient resources to the promotion of Sumavel DosePro, including by failing to develop, deploy or expand its sales force as necessary;
- Astellas could terminate the co-promotion agreement for any or no cause upon 180-days written notice at any time, which may negatively impact our ability to generate, or prevent us from generating, sufficient revenue;
- Astellas could fail to comply with applicable regulatory guidelines with respect to the promotion of Sumavel DosePro, which could result in administrative or judicially imposed sanctions, including warning letters, civil and criminal penalties, and injunctions; and
- disputes regarding the co-promotion agreement that negatively impact or terminate the commercialization efforts of Astellas may negatively impact or prevent the generation of sufficient revenue or result in significant litigation or arbitration.

For the three and six months ended June 30, 2011, the Astellas Segment represented approximately 40% of our net product revenue. Under the terms of the co-promotion agreement, Astellas could terminate the agreement for any or no reason upon 180-days written notice. The co-promotion agreement may also be terminated by Astellas or us for a number of other specified reasons, some of which are beyond our control. In the event Astellas terminates the agreement for specified reasons or a material uncured breach by us of our minimum sales effort obligations, we would be required to pay Astellas only the first of the two annual tail payments described above.

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In addition, either party may terminate the agreement based upon a failure of the Sumavel DosePro brand to achieve certain minimum sales levels in 2011 as defined in the co-promotion agreement. Based on our net product revenue through June 30, 2011, we do not expect to meet these 2011 minimum sales levels for Sumavel DosePro, and therefore expect that both we and Astellas will have the right to terminate the agreement on this basis. If either party were to exercise this termination right, it must provide 90 days written notice to the other party after the actual net sales of Sumavel DosePro through December 31, 2011 have been ascertained. In the event of such a termination relating to sales levels of Sumavel DosePro, we would be required to make two annual tail payments calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment.

In addition, Astellas may terminate the co-promotion agreement in the event we undergo a change of control (as defined in the agreement), if a governmental authority takes action that prevents or makes it unlawful for Astellas to perform its obligations under the agreement, in the event of our inability to supply commercial product, under certain circumstances where a third party asserts that the making or selling of Sumavel DosePro infringes the intellectual property rights of a third party, if we materially breach our minimum sales effort obligations and do not cure that breach within a specified period, upon the occurrence of a large scale recall or market withdrawal of Sumavel DosePro, upon a material uncured breach by us or in the event of our insolvency or bankruptcy or other event which affects our ability to perform our obligations under the agreement. Accordingly, we cannot assure you that Astellas will not terminate the agreement under these circumstances. As an alternative to termination, we and Astellas could agree to amend or otherwise restructure the current co-promotion agreement. Such amendment or restructuring could change the financial terms of our agreement, change our respective minimum sales force requirements, or otherwise materially alter our co-promotion relationship. Such an amendment or restructuring could require us to expand our sales force or otherwise invest significant additional financial resources in order to adequately support the successful sales and marketing of Sumavel DosePro.

In addition, our co-promotion agreement with Astellas expires on June 30, 2013, subject to a one-year extension at the option of Astellas. We cannot assure you that Astellas will enter into any extension of the agreement or, if it does so, that it will not condition any such extension upon changes in the agreement that could have a material adverse effect on us. If Astellas were to terminate the agreement or elect not to extend the agreement upon its expiration, we would lose the efforts of their sales force, and we would need to make arrangements with another third party to replace Astellas sales force, or significantly expand our sales and marketing organization. We may not be able to enter into such arrangements with third parties in a timely manner, on acceptable terms or at all. To the extent that we enter into another co-promotion or other licensing arrangement, our portion of retained product revenues is likely to be lower than if we directly marketed and sold Sumavel DosePro solely on our own, and a portion of those revenues generated will depend upon the efforts of such third parties similar to our dependence on Astellas, and these efforts may not be successful. If our co-promotion agreement with Astellas is terminated and we are unable to find another partner for the promotion of Sumavel DosePro in the primary care segment in the United States, we may not be able to expand our own sales and marketing capabilities to cover this segment and any such expansion could, in any event, substantially increase our expenses and capital requirements that we might not be able to fund.

If we are unable to successfully implement our commercialization plans and drive adoption by patients and physicians of Sumavel DosePro through our sales, marketing and commercialization efforts and the efforts of Astellas, then we will not be able to generate significant revenue which will have a material adverse effect on our business, results of operations, financial condition and prospects.

If Sumavel DosePro, Zohydro, if approved, or any other product candidate for which we receive regulatory approval does not achieve broad market acceptance or coverage by third-party payors, the revenues that we generate will be limited.

The commercial success of Sumavel DosePro, Zohydro, if approved, and any product candidates for which we obtain marketing approval from the U.S. Food and Drug Administration, or FDA, or other regulatory authorities will depend upon the acceptance of these products by physicians, patients, healthcare payors and the medical community. Coverage and reimbursement of our approved product by third-party payors is also necessary for commercial success. The degree of market acceptance of Sumavel DosePro and any other product candidates for which we may receive regulatory approval will depend on a number of factors, including:

- our ability to provide acceptable evidence of safety and efficacy;
- acceptance by physicians and patients of the product as a safe and effective treatment;
- the relative convenience and ease of administration;

the prevalence and severity of adverse side effects;

limitations or warnings contained in a product s FDA-approved labeling;

the clinical indications for which the product is approved;

in the case of product candidates that are controlled substances, the U.S. Drug Enforcement Agency, or DEA, scheduling classification;

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availability and perceived advantages of alternative treatments;

any negative publicity related to our or our competitors products;

the effectiveness of our or any current or future collaborators sales, marketing and distribution strategies;

pricing and cost effectiveness;

our ability to obtain sufficient third-party payor coverage or reimbursement; and

the willingness of patients to pay out of pocket in the absence of third-party payor coverage.

For example, while we believe the needle-free nature of our DosePro technology will appeal to patients, some patients may not react favorably to the subcutaneous delivery of drug products by DosePro. Our experience indicates that some patients will experience pain upon injection with the DosePro technology and/or reactions at the site of injection. Any undesirable side effects have the potential to limit market acceptance of our product candidates.

In addition, products used to treat and manage pain, especially in the case of opioids, are from time to time subject to negative publicity, including illegal use, overdoses, abuse, diversion, serious injury and death. These events have led to heightened regulatory scrutiny. Controlled substances are classified by the DEA as Schedule I through V substances, with Schedule I substances being prohibited for sale in the United States, Schedule II substances considered to present the highest risk of abuse and Schedule V substances being considered to present the lowest relative risk of abuse. Zohydro contains *hydrocodone*, and we anticipate it will be regulated as a Schedule II controlled substance, and despite the strict regulations on the marketing, prescribing and dispensing of such substances, illicit use and abuse of *hydrocodone* is well-documented. Thus, the regulatory approval process and the marketing of Zohydro may generate public controversy that may adversely affect regulatory approval and market acceptance of Zohydro.

Our efforts to educate the medical community and third-party payors on the benefits of Sumavel DosePro, Zohydro, if approved, and any of our product candidates for which we obtain marketing approval from the FDA or other regulatory authorities and gain broad market acceptance may require significant resources and may never be successful. If our products do not achieve an adequate level of acceptance by physicians, third-party payors and patients, we may not generate sufficient revenue from these products to become or remain profitable.

Our business and operations would suffer in the event of system failures.*

Despite the implementation of security measures, our internal computer systems and those of our current and any future partners, contractors and consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. For example, we recently experienced failures in our information systems and computer servers, which may have been the result of a cyber-attack. These failures resulted in an interruption of our normal business operations and required substantial expenditure of financial and administrative resources to remedy. We cannot be sure that similar failures will not occur in the future. System failures, accidents or security breaches can cause interruptions in our operations, and can result in a material disruption of our commercialization activities, drug development programs and our business operations. The loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Similarly, we rely on a large number of third parties to supply components for and manufacture our product and product candidates, warehouse and distribute Sumavel DosePro and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the commercialization of Sumavel DosePro and development of Zohydro could be delayed.

Our short operating history makes it difficult to evaluate our business and prospects.

We commenced our operations on August 25, 2006. Our operations to date have been limited to organizing and staffing our company, scaling up manufacturing operations with our third-party contract manufacturers, building a sales and marketing organization, conducting product

development activities for our product and product candidates, in-licensing rights to Zohydro and Relday, and commercializing Sumavel DosePro. Moreover, Sumavel DosePro is our only product that is approved for sale. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We depend on wholesale pharmaceutical distributors for retail distribution of Sumavel DosePro, and if we lose any of our significant wholesale pharmaceutical distributors, our business could be harmed.

The majority of our sales of Sumavel DosePro are to wholesale pharmaceutical distributors who, in turn, sell the products to pharmacies, hospitals and other customers. Three wholesale pharmaceutical distributors, Cardinal Health, Inc., McKesson Corporation

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and AmerisourceBergen Corporation, individually comprised 46.2%, 34.8% and 11.1%, respectively of our total gross sales of Sumavel DosePro for the six months ended June 30, 2011, which may result in substantial fluctuations in our results of operations from period to period. The loss of any of these wholesale pharmaceutical distributors accounts or a material reduction in their purchases could have a material adverse effect on our business, results of operations, financial condition and prospects.

In addition, these wholesale customers comprise a significant part of the distribution network for pharmaceutical products in the United States. This distribution network has undergone, and may continue to undergo, significant consolidation marked by mergers and acquisitions. As a result, a small number of large wholesale distributors control a significant share of the market. Consolidation of drug wholesalers has increased, and may continue to increase, competitive and pricing pressures on pharmaceutical products. In addition, at times, wholesaler purchases may exceed customer demand, resulting in reduced wholesaler purchases in later quarters, which may result in substantial fluctuations in our results of operations from period to period. We cannot assure you that we can manage these pricing pressures or that wholesaler purchases will not decrease as a result of this potential excess buying.

Our sales can be greatly affected by the inventory levels our wholesalers carry. We monitor wholesaler inventory of Sumavel DosePro using a combination of methods. Pursuant to distribution service agreements with our three largest wholesale customers, we receive inventory level reports. For most other wholesalers where we do not receive inventory level reports, however, our estimates of wholesaler inventories may differ significantly from actual inventory levels. Significant differences between actual and estimated inventory levels may result in excessive production (requiring us to hold substantial quantities of unsold inventory), inadequate supplies of products in distribution channels, insufficient product available at the retail level, and unexpected increases or decreases in orders from our wholesalers.

We expect intense competition, including from generic products, and if our competitors market and/or develop treatments for migraine or pain that are marketed more effectively, approved more quickly than our product candidates or demonstrated to be safer or more effective than our products, our commercial opportunities will be reduced or eliminated

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary therapeutics. We face competition from a number of sources, some of which may target the same indications as our product or product candidates, including large pharmaceutical companies, smaller pharmaceutical companies, biotechnology companies, academic institutions, government agencies and private and public research institutions, many of which have greater financial resources, marketing capabilities, including well-established sales forces, manufacturing capabilities, experience in obtaining regulatory approvals for product candidates and other resources than us. Many large, well-capitalized companies offer products in the United States that compete with Sumavel DosePro. Sumavel DosePro currently competes with branded products in the triptan class such as Imitrex and Treximet marketed by GlaxoSmithKline, or GSK, as well as six other branded triptan therapies being sold by AstraZeneca PLC, Endo Pharmaceuticals Holdings Inc., Johnson & Johnson, Merck & Co., Inc., and Pfizer Inc. Nautilus Neurosciences, Inc. also began selling Cambia, diclofenac potassium for oral solution, for the treatment of migraine in June 2010. In addition, we face competition from generic *sumatriptan* injection, now marketed in the United States as an authorized generic of the Imitrex STATdose System, or Imitrex STATdose, by Par Pharmaceutical Companies, Inc. and Sandoz Inc. (a Novartis AG company). In addition, in June 2010 the FDA approved Alsuma (*sumatriptan* injection), a needle-based autoinjector which was developed and is manufactured by Meridian Medical Technologies (now owned by Pfizer Inc.), and is being distributed by US WorldMeds, LLC. Finally, generic injectable sumatriptan in the form of vials and prefilled syringes is available from a number of pharmaceutical companies, and most recently, the FDA granted approval for a needle-based generic *sumatriptan* auto-injector from Sun Pharmaceutical Industries Limited in June 2011. Although these products may not be directly substituted for Sumavel DosePro, generic versions of *sumatriptan* injection and alternative autoinjector forms of *sumatriptan* injection may reduce the future adoption of Sumavel DosePro by third-party payors and consumers, as financial pressure to use generic products may encourage the use of a generic product over Sumavel DosePro. Sumavel DosePro is currently more expensive on a per dose basis than most of the competing branded and all of the generic triptan products for migraine, which may also limit the coverage and reimbursement by third-party payors, which could adversely affect adoption by physicians and patients.

If approved for the treatment of moderate to severe chronic pain, we anticipate that Zohydro would compete against other marketed branded and generic pain therapeutics. Opioid therapeutics generally fall into two classes: *codeines*, which include *oxycodones* and *hydrocodones,* and *morphines*. Zohydro is a *hydrocodone*, the most commonly prescribed opioid in the United States, and we expect Zohydro will compete with therapeutics within both the *codeine* and *morphine* classes. These therapeutics include both Schedule II and Schedule III products being marketed by companies such as Endo Pharmaceuticals Holdings Inc., Johnson & Johnson, Mallinckrodt Inc., Pfizer, Inc., Purdue Pharma L.P., Teva Pharmaceutical Industries Limited and Watson Pharmaceuticals, Inc.

In addition to already marketed therapeutics, we also face competition from product candidates that are or could be under development by many of the above-mentioned entities and others. For example, there are several products for the treatment of migraine under development by large pharmaceutical companies such as Merck & Co., Inc., and other smaller companies such as NuPathe, Inc. and MAP Pharmaceuticals, Inc. If approved, Zohydro may also compete with at least fifteen opioid product candidates under development, including abuse and diversion resistant formulations of currently available opioids, novel opioids and alternative

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delivery forms of various opioids under development at other pharmaceutical companies, including extended-release *hydrocodone* product candidates being developed by Cephalon, Inc., Egalet A/S and Pfizer, Inc. Zohydro may also face competition from non-opioid product candidates including new chemical entities, as well as alternative delivery forms of non-steroidal anti-inflammatory drugs. These new opioid and non-opioid product candidates are being developed by companies such as Acura Pharmaceuticals, Inc., Altea Therapeutics Corporation, Elite Pharmaceuticals, Inc., Javelin Pharmaceuticals, Inc., Pfizer Inc. and QRxPharma Ltd.

If approved for the treatment of schizophrenia and/or bipolar I disorder, we anticipate that Relday will compete against other marketed, branded and generic, typical and atypical antipsychotics, including both long-acting injectable and oral products. Currently marketed long-acting injectable atypical antipsychotic products include Risperdal Consta, and Invega Sustenna marketed by Johnson & Johnson, and Zyprexa Relprevv marketed by Eli Lilly & Company. Currently approved and marketed oral atypical antipsychotics include Risperdal (*risperidone*) and Invega (*paliperidone*) marketed by Johnson & Johnson, generic *risperidone*, Zyprexa (*olanzapine*) marketed by Eli Lilly and Company, Seroquel (*quetiapine*) marketed by AstraZeneca PLC, Abilify (*aripiprazole*) marketed by BMS/Otsuka Pharmaceutical Co., Ltd., Geodon (*ziprasidone*) marketed by Pfizer, Fanapt (Iloperidone) marketed by Novartis AG, Saphris (*asenapine*) marketed by Schering-Plough, Latuda (*lurasidone*) marketed by Dainippon Sumitomo Pharma, and generic *clozapine*. Finally, in addition to these currently marketed products, we may also face competition from additional long-acting injectable product candidates that could be developed by the large companies listed above, as well and by other pharmaceutical companies such as Alkermes, Inc., NuPathe, Inc., and Vanda Pharmaceuticals, Inc, each of which has announced they are developing long-acting antipsychotic product candidates.

We expect Sumavel DosePro and, if approved, Zohydro and any of our other product candidates to compete on the basis of, among other things, product efficacy and safety, time to market, price, patient reimbursement by third-party payors, extent of adverse side effects and convenience of treatment procedures. One or more of our competitors may develop needle-free injectable products, products to address chronic pain or other products that compete with ours, obtain necessary approvals for such products from the FDA, or other agencies, if required, more rapidly than us or develop alternative products or therapies that are safer, more effective and/or more cost effective than any products developed by us. If any of our product candidates receive the requisite regulatory approval and classification and are marketed, the competition which we will encounter will have, and the competition we are currently encountering with our Sumavel DosePro product has had and will continue to have, an effect on our product prices, market share and results of operations. We may not be able to differentiate any products that we are able to market from those of our competitors, successfully develop or introduce new products that are less costly or offer better results than those of our competitors, or offer purchasers of our products payment and other commercial terms as favorable as those offered by our competitors.

In addition, competitors may seek to develop alternative formulations of our product candidates and/or alternative drug delivery technologies that address our targeted indications. The commercial opportunity for Sumavel DosePro and our product candidates could be significantly harmed if competitors are able to develop alternative formulations and/or drug delivery technologies outside the scope of our products. Compared to us, many of our potential competitors have substantially greater:

- capital resources;
- research and development resources and experience, including personnel and technology;
- drug development, clinical trial and regulatory resources and experience;
- sales and marketing resources and experience;
- manufacturing and distribution resources and experience;
- name recognition; and

resources, experience and expertise in prosecution and enforcement of intellectual property rights.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we are able to or may obtain patent protection or other intellectual property rights that limit or block us from developing or commercializing our product candidates. Our competitors may also develop drugs that are more effective, more useful, better tolerated, subject to fewer or less severe side effects, more widely prescribed or accepted or less costly than ours and may also be more successful than us in manufacturing and marketing their products. If we are unable to compete effectively with the marketed therapeutics of our competitors or if such competitors are successful in developing products that compete with Sumavel DosePro or any of our product candidates that are approved, our business, results of operations, financial condition and prospects may be materially adversely affected.

We are dependent on numerous third parties in our supply chain, all of which are currently single source suppliers, for the commercial supply of Sumavel DosePro and a sole source supplier for clinical supply of Zohydro, and if we experience problems with any of these suppliers, the manufacturing of Sumavel DosePro and Zohydro could be delayed.

While we own most of the specialized equipment used to manufacture critical components of Sumavel DosePro, we do not own or operate manufacturing facilities and currently lack the in-house capability to manufacture Sumavel DosePro, Zohydro or any other

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products or product candidates. Our DosePro device and Sumavel DosePro are manufactured by contract manufacturers, component fabricators and secondary service providers. Final aseptic fill, finish, assembly and packaging of Sumavel DosePro are performed at Patheon UK Limited, Swindon, United Kingdom, a specialist in the aseptic fill/finish of injectables and other sterile pharmaceutical products. In addition, Nypro Limited, located in Bray, Ireland, manufactures the actuator assemblies and injection molded components for our DosePro device and MGlas AG, located in Münnerstadt, Germany, manufactures the specialized glass capsule that houses the *sumatriptan* active pharmaceutical ingredient, or API, in our DosePro device. Each of these manufacturers and each other company that supplies, fabricates or manufactures any component used in our DosePro device is currently the only qualified source of their respective components. We currently rely on Dr. Reddy s Laboratories as the only supplier of *sumatriptan* API for use in Sumavel DosePro. We also outsource all manufacturing and packaging of the clinical trial materials for Zohydro to third parties. Although we plan to qualify additional manufacturers and suppliers of some of the components used in Sumavel DosePro, there can be no assurance that we will be able to do so and the current manufacturers and suppliers of these components will likely be single source suppliers to us for a significant period of time. Similarly, under our license agreement, Elan Pharma International Ltd., or Elan, is the exclusive manufacturer of Zohydro. We may never be able to establish additional sources of supply for Zohydro.

Manufacturers and suppliers are subject to regulatory requirements covering, among other things, manufacturing, testing, quality control and record keeping relating to our product and product candidates, and are subject to ongoing inspections by regulatory agencies. Failure by any of our manufacturers or suppliers to comply with applicable regulations may result in long delays and interruptions to our manufacturing supply, and increase our costs, while we seek to secure another supplier who meets all regulatory requirements. Accordingly, the loss of any of our current third-party manufacturers or suppliers could have a material adverse effect on our business, results of operations, financial condition and prospects.

Reliance on third-party manufacturers and suppliers entails risks to which we would not be subject if we manufactured Sumavel DosePro or our product candidates ourselves, including:

- reliance on the third parties for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreements by the third parties because of factors beyond our control or the insolvency of any of these third parties or other financial difficulties, labor unrest, natural disasters or other factors adversely affecting their ability to conduct their business; and
- the possibility of termination or non-renewal of the agreements by the third parties, at a time that is costly or inconvenient for us, because of our breach of the manufacturing agreement or based on their own business priorities.

If our contract manufacturers or suppliers fail to deliver the required commercial quantities of Sumavel DosePro and its various components, the quantities of Zohydro or any of our other product candidates required for our clinical trials and, if approved, for commercial sale, on a timely basis and at commercially reasonable prices, and we are unable to find one or more replacement manufacturers or suppliers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality, and on a timely basis, we would likely be unable to meet demand for our products and would have to delay or terminate our pre-clinical or clinical trials, and we would lose potential revenue. It may also take a significant period of time to establish an alternative source of supply for our product, product candidates and components and to have any such new source approved by the FDA or any applicable foreign regulatory authorities. Furthermore, any of the above factors could cause the delay or suspension of initiation or completion of clinical trials, regulatory submissions or required approvals of our product candidates, cause us to incur higher costs and could prevent us from commercializing our product candidates successfully.

We may encounter delays in the manufacturing of Sumavel DosePro or fail to generate revenue if our supply of the components of our DosePro drug delivery system is interrupted.

Our DosePro drug delivery system is sourced, manufactured and assembled by multiple third parties across different geographic locations in Europe, including the United Kingdom, Germany and Ireland. All contract manufacturers and component suppliers have been selected for their specific competencies in the manufacturing processes and materials that make up the DosePro system. The components of DosePro include the actuator subassembly, capsule subassembly, and the setting mechanism. The actuator subassembly is comprised of nine individual components which are collectively supplied by six different third-party manufacturers. The capsule subassembly that houses the sterile drug formulation *sumatriptan* is comprised of five different components also supplied by four third-party manufacturers. Each of these third-party manufacturers is currently the single source of their respective components. If any of these manufacturers is unable to supply its respective component for any reason, including due to violations of the FDA s Quality System Regulation, or QSR, requirements, our ability to manufacture the finished

DosePro device will be adversely affected and our ability to meet the distribution requirements for any product sales of Sumavel DosePro and the resulting revenue therefrom will be negatively affected. Accordingly, there can be no assurance that any failure in any part of our supply chain will not have a material adverse effect on our ability to generate revenue from Sumavel DosePro, which in turn could have a material adverse effect on our business, results of operations, financial condition and prospects.

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We rely on third parties to perform many necessary services for our commercial products, including services related to the distribution, invoicing, storage and transportation of our products.

We have retained third-party service providers to perform a variety of functions related to the sale and distribution of our products, key aspects of which are out of our direct control. For example, we rely on Cardinal Health 105, Inc. (a/k/a Specialty Pharmaceutical Services) to provide key services related to logistics, warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management and call center management, and, as a result, most of our inventory is stored at a single warehouse maintained by the service provider. We place substantial reliance on this provider as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical damage or natural disaster at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired. In addition, we utilize third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services. If the quality or accuracy of the data maintained by these service providers is insufficient, our ability to continue to market our products could be jeopardized or we could be subject to regulatory sanctions. We do not currently have the internal capacity to perform these important commercial functions, and we may not be able to maintain commercial arrangements for these services on reasonable terms.

The perception that our DosePro needle-free drug delivery system should be pain free may limit patient adoption.

We believe that there is a perception among some patients, physicians and other customers that a needle-free delivery system should be pain free. While our experience indicates that some patients will experience pain upon injection with the DosePro technology, this pain sensation is consistent with the pain sensation associated with injection with a fine gauge needle and can be generally characterized as transient mild discomfort. In addition, some patients will experience local injection site signs and reactions following injection with DosePro. The fact that the use of our DosePro system may be accompanied by a certain amount of pain upon injection and local injection site signs and reactions may limit its adoption by patients, physicians and other customers.

Zohydro is subject to extensive regulation, and we cannot give any assurance that it or any of our other product candidates will receive regulatory approval or be successfully commercialized.

We currently are developing Zohydro for the treatment of moderate to severe chronic pain. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of opioid drug products, among other things, are subject to extensive regulation by the FDA, the DEA and other regulatory authorities in the United States. We are not permitted to market Zohydro in the United States unless and until we receive regulatory approval from the FDA. We cannot provide any assurance that we will obtain regulatory approval for Zohydro or any of our other product candidates, or that any such product candidates will be successfully commercialized.

We have not yet completed all necessary studies, nor submitted a new drug application, or NDA, or received marketing approval, for Zohydro. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA also has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. For example:

- the FDA may not deem a product candidate safe and effective;
- the FDA may not find the data from pre-clinical studies and clinical trials sufficient to support approval;
- the FDA may require additional pre-clinical studies or clinical trials;
- the FDA may not approve of our third-party manufacturers processes and facilities; or
- the FDA may change its approval policies or adopt new regulations.

Zohydro has undergone Phase 1 pharmacokinetics studies as well as Phase 2 clinical trials. However, these studies and trials were conducted by a third party and, accordingly, we did not directly participate in their design or execution. In addition, we will also need to successfully complete Phase 3 clinical trials to establish its safety and efficacy, additional Phase 1 studies, and additional pre-clinical studies prior to our submission of an NDA to the FDA for approval. We initiated the Phase 3 clinical development program for Zohydro in March 2010 and completed enrollment in our single pivotal Phase 3 efficacy trial, Study 801, in February 2011 and in our open-label Phase 3 trial, Study 802, in December 2010. Zohydro and any of our other product candidates may fail to achieve their specified endpoints in clinical trials. Furthermore, product candidates such as Zohydro may not be approved even if they achieve their specified endpoints in clinical trials. The FDA may disagree with our trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. The FDA may also approve a product candidate for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post-approval clinical trials. In addition, the FDA may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates.

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If we are unable to obtain regulatory approval for Zohydro or any other product candidates on the timeline we anticipate, we will not be able to execute our business strategy effectively and our ability to generate additional revenues beyond Sumavel DosePro will be limited, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

Our clinical trials may fail to demonstrate acceptable levels of safety and efficacy of Zohydro or any of our other product candidates, which could prevent or significantly delay their regulatory approval.

Our Zohydro product candidate and our other product candidates are prone to the risks of failure inherent in drug development. Before obtaining U.S. regulatory approval for the commercial sale of Zohydro or any other product candidate, we must gather substantial evidence from well-controlled clinical trials that demonstrate to the satisfaction of the FDA that the product candidate is safe and effective, and similar regulatory approvals would be necessary to commercialize the product candidate in other countries.

In light of widely publicized events concerning the safety risk of certain drug products, particularly opioid drug products, regulatory authorities, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products after approval. In addition, the Federal Food, Drug, and Cosmetic Act, or FFDCA, as amended by the Food and Drug Administration Amendments Act of 2007, grants significant expanded authority to the FDA, much of which is aimed at improving the safety of drug products before and after approval. In particular, the FFDCA authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require a risk evaluation and mitigation strategy, or REMS, for certain drugs, including certain currently approved drugs. It also significantly expands the federal government s clinical trial registry and results databank, which we expect will result in significantly increased government oversight of clinical trials. Under the FFDCA, companies that violate these and other provisions of the law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties.

The increased attention to drug safety issues may result in a more cautious approach by the FDA in its review of our clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

With regard to Zohydro, data from a Phase 2 clinical trial in osteoarthritis patients has shown what we believe is a clinically acceptable safety profile and a pharmacodynamic profile which supports further product development for the treatment of moderate to severe chronic pain in patients requiring around-the-clock opioid therapy for an extended period of time. In the two Phase 2 clinical trials conducted to date, patients experienced mild to moderate adverse events, including nausea, vomiting, headache, dizziness, sweating, constipation and drowsiness, which are similar to the reported side effects of opioids currently prescribed for chronic pain. However, our licensor, Elan conducted these trials and we have not independently verified the data or completed any of our own Phase 2 or Phase 3 trials for this product candidate. In addition, these results may not be predictive of results obtained in our ongoing Phase 3 clinical trials or any other required future trials, and we may be unable to demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals or approvals for commercially viable uses. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. If Zohydro is not shown to be safe and effective in clinical trials, this program could be delayed or terminated, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Delays in the commencement or completion of clinical testing for Zohydro or pre-clinical or clinical testing for any of our other product candidates could result in increased costs to us and delay or limit our ability to pursue regulatory approval or generate revenues. *

Clinical trials are very expensive, time consuming and difficult to design and implement. Delays in the commencement or completion of clinical testing for Zohydro or pre-clinical or clinical testing for Relday or any of our other product candidates could significantly affect our product development costs and business plan. In March 2010, we initiated a Phase 3 clinical development program for Zohydro, including a pivotal efficacy trial. Phase 3 clinical efficacy trials, in general, are significantly more complex and time-consuming and involve more patients than the Phase 1 and 2 clinical trials that have been completed to date. We do not know whether our Phase 3 clinical trials of Zohydro will be completed on schedule, if at all. We expect to initiate clinical testing for Relday in patients in schizophrenia in early 2012. In addition, we do not know whether any other pre-clinical or clinical trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- obtaining regulatory authorization to commence a clinical trial;

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reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, clinical investigators and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs, clinical investigators and trial sites;

manufacturing or obtaining sufficient quantities of a product candidate for use in clinical trials;

obtaining institutional review board, or IRB, approval to initiate and conduct a clinical trial at a prospective site;

identifying, recruiting and training suitable clinical investigators;

identifying, recruiting and enrolling subjects to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for the treatment of pain, migraine or similar indications;

retaining patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy, personal issues, or for any other reason they choose, or who are lost to further follow-up;

uncertainty regarding proper dosing; and

scheduling conflicts with participating clinicians and clinical institutions.

We believe that we have planned and designed an adequate Phase 3 clinical trial program for Zohydro, and we presented the trial design for our Phase 3 trials to the FDA at our End of Phase 2 meeting in June 2008. Although we believe the FDA has generally agreed with the design of our Phase 3 clinical trial program, the FDA could still determine that it is not satisfied with our plan or the details of our pivotal clinical trial protocols and designs. While the FDA has provided us with a written record of our discussions and responses to our questions at our End of Phase 2 meeting, such records and responses do not guarantee that the FDA will deem our trial design to be sufficient for the purpose of obtaining marketing approval for Zohydro. We did not seek a Special Protocol Assessment from the FDA for our ongoing pivotal Phase 3 efficacy study for Zohydro (Study 801).

In addition, while we completed enrollment in Study 801 in February 2011 and in our open-label Phase 3 trial, Study 802, in December 2010, chronic pain patients have historically been difficult to keep enrolled in clinical trials. If a significant number of patients fail to stay enrolled in any of our current or future clinical trials of Zohydro and such failure is not adequately accounted for in our trial design and enrollment assumptions, our clinical development program could be delayed. Clinical trials may also be delayed or repeated as a result of ambiguous or negative interim results or unforeseen complications in testing. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or other regulatory authorities due to a number of factors, including:

failure to design appropriate clinical trial protocols;

failure by us, our employees, our CROs or their employees to conduct the clinical trial in accordance with all applicable FDA, DEA or other regulatory requirements or our clinical protocols;

inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;

discovery of serious or unexpected toxicities or side effects experienced by study participants or other unforeseen safety issues;

lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties;

lack of effectiveness of any product candidate during clinical trials;

slower than expected rates of subject recruitment and enrollment rates in clinical trials;

failure of our CROs or other third-party contractors to comply with all contractual requirements or to perform their services in a timely or acceptable manner;

inability or unwillingness of medical investigators to follow our clinical protocols;

in the case of Zohydro, regulatory concerns with opioid products generally and the potential for abuse and diversion of the drugs; and

unfavorable results from on-going clinical trials and pre-clinical studies.

Additionally, changes in applicable regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for Zohydro and our other product candidates may be harmed, which may have a material adverse effect on our business, results of operations, financial condition and prospects.

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Our competitors could receive FDA approval for an extended-release hydrocodone product before we receive FDA approval for Zohydro, and thus could be granted regulatory exclusivity that could significantly delay our ability to receive approval for and commercialize Zohydro and therefore dramatically reduce its market potential. Our competitors could also pursue regulatory and other strategies to combat competition from 505(b)(2) products, which also may negatively affect the approval and commercialization of Zohydro and any of our other product candidates.

The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the FFDCA, or Section 505(b)(2). Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. For example, we obtained FDA marketing approval of Sumavel DosePro under Section 505(b)(2), and we intend to submit the NDA for Zohydro under Section 505(b)(2), and as such the NDA will rely, in part, on the FDA s previous findings of safety and effectiveness for *hydrocodone*.

Certain of our competitors may file a 505(b)(2) application for extended-release *hydrocodone* either before or shortly after we submit our own NDA for Zohydro. The first approved 505(b)(2) applicant for a particular condition of use, or change to a marketed product, such as a new extended-release formulation for a previously approved product, may be granted three-year Hatch-Waxman exclusivity if one or more clinical studies, other than bioavailability or bioequivalence studies, was essential to the approval of the application and was conducted/sponsored by the applicant. Three-year Hatch-Waxman exclusivity delays the FDA s approval of other 505(b)(2) applicants for the same condition of use or change to the drug product that was granted exclusivity, regardless of the date of submission of each NDA. We believe that several competitors are developing extended-release *hydrocodone* products, and if the FDA approves a competitor s 505(b)(2) application for its extended-release *hydrocodone* product before our application, and granted the competitor three-year exclusivity, the FDA would be precluded from making effective our NDA for Zohydro until after that three-year exclusivity period has run, and such delay would dramatically reduce our expected market potential for Zohydro. Additionally, even if our 505(b)(2) application for extended-release *hydrocodone* is approved first, we may still be subject to competition by other *hydrocodone* products, including approved products or other 505(b)(2) applications for different conditions of use that would not be restricted by the three-year exclusivity.

In addition, approval under Section 505(b)(2) generally requires the absence of any other patents covering the product candidate in question and competitors and others have the ability to take numerous steps to block or delay approval of product candidates under Section 505(b)(2), including:

- extending patent protection for existing products that would block Section 505(b)(2) approval of the product candidate by pursuing new patents for existing products that may be granted just before the expiration of one patent, which could extend patent protection for a number of years or otherwise delay the launch of generic, 505(b)(2) or other competing products;
- submitting Citizen Petitions to request the FDA to take adverse administrative action with respect to approval of a generic, 505(b)(2) or other competing product;
- filing patent infringement lawsuits, whether or not meritorious, to trigger up to a 30-month stay in the approval of a generic, 505(b)(2) or other competing product; and
- engaging in state-by-state initiatives to enact legislation or regulatory policies that restrict the substitution of some generic, 505(b)(2) or other competing drugs for brand-name drugs.

If any of these strategies are successful, our ability to obtain approval of and commercialize Zohydro and any of our other product candidates for which we rely on Section 505(b)(2) will be adversely affected.

We rely on third parties to conduct our pre-clinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have agreements with third-party CROs to conduct our ongoing Phase 3 trials for Zohydro, and anticipate that we may enter into other such agreements in the future regarding any of our other product candidates. We rely heavily on these parties for the execution of our clinical and pre-clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol. We and our CROs are required to comply with current good clinical practices, or GCPs. The FDA enforces these GCP regulations through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCP regulations, the data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA and similar foreign regulators will determine that any of our clinical trials comply or complied with GCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or cGMPs, regulations, and require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

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If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs on commercially reasonable terms, or at all. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate additional revenues could be delayed.

Switching or adding additional CROs can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, results of operations, financial condition and prospects.

The development of a REMS for Zohydro could cause significant delays in the approval process for Zohydro and will add additional layers of regulatory requirements, including the requirement for a Medication Guide and educational requirements for prescribers and patients, which could significantly impact our ability to commercialize Zohydro and dramatically reduce its market potential. *

The Food and Drug Administration Amendments Act, or FDAAA, added Section 505-1 to the FFDCA. Section 505-1 permits FDA to require a REMS for a drug product to ensure the safe use of the drug. A REMS is a strategic safety program that the FDA requires to ensure that the benefits of a drug outweigh its risks. In determining whether a REMS is necessary, the FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. If the FDA determines a REMS is necessary, the drug sponsor must agree to the REMS plan at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug s risks, limitations on who may prescribe or dispense the drug, requirements that patients enroll in a registry or undergo certain health evaluations or other measures that the FDA deems necessary to assure the safe use of the drug. In addition, the REMS must include a timetable to assess the strategy at 18 months, three years and seven years after the strategy s approval.

In February 2009, the FDA informed drug manufacturers that it will require a class-wide REMS for all long-acting and sustained-release opioid drug products. The FDA has since initiated efforts to develop a new standardized REMS for these opioid medications to ensure their safe use. In April 2011, FDA announced that it had finalized the elements of a class-wide REMS for these products. The central component of the opioid REMS program is an education program for prescribers and patients. Specifically, the REMS for these products must include a Medication Guide available for distribution to patients who are dispensed the drug, as well as a number of elements to assure safe use. These elements include training for prescribers who prescribe the drug; information provided to prescribers that prescribers can use to educate patients in the safe use, storage, and disposal of opioids; and information provided to prescribers of the existence of the REMS and the need to successfully complete the necessary training. Moreover, the REMS must include a timetable for submission of assessments that shall be no less frequent than 6 months, 12 months, and annually after the REMS is approved to assess the extent to which the elements to assure safe use are meeting the goals of the REMS and whether the goals or elements should be modified. The FDA expects that manufacturers of long-acting and extended-release opioids work together to provide educational materials as part of a class-wide single shared system to reduce the burden of the REMS on the healthcare system.

An extended-release formulation of *hydrocodone*, such as Zohydro, will be required to have a REMS that contains the elements of the recently-issued class-wide REMS for long-acting and sustained-release opioids. We intend to submit a REMS at the time of the NDA submission for Zohydro. The development of the REMS could cause significant delays in the approval process for Zohydro, and the educational requirements and requirements for a Medication Guide for patients could significantly impact our ability to commercialize Zohydro and dramatically reduce its market potential.

Our commercialization partner for Sumavel DosePro in the European Union and three other countries, Desitin, may not successfully develop, obtain approval for or commercialize Sumavel DosePro in those territories, which may adversely affect our ability to commercialize Sumavel DosePro both inside and outside the United States.

In March 2008, we entered into a licensing and distribution agreement with Desitin pursuant to which we granted Desitin the exclusive right under our intellectual property rights related to Sumavel DosePro to develop, use, distribute, sell, offer for sale, and import Sumavel DosePro and any potential modified versions of Sumavel DosePro in the European Union, Norway, Switzerland and Turkey. In that regard, Desitin is not obligated under the agreement to pursue regulatory approval or commercialization of Sumavel DosePro in any of these countries except for Germany. Since we will depend on Desitin to develop, obtain regulatory approval for

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and, if regulatory approval is granted, commercialize Sumavel DosePro in these countries, we will have limited control over the success of Desitin s development, regulatory approval and commercialization efforts. Desitin submitted a Marketing Authorization Application for Sumavel DosePro to the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)) in Germany, the reference member state, through the Decentralized Procedure in October 2009, following completion of a European pivotal bioequivalence trial comparing needle-free Sumavel DosePro to a traditional needle-based autoinjector, Imigran-Inject, the European brand of Imitrex STATdose. In November 2010, Denmark became the first member of the European Union to approve marketing of Sumavel DosePro in that country. Subsequently, Sumavel DosePro has received marketing approval in Germany, Sweden, Norway and the United Kingdom.

Any additional clinical studies Desitin may be required to conduct as part of the regulatory approval process may not corroborate the results of the clinical studies we have conducted or may have adverse results or effects on our ability to maintain regulatory approvals in the United States or obtain them in other countries. In addition, although we believe that the U.S. market represents the largest commercial opportunity for Sumavel DosePro, Desitin may not develop Sumavel DosePro as fast or generate as large of a market as we would like or as the market may expect and Desitin may not seek to develop, obtain approval for or commercialize Sumavel DosePro in countries for which it has exclusive rights, other than in Germany, where Desitin is required to develop, seek approval for and commercialize Sumavel DosePro. Any failure by Desitin to successfully commercialize Sumavel DosePro or to successfully obtain applicable foreign regulatory approval for Sumavel DosePro would limit our opportunity to receive revenue from the territories licensed to Desitin. Furthermore, negative developments occurring in those territories controlled by Desitin could have a negative impact on physician and patient impressions of our product in the United States and elsewhere.

Our failure to successfully establish new partnerships with pharmaceutical companies or contract sales organizations to co-promote any additional product candidates that may receive regulatory approval may impair our ability to effectively market and sell such product candidates.

Major pharmaceutical companies usually employ groups of sales representatives numbering in the thousands to call on the large number of primary care physicians. In connection with the launch of Sumavel DosePro in January 2010 we built and marketing organization to promote Sumavel DosePro in the United States, including a focused sales force of approximately 80 representatives primarily targeting neurologists and other key prescribers of migraine medications, including headache clinics and headache specialists. We have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. In addition, in July 2009, we entered into an exclusive agreement with Astellas under which Sumavel DosePro is also being marketed by Astellas in the United States promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians, and urologists by approximately 400 Astellas sales representatives. In order to expand the market opportunity for any additional product candidates that receive regulatory approval into the broader primary care physician audiences, we will need to continue to expand our sales and marketing personnel and commercial infrastructure and/or establish partnerships with pharmaceutical companies or contract sales organizations to co-promote such product candidates. We currently, and on an ongoing basis will have to, compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. We also face competition in our search for collaborators and potential co-promoters. To the extent we rely on additional third parties to commercialize any product candidates that may receive regulatory approval, we are likely to receive less revenues than if we commercialized these products ourselves. Further, by entering into strategic partnerships or similar arrangements, we may rely in part on such third parties for financial and commercialization resources. Even if we are able to identify suitable partners to assist in the commercialization of our product candidates, they may fail to devote the resources necessary to realize the full commercial potential of our products. In addition, we may lack the financial and managerial resources to increase the size of our sales and marketing organization to adequately commercialize any product candidates that may be approved, and any increase in our sales force would result in an increase in our expenses, which could be significant before we generate revenues from any newly approved product candidate. If we are unable to expand our sales and marketing infrastructure or enter into a third-party arrangement, we would not be able to successfully commercialize any approved products. Even if we are able to expand our sales and marketing personnel or successfully establish partnership arrangements, such sales force and marketing teams may not be successful in commercializing our products, which would adversely affect our ability to generate revenue for such products, which will have a material adverse effect on our business, results of operations, financial condition and prospects.

Our failure to successfully acquire, develop and market additional product candidates or approved products would impair our ability to grow our business. In that regard, our DosePro delivery system cannot be used with drug formulation volumes greater than 0.5 mL, which will likely limit its use with drugs requiring larger formulation volumes. *

As part of our growth strategy we intend to seek to expand our product pipeline by exploring acquisition or in-licensing opportunities of proven drugs that can be paired with our DosePro needle-free drug delivery system. However, the current version of our DosePro drug delivery system cannot be used with drug formulation volumes greater than 0.5 mL. Many marketed and development-stage injectable products, including most biologics, have formulation volumes greater than 0.5 mL and would require reformulation, if possible, to accommodate the approved doses in smaller volumes that are compatible with DosePro. Any reformulation may increase the risk of failure during development, extend the development timelines, increase development costs and

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add complexity to the regulatory approval process and in some cases reformulation may not be possible. If we are not able to identify additional drug compounds that can be delivered via the current version of our DosePro technology, or if we are unable to successfully develop higher dose versions of this technology, our ability to develop additional product candidates and grow our business would be adversely affected. We will also seek opportunities to out-license the DosePro technology to partners seeking to enhance, differentiate, or extend the life-cycle of their injectable products. If we are unable to secure partnerships with companies that have compounds that can be delivered via the current version of our DosePro technology, or if we are unable to successfully develop higher dose versions of this technology, we will not be able to generate revenues from out-licensing our DosePro technology.

We have initiated early stage design and development of a larger volume, second generation version of our DosePro technology to accommodate drug formulation volumes greater than 0.5 mL, which if successfully developed, would allow for a broader range of potential applications for our technology. However, the full development of such technology will require substantial investment and we may consider entering into a third-party collaboration in order to obtain third-party financing to help fully develop such technology. There is no guarantee that we or any potential future third-party collaborator will be able to successfully develop such a device technology, whether for financial or technical reasons or otherwise.

Furthermore, we intend to in-license, acquire, develop and/or market additional products and product candidates in the areas of pain and central nervous system, or CNS, disorders. For example, in July 2011, we entered into a development and license agreement with Durect Corporation for a proprietary, long-acting, injectable formulation of risperidone using Durect s SABER controlled-release formulation technology in combination with our DosePro technology. Durect will be responsible for non-clinical, formulation and CMC development responsibilities. As a result, we will be dependent on Durect s successful completion of its responsibilities for Relday. In addition, because our internal research and development capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify and select promising pharmaceutical product candidates and products, negotiate licensing or acquisition agreements with their current owners and finance these arrangements.

The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing, sales and other resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates, or license the rights to our DosePro technology, on terms that we find acceptable, or at all.

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including pre-clinical or clinical testing and approval by the FDA and applicable foreign regulatory authorities. We expect to initiate clinical testing for Relday in patients in schizophrenia in early 2012. We may not be able to obtain necessary approvals to initiate such clinical testing in a timely manner or at all. In addition, all product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any products that we develop or approved products that we acquire will be manufactured or sold profitably or achieve market acceptance.

If we are unable to license or acquire additional product candidates or approved products and successfully develop and commercialize them, or if we are otherwise unable to pair our DosePro delivery system with other drugs or out-license the DosePro technology to others, it would likely have a material adverse effect on our business, results of operations, financial condition and prospects.

We may need to continue to increase the size of our organization, and we may experience difficulties in managing and financing growth.

We increased our full-time employees from 48 as of October 31, 2009 to 146 as of June 30, 2011. In addition, we have initiated activities to expand our sales force in the United States from approximately 80 sales representatives to approximately 95 sales representatives by the end of the third quarter of 2011. We may need to continue to expand our managerial, operational and other resources in order to grow, manage and fund our existing business. Our management and personnel, systems and facilities currently in place may not be adequate to support this recent and any future growth, and we may be unable to fund the costs and expenses required to increase our necessary headcount and infrastructure. Our need to effectively manage our operations, any future growth and various projects requires that we:

manage our internal and external commercialization efforts for Sumavel DosePro effectively while carrying out our contractual obligations to Astellas and other third parties and complying with all applicable laws, rules and regulations;

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manage our internal development efforts for Zohydro, Relday and our other product candidates effectively while carrying out our contractual obligations to licensors, collaborators and other third parties and complying with all applicable laws, rules and regulations;

continue to improve our operational, financial and management controls, reporting systems and procedures; and

attract and retain sufficient numbers of talented employees.

We may be unable to successfully implement or fund these tasks on a larger scale and, accordingly, may not achieve our commercialization and development goals. In addition, our management may have to divert a disproportionate amount of its attention away from day-to-day activities and towards managing these growth-related activities. Our future financial performance and our ability to execute on our business plan will depend, in part, on our ability to effectively manage any future growth and our failure to effectively manage any growth could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we are unable to attract and retain key personnel, we may not be able to manage our business effectively or develop our product candidates or commercialize our product.

Our success depends on our continued ability to attract, retain and motivate highly qualified management and key clinical development, regulatory, sales and marketing and other personnel. We are highly dependent on the development, regulatory, commercial and financial expertise of our senior management team. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the areas in Southern and Northern California, where we currently operate. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercialization objectives, our ability to raise additional capital and our ability to implement our business strategy. The loss of the services of any members of our senior management team, especially our Chief Executive Officer, Roger L. Hawley, and President and Chief Operating Officer, Stephen J. Farr, Ph.D., could negatively impact the commercialization of Sumavel DosePro and could delay or prevent the development and commercialization of any other product candidates, including Zohydro. In addition, under the terms of our amended and restated loan and security agreement with Oxford and SVB, if our Chief Executive Officer, Chief Financial Officer or President resigns, is terminated or is no longer actively involved in his or her current position and is not replaced by a person acceptable to our board of directors within 120 days, an event of default would be triggered under the agreement, and the lenders would be able to demand immediate repayment of all borrowings outstanding under the agreement. Further, if we lose any members of our senior management team, we may not be able to find suitable replacements, and our business may be harmed as a result. In addition to the competition for personnel, our locations in California in particular are characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Although we have employment agreements with each of our executive officers, these agreements are terminable by them at will at any time with or without notice and, therefore, do not provide any assurance that we will be able to retain their services. We do not maintain key man insurance policies on the lives of our senior management team or the lives of any of our other employees. In addition, we have clinical advisors who assist us in formulating our clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours. If we are unable to attract and retain key personnel, our business, results of operations, financial condition and prospects will be adversely affected.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

exposure to unknown liabilities;

disruption of our business and diversion of our management s time and attention in order to develop acquired products, product candidates or technologies;

incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;

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- higher than expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we are unable to achieve and maintain adequate levels of coverage and reimbursement for Sumavel DosePro, Zohydro, if approved, or any of our other product candidates for which we may receive regulatory approval on reasonable pricing terms, their commercial success may be severely hindered.

Successful sales of our products depend on the availability of adequate coverage and reimbursement from third-party payors. Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

In addition, the market for our products will depend significantly on access to third-party payors drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor.

Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third-party coverage and reimbursement for Sumavel DosePro or any of our other product candidates for which we may receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability if our insurance coverage for those claims is inadequate.

The commercial use of our product and clinical use of our product and product candidates expose us to the risk of product liability claims. This risk exists even if a product is approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA, such as the case with Sumavel DosePro, or an applicable foreign regulatory authority. Our product and product candidates are designed to affect important bodily functions and processes. Any side effects, manufacturing defects, misuse or abuse associated with Sumavel DosePro or our

product candidates could result in injury to a patient or even death. For example, because our DosePro technology is designed to be self-administered by patients, it is possible that a patient could fail to follow instructions and as a result apply a dose in a manner that results in injury. In addition, Zohydro is an opioid pain reliever that contains *hydrocodone*, which is a regulated controlled substance under the Controlled Substances Act of 1970, or CSA, and could result in harm to patients relating to its potential for abuse. In addition, a liability claim may be brought against us even if our product or product candidates merely appear to have caused an injury. Product liability claims may be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our product candidates, among others. If we cannot successfully defend ourselves against product liability claims we will incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

the inability to commercialize our product or product candidates;

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decreased demand for our product or product candidates;

impairment of our business reputation;

product recall or withdrawal from the market;

withdrawal of clinical trial participants;

costs of related litigation;

distraction of management s attention from our primary business;

substantial monetary awards to patients or other claimants; or

loss of revenues.

We have obtained product liability insurance coverage for commercial product sales and clinical trials with a $10 million per occurrence and a $10 million annual aggregate coverage limit. Our insurance coverage may not be sufficient to cover all of our product liability related expenses or losses and may not cover us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost, in sufficient amounts or upon adequate terms to protect us against losses due to product liability. If we determine that it is prudent to increase our product liability coverage based on sales of Sumavel DosePro, approval of Zohydro or otherwise, we may be unable to obtain this increased product liability insurance on commercially reasonable terms or at all. Large judgments have been awarded in class action or individual lawsuits based on drugs that had unanticipated side effects, including side effects that are less severe than those of Sumavel DosePro and our product candidates. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and have a material adverse affect our business, results of operations, financial condition and prospects.

We may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and other facilities are located in San Diego and the San Francisco Bay Area, which in the past have both experienced severe earthquakes. We do not carry earthquake insurance. As a result, earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

Our enterprise financial systems are located in our San Diego, California headquarters. Our manufacturing resource planning and enterprise quality systems are located in our Emeryville, California facility. If a disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters or our Emeryville facility, that damaged critical infrastructure, such as enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations at either location, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

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

Our research and development activities and our third-party manufacturers and suppliers activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product and product candidates and other hazardous compounds.

We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers facilities pending use and disposal. We cannot completely eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, injury to our employees and others, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources. We do not currently carry biological or hazardous waste insurance coverage.

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In connection with the reporting of our financial condition and results of operations, we are required to make estimates and judgments which involve uncertainties, and any significant differences between our estimates and actual results could have an adverse impact on our financial position, results of operations and cash flows.

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosure of contingent assets and liabilities. In particular, as part of our revenue recognition policy, our estimates of product returns, rebates and chargebacks require our most subjective and complex judgment due to the need to make estimates about matters that are inherently uncertain. Any significant differences between our actual results and our estimates and assumptions could negatively impact our financial position, results of operations and cash flows.

Changes in accounting standards and their interpretations could adversely affect our operating results.

GAAP are subject to interpretation by the Financial Accounting Standards Board, the American Institute of Certified Public Accountants, the Securities and Exchange Commission, or SEC, and various other bodies that promulgate and interpret appropriate accounting principles. These principles and related implementation guidelines and interpretations can be highly complex and involve subjective judgments. A change in these principles or interpretations could have a significant effect on our reported financial results, and could affect the reporting of transactions completed before the announcement of a change.

Fluctuations in the value of the Euro or U.K. pound sterling could negatively impact our results of operations and increase our costs.

Payments to our material suppliers and contract manufactures are denominated in the Euro and U.K. pounds sterling. Our reporting currency is the U.S. dollar and to date all of the revenues generated by sales of Sumavel DosePro have been in U.S. dollars. For the six months ended June 30, 2011, $5.3 million (based on exchange rates as of June 30, 2011) of our materials, contract manufacturing costs and other manufacturing-related costs were denominated in foreign currencies. As a result, we are exposed to foreign exchange risk, and our results of operations may be negatively impacted by fluctuations in the exchange rate between the U.S. dollar and the Euro or U.K. pound sterling. A significant appreciation in the Euro or U.K. pound sterling relative to the U.S. dollar will result in higher expenses and cause increases in our net losses. Likewise, to the extent that we generate any revenues denominated in foreign currencies, or become required to make payments in other foreign currencies, fluctuations in the exchange rate between the U.S. dollar and those foreign currencies could also negatively impact our results of operations. We currently have not entered into any foreign currency hedging contracts to reduce the effect of changes in foreign currency exchange rates, and foreign currency hedging is inherently risky and may result in unanticipated losses.

Our operating results are partially dependent on freight costs and our costs may increase significantly if we are unable to ship and transport finished products efficiently and economically across long distances and international borders.

Our Sumavel DosePro product is manufactured in Europe and we transport significant volumes of that product across long distances and international borders. As a result, our operating results can be affected by changes in transportation costs. We generally ship our product by air freight, and freight rates can vary significantly due to a large number of factors beyond our control, including changes in fuel prices or general economic conditions. If demand for air freight should increase substantially, it could make it difficult for us to procure transportation space at prices we consider acceptable.

Because our products must cross international borders, we are subject to risk of delay due to customs inspection, if our documentation does not comply with customs rules and regulations or for similar reasons. In addition, any increases in customs duties or tariffs, as a result of changes to existing trade agreements between countries or otherwise, could increase our costs or the final cost of our products to our customers or increase our expenses. The laws governing customs and tariffs in many countries are complex, subject to many interpretations and often includes substantial penalties for noncompliance.

Risks Related to Our Financial Position and Capital Requirements

We have never generated net income or positive cash flow from operations and are dependent upon external sources of financing to fund our business and development.*

We launched our only approved product, Sumavel DosePro, in January 2010. Without a long history of sales, we may not accurately predict future sales, and we may never be able to significantly increase these sales, especially in light of our reliance on our partnership with Astellas to co-promote Sumavel DosePro. We have financed our operations almost exclusively through the proceeds from the issuance of our common and

preferred stock, including the proceeds from our initial public offering completed in November 2010, and debt, and have incurred losses and negative cash flow from operations in each year since our inception. Our net loss applicable to common stockholders was $45.9 million in 2009, $73.6 million in 2010, and $38.2 million for the six months ended June 30, 2011 and our cash used in operating activities was $32.4 million in 2009, $72.0 million in 2010 and $40.5 million for the six

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months ended June 30, 2011. As of June 30, 2011, we had an accumulated deficit of $236.3 million. These losses and negative cash flow from operations have had a material adverse effect on our stockholders equity and working capital. Further, despite the revenues from Sumavel DosePro, we expect our losses to continue for at least the next several years as a result of the development expenses incurred in connection with our ongoing clinical development for Zohydro, the initiation of clinical development for Relday and the cost of the sales and marketing expense associated with Sumavel DosePro. In addition, if we obtain regulatory approval for Zohydro or any of our other product candidates, we expect to incur significant sales, marketing and manufacturing expenses as well as continued development expenses. As a result, we are and will remain dependent upon external sources of financing to finance our business and the development and commercialization of our approved product and product candidates. We cannot assure you that debt or equity financing will be available to us in amounts, at times or on terms that will be acceptable to us, or at all. Any shortfall in our cash resources could require that we delay or abandon certain development and commercialization activities and could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Our independent registered public accounting firm has expressed substantial doubt as to our ability to continue as a going concern.

In its report accompanying our audited consolidated financial statements for the year ended December 31, 2010, our independent registered public accounting firm included an explanatory paragraph stating that our recurring losses from operations and lack of sufficient working capital raise substantial doubt as to our ability to continue as a going concern. A going concern opinion could impair our ability to finance our operations through the sale of debt or equity securities or commercial bank loans. Our ability to continue as a going concern will depend, in large part, on our ability to generate positive cash flow from operations and obtain additional financing, neither of which is certain. If we are unable to achieve these goals, our business would be jeopardized and we may not be able to continue operations and may have to liquidate our assets and may receive less than the value at which those assets are carried on our consolidated financial statements, and it is likely that investors will lose all or a part of their investment. In addition, our amended loan and security agreement with Oxford and SVB includes a covenant that the audit reports accompanying our annual consolidated financial statements for fiscal year 2010 and thereafter not include a going concern qualification and any breach of that covenant would permit the lenders to demand immediate repayment of all loans outstanding under the agreement and to seize and sell the collateral. In March 2011, we obtained a waiver from Oxford and SVB for the breach caused by the receipt of the 2010 audit report from our independent registered public accounting firm which includes a modification of standard report for going concern uncertainty.

Our level of indebtedness could adversely affect our ability to raise additional capital to fund our operations, limit our ability to react to changes in the economy or our industry and prevent us from meeting our obligations.

As of June 30, 2011, the principal amount of our total indebtedness was approximately $26.7 million. In July 2011, we completed the royalty financing transaction with Cowen Royalty, which increased our total indebtedness by an additional $30.0 million. We have and expect to continue to make borrowings under our $10.0 million revolving credit facility to fund working capital and other cash needs and we may incur substantial additional indebtedness in the future, both under our $10.0 million revolving credit facility and any other debt facilities we may enter into in the future. Our outstanding debt and related debt service obligations could have important adverse consequences to us, including:

- heightening our vulnerability to downturns in our business or our industry or the general economy and restricting us from making improvements or acquisitions, or exploring business opportunities;
- requiring a significant portion of our available cash to be dedicated to the payment of principal and interest on our indebtedness, therefore reducing our ability to use our available cash to fund our operations, capital expenditures and future business opportunities;
- limiting our ability to obtain additional financing for working capital, capital expenditures, debt service requirements, acquisitions and general corporate or other purposes;
- limiting our ability to adjust to changing market conditions and placing us at a competitive disadvantage compared to our competitors who have greater capital resources; and
- subjecting us to financial and other restrictive covenants in our debt instruments, the failure with which to comply could result in an event of default under the applicable debt instrument that allows the lender to demand immediate repayment of the related debt.

If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay product development, sales and marketing, capital and other expenditures, sell assets, seek additional capital or restructure or refinance our indebtedness. These alternative measures may not be successful and may not permit us to meet our scheduled debt service obligations. This risk is increased by the fact that borrowings under certain of our credit facilities bear interest at a variable rates, exposing us to the risk that the amount of cash required to pay interest will increase to the extent that market interest rates increase.

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Our debt instruments contain a number of financial covenants and other provisions, including a requirement that we attain specified future levels of revenues, which, if violated, could result in the immediate acceleration of our outstanding indebtedness. *

Our $35.0 million amended and restated loan and security agreement with Oxford and SVB includes covenants requiring, among other things, that (1) we achieve, as of the last day of each month, measured on a trailing three-month basis, actual revenues of at least a specified percentage of our projected revenue as provided to Oxford and SVB in the event we fail to maintain a liquidity ratio (defined, in general, as the ratio of (a) cash and cash equivalents deposited with SVB plus unused borrowing capacity under that agreement to (b) all debt, capital lease obligations and contingent obligations owed to the lenders) of 1.25 to 1.00, and (2) the audit report accompanying our year-end consolidated financial statements for fiscal year 2010 and thereafter not include a going concern qualification. As discussed above, the audit report from our independent registered public accounting firm accompanying our 2010 consolidated financial statements includes a modification of the standard report for the going concern uncertainty, as a result, our results of operations and financial condition will have to improve to a point where our auditors can deliver their audit report without this qualification in order to avoid a breach of this covenant. In addition, the amended loan agreement prohibits us from (1) incurring any debt other than, among other things, debt under the amended loan agreement, (2) entering into sale and leaseback transactions (3) a change in our management such that our Chief Executive Officer, Chief Financial Officer or President resigns, is terminated or is no longer actively involved in our management in his or her current position and is not replaced with a person acceptable to our board of directors within 120 days and (4) entering into mergers with, or acquisitions of all or substantially all the assets of, another entity with a value in excess of $100,000, and also prohibits the occurrence of a change in control of our company. Under the amended loan agreement, a change in control will be deemed to occur if, among other things, our stockholders as of the effective date of the amended loan agreement cease to hold (a) at least 60% of our capital stock or (b) capital stock having a majority of the ordinary voting power in the election of our directors. The agreement provides that an event of default will occur if, among other customary events of default, (1) there is a material adverse change in our business, operations or condition (financial or otherwise) or material impairment in the prospects of us repaying any portion of our obligations under the agreement, (2) there is a material impairment in the value of the collateral pledged to secure our obligations under the agreement, (3) we default in the payment of any amount payable under the agreement when due, or (4) we breach any covenant in the agreement (subject to a grace period in some cases). In connection with the Cowen Royalty transaction, we paid off all outstanding amounts under our loan and security agreement with GE Capital. In 2009, 2010 and 2011, we were required to obtain amendments or waivers under our credit facilities, and we may in the future need to obtain waivers or amendments under our credit facilities or other debt instruments, in order to avoid a breach or default, particularly if our business deteriorates or does not perform in accordance with our expectations.

Our $30.0 million royalty financing agreement with Cowen Royalty obligates us to make payments to Cowen Royalty of $10.0 million on each of January 31, 2015, 2016 and 2017, as well as fixed percentages of amounts received or recorded from our products sales. Our $35.0 million amended and restated loan and security agreement with Oxford and is secured by all our assets (including, among other things, intellectual property, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash). Our obligations under the Cowen Royalty financing agreement are secured under a security agreement by a second priority security interest (junior to the security interest of Oxford and SVB under the amended and restated loan and security agreement) in all of our assets, including intellectual property and other rights to the extent necessary or used to commercialize our products. The security interest will be extinguished once the aggregate payments made by us to Cowen Royalty equals $75.0 million. Each agreement contains provisions which allow the lenders to demand immediate repayment of the debt and to seize and sell the collateral to pay that debt upon the occurrence of an event of default under the agreement. If we are unable to pay the indebtedness secured by collateral when due, whether at maturity or if declared due and payable by the lender following a default, the lender generally has the right to seize and sell the collateral securing that indebtedness.

In addition, Cowen Royalty has the option to terminate the royalty financing agreement at its election in connection with our change of control (which includes the sale, transfer, assignment or licensing of our rights in the United States to either Sumavel DosePro or Zohydro), a bankruptcy event with respect to us or an event of default under the royalty financing agreement. Upon such a termination by Cowen Royalty, we are obligated to make a payment of a base amount of $45.0 million, or, if higher, an amount that generates a 17% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the payments received by Cowen Royalty up to the date of prepayment. If we were required to accelerate the payment of these amounts upon a default, we would be required to find an alternate source of capital from which to draw funds and there can be no assurances that we would be able to do so on terms acceptable to us, or at all.

There can be no assurance that we will not breach the covenants or other terms of, or that an event of default will not occur under, our credit facilities or any other debt instruments and, if a breach or event of default occurs, there can be no assurance that we will be able to obtain necessary waivers or amendments from the lenders or refinance the related indebtedness on terms we find acceptable, or at all.

As a result, any failure to pay our debt service obligations when due, any breach or default of our covenants or other obligations under debt instruments, or any other event that allows any lender to demand immediate repayment of borrowings, could have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, the arrangement under

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the royalty financing agreement with Cowen Royalty may make us less attractive to potential acquirers, and in the event that we exercised our change of control pay-off option in order to carry out a change of control, the payment of such funds out of our available cash or acquisition proceeds would reduce acquisition proceeds for our stockholders.

Our results of operations and liquidity needs could be materially negatively affected by market fluctuations and economic downturn.

Our results of operations and liquidity could be materially negatively affected by economic conditions generally, both in the United States and elsewhere around the world. Domestic and international equity and debt markets have experienced and may continue to experience heightened volatility and turmoil based on domestic and international economic conditions and concerns. In the event these economic conditions and concerns continue or worsen and the markets continue to remain volatile, our results of operations and liquidity could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may decline. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are not federally insured. If economic instability continues, we cannot provide assurance that we will not experience losses on these investments.

Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

We may raise additional funds through public or private equity offerings, debt financings, receivables or royalty financings or corporate collaboration and licensing arrangements. To the extent that we raise additional capital by issuing equity securities or convertible debt, your ownership interest in us will be diluted. Debt financing typically contains covenants that restrict operating activities. Our amended and restated loan and security agreement with Oxford and SVB is secured by all our assets, including, among other things, intellectual property, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general and tangibles and cash. Our obligations under the Cowen Royalty financing agreement are secured under a security agreement by a second priority security interest (junior to the security interest of Oxford and SVB under the amended and restated loan and security agreement) in all assets of our, including intellectual property and other rights to the extent necessary or used to commercialize our products. The security interest will be extinguished once the aggregate payments made by us to Cowen Royalty equals $75.0 million.

Each such agreement contains provisions which allow such lenders to accelerate the debt and seize and sell the collateral if, among other things, we fail to pay principal or interest when due or breach our obligations under the agreements or if a material adverse change in our business or any other event of default occurs. Any future debt financing we enter into may involve more onerous covenants that restrict our operations and will likely allow the lenders to accelerate the debt and seize and sell any collateral following a default. Our obligations under our outstanding debt agreements or any future debt financing will need to be repaid, which creates additional financial risk for our company, particularly if our business or prevailing financial market conditions are not conducive to paying-off or refinancing our outstanding debt obligations.

If we raise additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish potentially valuable rights to our current product or product candidates or proprietary technologies, or grant licenses on terms that are not favorable to us. If adequate funds are not available, our ability to achieve profitability or to respond to competitive pressures would be significantly limited and we may be required to delay, significantly curtail or eliminate the commercialization and development of our product or product candidates.

Our ability to utilize our net operating loss and research and development income tax credit carryforwards may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the IRC, substantial changes in our ownership may limit the amount of net operating loss and research and development income tax credit carryforwards that could be utilized annually in the future to offset taxable income, if any. Specifically, this limitation may arise in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such annual limitation may significantly reduce the utilization of the net operating loss carryforwards before they expire. We performed a Section 382 and 383 analysis and determined that we had one ownership change, as defined by IRC Sections 382 and 383, which occurred in August 2006 upon the issuance of Series A-1 preferred shares. As a result of this ownership change, we reduced our net operating loss carryforwards by $1.9 million and research and development income tax credit by $8,000. Any future equity financing transactions, together with our initial public offering, private placements and other transactions that have occurred since our inception, may trigger an ownership change pursuant to Sections 382 and 383, which could further limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset taxable income, if any. Any such limitation, whether as the result of prior private placements, sales of common stock by our existing stockholders or additional sales of common stock by us, could have an adverse effect on our results of operations.

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Risks Related to Regulation of our Product and Product Candidates

Our currently marketed product, Sumavel DosePro, is and any of our other product candidates that receive regulatory approval will be subject to ongoing and continued regulatory review, which may result in significant expense and limit our ability to commercialize such products.

Even after we achieve U.S. regulatory approval for a product, the FDA may still impose significant restrictions on the approved indicated uses for which the product may be marketed or on the conditions of approval. For example, a product s approval may contain requirements for potentially costly post-approval studies and surveillance, including Phase 4 clinical trials, to monitor the safety and efficacy of the product. We will also be subject to ongoing FDA obligations and continued regulatory review with respect to the manufacturing, processing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and with GCPs and good laboratory practices, which are regulations and guidelines enforced by the FDA for all of our products in clinical and pre-clinical development, and for any clinical trials that we conduct post-approval. To the extent that a product is approved for sale in other countries, we may be subject to similar restrictions and requirements imposed by laws and government regulators in those countries.

In the case of Zohydro and any other product candidates or products containing controlled substances, we and our contract manufacturers will also be subject to ongoing DEA regulatory obligations, including, among other things, annual registration renewal, security, recordkeeping, theft and loss reporting, periodic inspection and annual quota allotments for the raw material for commercial production of our products. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations, QSR requirements for medical device components or similar requirements, if applicable. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where, or processes by which, the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturer or us, including requiring product recall, notice to physicians, withdrawal of the product from the market or suspension of manufacturing. In that regard, because all of our contract manufacturers for Sumavel DosePro are located outside the United States, they may be subject to foreign laws and regulations governing the manufacture of drugs and devices, and any failure by them to comply with those laws and regulations may delay or interrupt supplies of our product.

If we, our product or product candidates or the manufacturing facilities for our product or product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- impose restrictions on the marketing or manufacturing of the product, suspend or withdraw product approvals or revoke necessary licenses;
- issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- commence criminal investigations and prosecutions;
- impose injunctions, suspensions or revocations of necessary approvals or other licenses;
- impose fines or other civil or criminal penalties;
- suspend any ongoing clinical trials;
- deny or reduce quota allotments for the raw material for commercial production of our controlled substance products;

delay or refuse to approve pending applications or supplements to approved applications filed by us;

refuse to permit drugs or precursor chemicals to be imported or exported to or from the United States;

suspend or impose restrictions on operations, including costly new manufacturing requirements; or

seize or detain products or require us to initiate a product recall.

In addition, our product labeling, advertising and promotion are subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription drug products. In particular, a drug may not be promoted for uses that are not approved by the FDA as reflected in the product s approved labeling, although the FDA does not regulate the prescribing practices of physicians. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including substantial monetary penalties and criminal prosecution.

The FDA s regulations, policies or guidance may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are not able to achieve and maintain regulatory compliance, we may

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not be permitted to market our drugs, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

Sumavel DosePro, Zohydro and our other product candidates may cause undesirable side effects or have other unexpected properties that could result in post-approval regulatory action.

If we or others identify undesirable side effects, or other previously unknown problems, caused by our products, other products or our product candidates with the same or related active ingredients, after obtaining U.S. regulatory approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require us to recall product;
- regulatory authorities may require the addition of warnings in the product label or narrowing of the indication in the product label;
- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way the product is administered or modify the product in some other way;
- the FDA may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of the product;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

The most common treatment-emergent adverse reactions (reported by at least 5% of patients) for *sumatriptan* injection as described in the Sumavel DosePro Prescribing Information summarizing two large placebo-controlled clinical trials were injection site reaction (59%), atypical sensations (42%), dizziness (12%), flushing (7%), chest discomfort (5%), weakness (5%), and neck pain/stiffness (5%).

While the adverse reaction profile for Zohydro has not yet been fully characterized in Phase 3 clinical trials, in two completed Phase 2 studies of Zohydro patients experienced mild to moderate adverse events, such as nausea, vomiting, headache, dizziness, sweating, constipation and drowsiness, which are similar to the reported effects of opioids currently prescribed for chronic pain.

Any of the above events resulting from undesirable side effects or other previously unknown problems could prevent us from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our product candidates.

Our development and commercialization strategy for Zohydro depends upon the FDA s prior findings of safety and effectiveness of Zohydro based on data not developed by us, but which the FDA may rely upon in reviewing our NDA.

The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the FFDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Under this statutory provision, the FDA may rely, for purposes of approving an NDA, on findings of safety and effectiveness based on data not developed by the filer of the NDA. Similar to Sumavel DosePro, we intend to submit the NDA for Zohydro under Section 505(b)(2), and as such the NDA will

rely, in part, on the FDA s previous findings of safety and effectiveness for *hydrocodone*. Even though we may be able to take advantage of Section 505(b)(2) to support potential U.S. approval for Zohydro, the FDA may require us, and did require us with respect to Sumavel DosePro, to perform additional studies or measurements to support approval. In addition, the FDA s interpretation and use of Section 505(b)(2) has been controversial and has previously been challenged in court, but without a definitive ruling on the propriety of the FDA s approach. Future challenges, including a direct challenge to the approval of our products, may be possible and, if successful, could limit or eliminate our ability to rely on the Section 505(b)(2) pathway for the approval of our products. Such a result could require us to conduct additional testing and costly clinical trials, which could substantially delay or prevent the approval and launch of our products.

Zohydro will be subject to DEA regulations and, failure to comply with these regulations, or the cost of compliance with these regulations, may adversely affect our business.

Zohydro contains *hydrocodone*, a regulated controlled substance under the CSA, which establishes, among other things, certain registration, production quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as

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Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Zohydro, because it is a single-entity *hydrocodone* product, is expected to be regulated by the DEA as a Schedule II controlled substance under the CSA. All Schedule II substance prescriptions, such as prescriptions for Zohydro, must be in writing and signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription.

The manufacture, shipment, storage, sale and use, among other things, of controlled substances that are pharmaceutical products are subject to a high degree of regulation, including security, record-keeping and reporting obligations enforced by the DEA. Our failure to comply with these requirements could result in the loss of our DEA registration, significant restrictions on Zohydro, civil penalties or criminal prosecution.

The DEA, and some states, also conduct periodic inspections of registered establishments that handle controlled substances. Facilities that conduct research, manufacture, store, distribute, import or export controlled substances must be registered to perform these activities and have the security, control and inventory mechanisms required by the DEA to prevent drug loss and diversion. Failure to maintain compliance, particularly non-compliance resulting in loss or diversion, can result in regulatory action that could have a material adverse effect on our business, results of operations, financial condition and prospects. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal proceedings.

Individual states also have controlled substances laws. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs, as well. While some states automatically schedule a drug when the DEA does so, in other states there has to be rulemaking or a legislative action. State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could have a material adverse effect on the commercial attractiveness of such product. We or our partners must also obtain separate state registrations in order to be able to obtain, handle, and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

The FDA, in consultation with the DEA, will require us to develop a comprehensive risk management program to reduce the inappropriate use of our product candidate, including restrictions on the manner in which it is marketed and sold, so as to reduce the risk of improper patient selection and diversion or abuse of the product. Developing such a program in consultation with the FDA may be a time-consuming process and could delay approval of our product candidate. Such a program or delays of any approval from the FDA could limit market acceptance of the product.

Under the terms of our license agreement with Elan, Elan has the exclusive right to manufacture and supply both clinical and commercial supplies of Zohydro. While Elan is required to comply with applicable laws and regulations regarding controlled substances, we do not have any direct control over Elan s compliance in these regards, and any failure by Elan to comply with those laws and regulations could result in a reduction or cessation of production of Zohydro.

Annual DEA quotas on the amount of hydrocodone allowed to be produced in the United States and our specific allocation of hydrocodone by the DEA could significantly limit the clinical development of Zohydro as well as the production or sale of Zohydro even if we obtain FDA approval.

The DEA limits the availability and production of all Schedule II substances through a quota system which includes a national aggregate quota and individual quotas. Because *hydrocodone* is subject to the DEA s production and procurement quota scheme, the DEA establishes annually an aggregate quota for how much *hydrocodone* may be produced in total in the United States based on the DEA s estimate of the quantity needed to meet legitimate scientific and medicinal needs. This limited aggregate amount of *hydrocodone* that the DEA allows to be produced in the United States each year is allocated among individual companies, who must submit applications annually to the DEA for individual production and procurement quotas. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments. Elan, which has licensed us the right to sell Zohydro in the United States, if approved, was allocated a sufficient quantity of *hydrocodone* to meet our planned clinical and pre-clinical needs during 2010. However, in future years, we may need greater amounts of *hydrocodone* to sustain and complete our Phase 3 development program for Zohydro which we commenced in March 2010, and we will need significantly greater amounts of *hydrocodone* to implement our commercialization plans if the FDA approves Zohydro.

Moreover, we do not know what amounts of *hydrocodone* other companies developing product candidates containing *hydrocodone* may request for future years. The DEA, in assessing factors such as medical need, abuse and diversion potential and other policy considerations, may choose to set the aggregate *hydrocodone* quota lower than the total amount requested by the

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companies. Elan is permitted to petition the DEA to increase the annual aggregate quota after it is initially established, but there is no guarantee that the DEA would act favorably upon such a petition. Our procurement quota of *hydrocodone* may not be sufficient to meet our future clinical development needs or commercial demand if we receive regulatory approval for Zohydro. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in our quota for *hydrocodone* or a failure to increase it over time as we anticipate could delay or stop the clinical development of Zohydro or if approved, the product launch or commercial sale of Zohydro or cause us to fail to achieve our expected operating results, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

We will need to obtain FDA approval of our proposed product trade names and any failure or delay associated with such approval may adversely impact our business.

Any trade name we intend to use for our products will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or PTO. The FDA typically conducts a rigorous review of proposed trade names, including an evaluation of potential for confusion with other trade names. The FDA may also object to a trade name if it believes the name inappropriately implies medical claims. If the FDA objects to our proposed trade names, we may be required to adopt an alternative name for our product candidate. If we adopt an alternative name, we would lose the benefit of our existing trademark applications and may be required to expend significant additional resources in an effort to identify a suitable trade name that would qualify under applicable trademark laws, and not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to generate revenues from our products.

Even though Sumavel DosePro has received regulatory approval in the United States, we, Desitin, or any other potential partners may never receive approval or commercialize our products outside of the United States.

We have established an exclusive commercial partnership for Sumavel DosePro with Desitin in the European Union and three other countries in order to seek to accelerate the development and regulatory approvals in those territories. We may also seek to establish commercial partnerships for Sumavel DosePro in other foreign countries. In order to market Sumavel DosePro or any other products outside of the United States, we, Desitin, or any potential partner must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our products. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed in these Risk Factors and elsewhere in this Quarterly Report on Form 10-Q regarding FDA approval in the United States, as well as other risks. For example, legislation analogous to Section 505(b)(2) of the FFDCA in the United States does not exist in other countries. In territories where data is not freely available, we or our partners may not have the ability to commercialize our products without negotiating rights from third parties to refer to their clinical data in our regulatory applications, which could require the expenditure of significant additional funds. We, Desitin, or any potential partner may be unable to obtain rights to the necessary clinical data and may be required to develop our own proprietary safety effectiveness dossiers. Desitin submitted a Marketing Authorization Application for Sumavel DosePro to the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)) in Germany, the reference member state, through the Decentralized Procedure in October 2009, following completion of a European pivotal bioequivalence trial comparing needle-free Sumavel DosePro to a traditional needle-based autoinjector, Imigran-Inject, the European brand of Imitrex STATdose. However, regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others.

Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed in these Risk Factors and elsewhere in this Quarterly Report on Form 10-Q regarding FDA approval in the United States. As described above, such effects include the risks that our product candidates may not be approved at all or for all requested indications, which could limit the uses of our product candidates and have an adverse effect on their commercial potential or require costly, post-marketing studies. In addition, we, Desitin, or any potential partner may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution if we fail to comply with applicable foreign regulatory requirements.

Health care reform measures and changes in policies, funding, staffing and leadership at the FDA and other agencies could hinder or prevent the commercial success of Sumavel DosePro and any of our product candidates that may be approved by the FDA.

In the United States, there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our future results of operations and the future results of operations of our potential customers. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established a new Part D prescription drug benefit, which became effective January 1, 2006. Under the prescription drug benefit, Medicare beneficiaries can obtain prescription drug coverage from

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private sector plans that are permitted to limit the number of prescription drugs that are covered in each therapeutic category and class on their formularies. If Sumavel DosePro or any of our product candidates that are approved by the FDA are not widely included on the formularies of these plans, our ability to market our products to the Medicare population could suffer.

Furthermore, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs. Most recently, in March 2010, President Obama signed into law the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA, which includes measures to significantly change the way health care is financed by both governmental and private insurers. Among the provisions of the PPACA of greatest importance to the pharmaceutical industry are the following:

an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, beginning in 2011;

an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively;

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D, beginning in 2011;

extension of manufacturers Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, effective March 23, 2010;

expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in April 2010 and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing both the volume of sales and manufacturers Medicaid rebate liability;

expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective in January 2010;

new requirements to report certain financial arrangements with physicians and others, including reporting any transfer of value made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2012, with reporting starting in 2013;

a new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;

a licensure framework for follow-on biologic products;

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and

establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending beginning by January 1, 2011.

Many of the details regarding the implementation of the PPACA are yet to be determined, and at this time, it remains unclear the full effect that the PPACA would have on our business.

Additionally, individual states have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects.

In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This can reduce demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

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In certain foreign markets, the pricing of prescription drugs is subject to government control and reimbursement and may, in some cases, be unavailable. In the United States, the commercial success of Sumavel DosePro and our product candidates, if and when commercialized, will depend, in part, upon the availability of coverage and reimbursement from third-party payors at the federal, state and private levels. Third-party payors include governmental programs such as Medicare or Medicaid, private insurance plans and managed care plans. These third-party payors may deny coverage or reimbursement for a product or therapy in whole or in part if they determine that the product or therapy was not medically appropriate or necessary. Also, third-party payors have attempted to control costs by limiting coverage through the use of formularies and other cost-containment mechanisms and the amount of reimbursement for particular procedures or drug treatments.

Additionally, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to market our products and generate revenues. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation or re-importation of pharmaceutical products from foreign countries into the United States, including from countries where the products are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could lead to a decision to decrease our prices to better compete, which, in turn, could adversely affect our business, results of operations, financial condition and prospects. Alternatively, in response to legislation such as this, we might elect not to seek approval for or market our products in foreign jurisdictions in order to minimize the risk of re-importation, which could also reduce the revenue we generate from our product sales. It is also possible that other legislative proposals having similar effects will be adopted.

Furthermore, regulatory authorities assessment of the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects. For example, average review times at the FDA for marketing approval applications have fluctuated over the last ten years, and we cannot predict the review time for any of our submissions with any regulatory authorities. In addition, review times can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes.

We may incur liability if our continuing medical or health education programs and/or product promotions are determined, or are perceived, to be inconsistent with regulatory guidelines.

The FDA provides guidelines with respect to appropriate promotion and continuing medical and health education activities. Although we endeavor to follow these guidelines, the FDA or the Office of the Inspector General: U.S. Department of Health and Human Services may disagree, and we may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. In addition, management s attention could be diverted and our reputation could be damaged.

If we fail to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Law, which constrains our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to entities like us which provide coding and billing advice to customers;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and its implementing regulations, and the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, which prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare

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matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;

federal physician self-referral laws, such as the Stark law, which prohibit a physician from making a referral to a provider of certain health services with which the physician or the physician s family member has a financial interest, and prohibit submission of a claim for reimbursement pursuant to a prohibited referral; and

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under the U.S. federal Anti-Kickback Statute, it is possible that some of our business activities could be subject to challenge under one or more of such laws. To the extent that any product we make is sold in a foreign country, we may be subject to similar foreign laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in U.S. federal or state health care programs, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management s attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Import/export regulations and tariffs may change and increase our costs.

We are subject to risks associated with the regulations relating to the import and export of products and materials. We cannot predict whether the import and/or export of our products will be adversely affected by changes in, or enactment of, new quotas, duties, taxes or other charges or restrictions imposed by India (where our supplier of the *sumatriptan* used in Sumavel DosePro is located), the United Kingdom (where the assembly of Sumavel DosePro takes place) or any other country in the future. Any of these factors could adversely affect our business, results of operations, financial condition and prospects.

Risks Related to Intellectual Property

Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection. *

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our product, Sumavel DosePro, and our product candidate, Zohydro, their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing Sumavel DosePro or our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

We in-license certain intellectual property for Zohydro from Elan, and certain intellectual property for Relday from Durect. We rely on these licensors to file and prosecute patent applications and maintain patents and otherwise protect the licensed intellectual property. We have not had and do not have primary control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, with respect to our license agreement with Elan, we cannot be certain that such activities by Elan have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. Elan has retained the first right, but not the obligation, to initiate an infringement proceeding against a third-party infringer of the intellectual property rights that Elan has licensed to us, and enforcement of our licensed patents or defense of any claims asserting the invalidity or unenforceability of these patents would also be subject to the control or cooperation of Elan. We are not entitled to control the manner in which Elan may defend the intellectual property that is licensed to us and it is possible that their defense activities may be less vigorous than had we conducted the defense ourselves.

Most of our patents related to DosePro were acquired from Aradigm, who acquired those patents from a predecessor owner. Our patents related to Zohydro are licensed from Elan. Thus, most of our patents, as well as many of our pending patent applications, were not written by us or our attorneys, and we did not have control over the drafting and prosecution of these patents. Further, the former patent owners and our licensor might not have given the same attention to the drafting and prosecution of these patents and applications as we would have if we had been the owners of the patents and applications and had control over the drafting and prosecution. In addition, the former patent owners and Elan may not have been completely familiar with U.S. patent law, possibly resulting in inadequate disclosure and/or claims. This could possibly result in findings of invalidity or unenforceability of the patents we own and in-license, patents issuing with reduced claim scope, or in pending applications not issuing as patents.

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In addition, as part of the agreement where we acquired patents related to DosePro from Aradigm, Aradigm retained, and we granted to Aradigm, a non-exclusive, worldwide, royalty free license to the acquired patents solely for purposes of the delivery of one or more aerosolized APIs directly into the bronchia or lungs. The agreement with Aradigm also includes a covenant not to compete with us regarding technologies or products for the delivery of one or more APIs via needle free injection. That covenant expired on August 26, 2010, giving Aradigm or its licensees the right to develop and sell other needle-free injection technologies and products.

The patent positions of pharmaceutical, biopharmaceutical and medical device companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in patents in these fields has emerged to date in the United States. There have been recent changes regarding how patent laws are interpreted, and both the PTO and Congress have recently proposed radical changes to the patent system. We cannot accurately predict future changes in the interpretation of patent laws or changes to patent laws which might be enacted into law. Those changes may materially affect our patents, our ability to obtain patents and/or the patents and applications of our collaborators and licensors. The patent situation in these fields outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in the patents we own or to which we have a license or third-party patents.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the pharmaceutical compounds used in Sumavel DosePro and our product candidates but that are not covered by the claims of our patents;
- the APIs in Sumavel DosePro and our current product candidates are, or will soon become, commercially available in generic drug products, and no patent protection will be available without regard to formulation or method of use;
- we or our licensor, as the case may be, may not be able to detect infringement against our in-licensed patents, which may be especially difficult for manufacturing processes or formulation patents;
- we or our licensor, as the case may be, might not have been the first to make the inventions covered by our owned or in-licensed issued patents or pending patent applications;
- we or our licensor, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are dominating patents to Sumavel DosePro or our product candidates of which we are not aware;
- it is possible that there are prior public disclosures that could invalidate our inventions, or our licensor s as the case may be, or parts of our inventions of which we or they are not aware;

it is possible that others may circumvent our owned or in-licensed patents;

it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;

the laws of foreign countries may not protect our or our licensor s, as the case may be, proprietary rights to the same extent as the laws of the United States;

the claims of our owned or in-licensed issued patents or patent applications when issued may not cover our device or product candidates;

our owned or in-licensed issued patents may not provide us with any competitive advantages, or may be narrowed in scope, be held invalid or unenforceable as a result of legal challenges by third parties;

we may not develop additional proprietary technologies for which we can obtain patent protection; or

the patents of others may have an adverse effect on our business.

We also may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, and we have limited control over the protection of trade secrets used by our licensors, collaborators and suppliers. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If our confidential or

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proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace will be harmed and our ability to successfully penetrate our target markets could be severely compromised.

If any of our owned or in-licensed patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Likewise, our patents covering certain technology used in our DosePro device are expected to expire on various dates from 2014 through 2026 and the patents licensed to us by Elan are expected to expire in 2019. Five of our patents, U.S. Patent Nos. 5,891,086, 5,957,886 6,135,979, 7,776,007 and 7,901,385 are expected to expire in 2014, 2016 2017, 2026 and 2026, respectively. U.S. Patent No. 5,891,086 covers a particular actuator mechanism forming a part of the needleless injector device; U.S. Patent No. 5,957,886 claims a needleless injector system using a viscous damping medium; U.S. Patent No. 6,137,979 covers the needleless injector with particular safety mechanisms; and US Patent Numbers 7,776,007 and 7,901,385 cover various elements of the setting mechanism that enables a user to prepare the product for administration in a few simple steps. Upon the expiration of these patents, we will lose the right to exclude others from practicing these inventions. Additionally, since these five patents are the only patents currently listed in the FDA Orange Book for Sumavel DosePro, their expiration will mean that we lose certain advantages that come with Orange Book listing of patents. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. Moreover, if Elan decides not to commence or continue any action relating to the defense of the patents they have licensed to us, they are required to notify us and we have the right to initiate proceedings after receiving their notice. Such proceedings will require the assistance of Elan, and we have limited control over the amount or timing of resources Elan devotes on our behalf or the priority they place on enforcing these patent rights.

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

We are a party to a license agreement with Elan, pursuant to which we license key intellectual property for Zohydro. We also recently entered into a license agreement with Durect, pursuant to which we license key intellectual property for Relday. These existing licenses imposes various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate the license, in which event we would not be able to develop or market the affected products. If we lose such license rights, our business, results of operations, financial condition and prospects may be materially adversely affected. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer similar consequences.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and we may be unable to protect our rights to our products and technology.

If we or our collaborators or licensors choose to go to court to stop a third party from using the inventions claimed in our owned or in-licensed patents, that third party may ask the court to rule that the patents are invalid and/or should not be enforced against that third party. These lawsuits are expensive and would consume time and other resources even if we or they, as the case may be, were successful in stopping the infringement of these patents. In addition, there is a risk that the court will decide that these patents are not valid and that we or they, as the case may be, do not have the right to stop others from using the inventions.

There is also the risk that, even if the validity of these patents is upheld, the court will refuse to stop the third party on the ground that such third-party s activities do not infringe our owned or in-licensed patents. In addition, the U.S. Supreme Court has recently changed some tests regarding granting patents and assessing the validity of patents. As a consequence, issued patents may be found to contain invalid claims according to the newly revised standards. Some of our own or in-licensed patents may be subject to challenge and subsequent invalidation or significant narrowing of claim scope in a reexamination proceeding before the PTO, or during litigation, under the revised criteria which make it more difficult to obtain patents.

We may also not be able to detect infringement of our own or in-licensed patents, which may be especially difficult for methods of manufacturing or formulation products. While we intend to take actions reasonably necessary to enforce our patent rights, we depend, in part, on our licensors and collaborators to protect a substantial portion of our proprietary rights. For example, Elan, our licensor, is primarily responsible for the enforcement of the intellectual property rights related to Zohydro. Under the agreement, Elan has the first right, but not the obligation, to initiate an infringement proceeding against a third-party infringer. If Elan decides not to commence or continue any action, they are required to notify us and grant us step in rights to enforce the in-licensed intellectual property. Such enforcement will require the cooperation of Elan, and we will be responsible for Elan s reasonable expenses and attorney s fees incurred as a result of that cooperation. We have limited control over the amount or timing of resources Elan devotes on our behalf or the priority they place on enforcing these patent rights to our advantage.

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If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our device and product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields relating to Sumavel DosePro and our product candidates. As the medical device, biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our product or product candidates infringe the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of medical devices, drugs, products or their methods of use. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product, product candidates, technology or methods.

In addition, there may be issued patents of third parties of which we are currently unaware, that are infringed or are alleged to be infringed by our product, product candidates or proprietary technologies. Because some patent applications in the United States may be maintained in secrecy until the patents are issued, because patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing, and because publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the PTO to determine priority of invention in the United States. If another party has reason to assert a substantial new question of patentability against any of our claims in our owned and in-licensed U.S. patents, the third party can request that the PTO reexamine the patent claims, which may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential infringement claims, interference and reexamination proceedings, we may become a party to patent opposition proceedings in the European Patent Office where either our patents are challenged, or we are challenging the patents of others. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if the other party had independently arrived at the same or similar invention prior to our own or, if applicable, our licensor s invention, resulting in a loss of our U.S. patent position with respect to such inventions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our device and/or product candidates and/or proprietary technologies infringe their intellectual property rights. These lawsuits are costly and could adversely affect our results of operations and divert the attention of managerial and technical personnel. There is a risk that a court would decide that we or our commercialization partners are infringing the third party s patents and would order us or our partners to stop the activities covered by the patents. In addition, there is a risk that a court will order us or our partners to pay the other party damages for having violated the other party s patents.

If a third-party s patents was found to cover our device and/or product candidates, proprietary technologies or their uses, we or our collaborators could be enjoined by a court and required to pay damages and could be unable to commercialize Sumavel DosePro or our product candidates or use our proprietary technologies unless we or they obtained a license to the patent. A license may not be available to us or our collaborators on acceptable terms, if at all. In addition, during litigation, the patent holder could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our products, technologies or methods pending a trial on the merits, which could be years away.

There is a substantial amount of litigation involving patent and other intellectual property rights in the device, biotechnology and pharmaceutical industries generally. If a third party claims that we or our collaborators infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management s attention from our core business;

- substantial damages for infringement, which we may have to pay if a court decides that the product at issue infringes on or violates the third party s rights, and if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner s attorneys fees;

a court prohibiting us from selling or licensing the product unless the third party licenses its product rights to us, which it is not required to do;

if a license is available from a third party, we may have to pay substantial royalties, upfront fees and/or grant cross-licenses to intellectual property rights for our products; and

redesigning our products or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

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Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Although we own worldwide rights to Sumavel DosePro, we do not have patent protection for the product in a significant number of countries, and we will be unable to prevent infringement in those countries.

Our patent portfolio related to DosePro includes patents in the United States, Canada, Germany, Spain, France, the United Kingdom, Italy, and Japan. The covered technology and the scope of coverage varies from country to country. For those countries where we do not have granted patents, we have no ability to prevent the unauthorized use of our intellectual property, and third parties in those countries may be able to make, use, or sell products identical to, or substantially similar to DosePro.

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

Periodic maintenance fees on our owned and in-licensed patents are due to be paid to the PTO in several stages over the lifetime of the patents. Future maintenance fees will also need to be paid on other patents which may be issued to us. We have systems in place to remind us to pay these fees, and we employ outside firms to remind us or our in-licensor to pay annuity fees due to foreign patent agencies on our pending foreign patent applications. The PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

For the patents and patent applications related to Zohydro, Elan is obligated to maintain our in-licensed patents in the United States under our license agreement. Should Elan fail to pursue maintenance of our licensed patents and patent applications, Elan is obligated to notify us and, at that time, we will be granted an opportunity to maintain the prosecution and avoid withdrawal, cancellation, expiration or abandonment of the licensed U.S. patents and applications.

We also may rely on trade secrets and confidentiality agreements to protect our technology and know-how, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, and we have limited control over the protection of trade secrets used by our licensors, collaborators and suppliers. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If our confidential or proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace will be harmed and our ability to successfully generate revenues from Sumavel DosePro and, if approved by the FDA or other regulatory authorities, our product candidates could be adversely affected.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the device, biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other device, biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management, which would adversely affect our financial condition.

Risks Relating to the Securities Markets and an Investment in Our Stock

The market price of our common stock has fluctuated and is likely to continue to fluctuate.

The market prices for securities of biotechnology and pharmaceutical companies have historically been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Since the commencement of trading in connection with our initial public offering in November 2010, the publicly traded shares of our common stock have themselves experienced significant price and volume fluctuations. During this quarter ended June 30, 2011, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price

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of $3.59 to a high sale price of $5.12. This market volatility is likely to continue and could reduce the market price of our common stock, regardless of our operating performance. In addition, the trading price of our common stock could change significantly over short periods of time due to many factors, including those described elsewhere in this Risk Factors section and the following:

- announcements concerning our and Astellas commercial progress in promoting and selling Sumavel DosePro, including sales and revenue trends;
- the development status of Zohydro or any of our other product candidates, including the results from our clinical trials;
- FDA or international regulatory actions, including whether and when we receive regulatory approval, for any of our product candidates;
- other regulatory developments, including the FDA s potential grant of regulatory exclusivity to a competitor who receives FDA approval before us for an extended-release *hydrocodone* product, which could significantly delay our ability to receive approval for Zohydro;
- announcements of the introduction of new products by us or our competitors;
- announcements concerning product development results or intellectual property rights of others;
- announcements relating to litigation, intellectual property or our business, and the public s response to press releases or other public announcements by us or third parties;
- variations in the level of expenses related to Zohydro or any of our other product candidates or clinical development programs, including relating to the timing of invoices from, and other billing practices of, our CROs and clinical trial sites;
- market conditions or trends in the pharmaceutical sector or the economy as a whole;
- changes in operating performance and stock market valuations of other pharmaceutical companies and price and volume fluctuations in the overall stock market;
- litigation or public concern about the safety of Sumavel DosePro or our product candidates;
- actual and anticipated fluctuations in our quarterly operating results;
- the financial projections we may provide to the public, any changes in these projections or our failure to meet these projections;

deviations from securities analysts estimates or the impact of other analyst comments;

ratings downgrades by any securities analysts who follow our common stock;

additions or departures of key personnel;

third-party payor coverage and reimbursement policies;

developments concerning current or future strategic collaborations, and the timing of payments we may make or receive under these arrangements;

developments affecting our contract manufacturers, component fabricators and service providers;

the development and sustainability of an active trading market for our common stock;

future sales of our common stock by our officers, directors and significant stockholders;

other events or factors, including those resulting from war, incidents of terrorism, natural disasters, security breaches or responses to these events;

changes in accounting principles; and

discussion of us or our stock price by the financial and scientific press and in online investor communities.

In addition, the stock markets, and in particular the Nasdaq Global Market, have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many pharmaceutical companies. Stock prices of many pharmaceutical companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. The realization of any of the above risks or any of a broad range of other risks, including those or any of a broad range of other risks, including those described in these Risk Factors, could have a dramatic and material adverse impact on the market price of our common stock.

There may not be a viable public market for our common stock.

Our common stock had not been publicly traded prior to our initial public offering in November 2010, and an active trading market may not be developed or sustained. We cannot predict the extent to which investor interest in our company will lead to the

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development of an active trading market on the Nasdaq Global Market or otherwise or how liquid that market might become. If an active public market does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at a price that is attractive to you, or at all. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products, product candidates or technologies by using our shares of common stock as consideration.

We may invest or spend our cash in ways with which you may not agree or in ways which may not yield a significant return.

Our management has considerable discretion in the use of our cash. Our cash may be used for purposes that do not increase our operating results or market value. Until the cash is used, it may be placed in investments that do not produce significant income or that may lose value. The failure of our management to invest or spend our cash effectively could result in unfavorable returns and uncertainty about our prospects, each of which could cause the price of our common stock to decline.

Our quarterly operating results may fluctuate significantly.

Our quarterly operating results are difficult to predict and may fluctuate significantly from period to period, particularly because the commercial success of, and demand for, Sumavel DosePro, as well as the success and costs of our Zohydro and other product candidate development programs are uncertain and therefore our future prospects are uncertain. Our net loss and other operating results will be affected by numerous factors, including:

- fluctuations in the quarterly revenues of Sumavel DosePro, including our distributors inventory management practices and buying patterns and the performance by Astellas;
- the level of underlying demand for Sumavel DosePro or any of our other product candidates that may receive regulatory approval;
- ability to control production spending and underutilization of production capacity;
- variations in the level of development expenses related to Zohydro or other development programs;
- results of clinical trials for Zohydro;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments and legislative changes, including healthcare reform, affecting our product and product candidates or those of our competitors; and
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

We may become involved in securities class action litigation that could divert management s attention and adversely affect our business and could subject us to significant liabilities.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations as well a broad range of other factors, including the realization of any of the risks described in these Risk Factors, may cause the market price of our common stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies generally experience significant stock price volatility. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management s attention and resources, which could adversely affect our business. Any adverse determination in any such litigation or any amounts paid to settle any such actual or threatened litigation could require that we make significant payments.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no securities or industry analysts commence coverage of our company, the trading price for our stock would be negatively impacted. If we obtain securities or industry analyst coverage and if one or more of the analysts who covers us downgrades our stock, publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts

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ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

Our executive officers and directors and their affiliates will exercise significant control over stockholder voting matters in a manner that may not be in the best interests of all of our stockholders.*

Our executive officers and directors and their affiliates together control approximately 76% of our outstanding common stock, assuming no exercise of outstanding options or warrants. Four of our non-employee directors are, or are representatives designated by, significant stockholders and two of our directors are executive officers. As a result, these stockholders will collectively be able to significantly influence and may be able to control all matters requiring approval of our stockholders, including the election of directors and approval of significant corporate transactions such as mergers, consolidations or the sale of all or substantially all of our assets. The concentration of ownership may delay, prevent or deter a change in control of our company even when such a change may be in the best interests of some stockholders, impede a merger, consolidation, takeover or other business combination involving us, or could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might adversely affect the prevailing market price of our common stock.

In addition, sales of shares beneficially owned by executive officers and directors and their affiliates could be viewed negatively by third parties and have a negative impact on our stock price. Moreover, we cannot assure you as to how these shares will may be distributed and subsequently voted.

Future sales of our common stock or securities convertible or exchangeable for our common stock may depress our stock price.*

Persons who were our stockholders prior to the sale of shares in our initial public offering continue to hold a substantial number of shares of our common stock that they will be able to sell in the public market in the near future. Significant portions of these shares are held by a small number of stockholders. If these stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale resulting from our recent initial public offering lapse, the trading price of our common stock could decline. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. As of June 30, 2011, we had 34,021,708 shares of common stock outstanding. Of these shares, approximately 14,436,493 are freely tradable, without restriction, in the public market.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act and, in any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of shares of our common stock, warrants to purchase our capital stock and the shares of common stock issuable upon exercise of those warrants are entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. In addition, after the lock-up agreements described above expire, our directors may and we expect that our executive officers will establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for the purpose of effecting sales of our common stock. Any sales of securities by these stockholders, or the perception that those sales may occur, including the entry into such programmed selling plans, could have a material adverse effect on the trading price of our common stock.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;

a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;

a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;

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advance notice requirements for stockholder proposals and nominations for election to our board of directors;

a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than $66^{2}/_{3}\%$ of all outstanding shares of our voting stock then entitled to vote in the election of directors;

a requirement of approval of not less than $66\,^{2}/_{3}\%$ of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and

the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

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

The continued operation and expansion of our business will require substantial funding. Investors seeking cash dividends in the foreseeable future should not purchase our common stock. We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our available cash to fund the development and growth of our business. Any determination to pay dividends in the future will be at the discretion of our board of directors and will depend upon results of operations, financial condition, contractual restrictions, restrictions imposed by applicable law and other factors our board of directors deems relevant. In addition, our ability to pay cash dividends is currently prohibited by the terms of our loan and security agreements. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock, which may never occur.

We incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to meet compliance obligations .*

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the Nasdaq Stock Market, or Nasdaq, that impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition. In addition, on July 21, 2010, the Dodd-Frank Wall Street Reform and Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as say on pay and proxy access. The requirements of these rules and regulations will increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and may also place undue strain on our personnel, systems and resources. Our management and other personnel will need to devote a substantial amount of time to these new compliance initiatives. In addition, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Ensuring that we have adequate internal financial and accounting controls and procedures in place is a costly and time-consuming effort that needs to be re-evaluated frequently. In particular, commencing in fiscal 2011, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act, or Section 404. Our testing, or the subsequent testing by our

independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. We expect to incur significant expense and devote substantial management effort toward ensuring compliance with Section 404. We currently do not have an internal audit function, and we may need to hire additional accounting and financial staff with appropriate public company

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experience and technical accounting knowledge. Implementing any appropriate changes to our internal controls may require specific compliance training for our directors, officers and employees, entail substantial costs to modify our existing accounting systems, and take a significant period of time to complete. Such changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate consolidated financial statements or other reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business. Moreover, effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent fraud. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would entail expenditure of additional financial and management resources.

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

Unregistered Sales of Equity Securities

Not Applicable.

Use of Proceeds

Our initial public offering of common stock was effected through a Registration Statement on Form S-1 (File No. 333-169210) that was declared effective by the Securities and Exchange Commission on November 22, 2010, which registered an aggregate of 16,100,000 shares of our common stock. On November 29, 2010, 14,000,000 shares of common stock were sold on our behalf at an initial public offering price of $4.00 per share, for aggregate gross proceeds of $56.0 million, managed by Wells Fargo Securities, Leerink Swann, Oppenheimer & Co. and Stifel Nicolaus Weisel. On December 27, 2010, in connection with the exercise of the underwriters over-allotment option, 436,493 additional shares of common stock were sold on our behalf at the initial public offering price of $4.00 per share, for aggregate gross proceeds of $1.7 million. Following the sale of the 14,436,493 shares of common stock, the offering terminated.

We paid to the underwriters underwriting discounts and commissions totaling approximately $2.7 million in connection with the offering. In addition, we incurred expenses of approximately $3.3 million in connection with the offering, which when added to the underwriting discounts and commissions paid by us, amounts to total expenses of approximately $6.0 million. Thus, the net offering proceeds to us, after deducting underwriting discounts and commissions and offering expenses, were approximately $51.7 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of June 30, 2011, we had used $44.9 million of the $51.7 million net proceeds from our initial public offering. We used $11.6 million of these proceeds to fund Phase 3 clinical trials and related development activities for Zohydro, and $33.3 million to fund ongoing commercialization of Sumavel DosePro, and for working capital and other general corporate purposes. We invested the remainder of the proceeds in short and intermediate-term, interest-bearing obligations, investment-grade instruments or direct or guaranteed obligations of the U.S. government.

Item 3. Defaults Upon Senior Securities

Not applicable.

Item 4. Removed and Reserved

Item 5. Other Information

Not applicable.

Item 6. Exhibits

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) 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.

ZOGENIX, INC.

Date: August 11, 2011

By: /s/ Roger L. Hawley
Chief Executive Officer

Date: August 11, 2011

By: /s/ Ann D. Rhoads
Executive Vice President, Chief Financial

Officer, Treasurer and Secretary

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EXHIBIT INDEX

Exhibit Number	Description
3.1(2)	Fifth Amended and Restated Certificate of Incorporation of the Registrant
3.2(2)	Amended and Restated Bylaws of the Registrant
4.1(3)	Form of the Registrant s Common Stock Certificate
4.2(1)	Third Amended and Restated Investors Rights Agreement dated December 2, 2009
4.3(1)	Amendment to Third Amended and Restated Investors Rights Agreement dated as of July 1, 2010
4.4(1)	Warrant dated March 5, 2007 issued by the Registrant to General Electric Capital Corporation
4.5(1)	Warrant dated June 30, 2008 issued by the Registrant to Oxford Finance Corporation
4.6(1)	Warrant dated June 30, 2008 issued by the Registrant to CIT Healthcare LLC (subsequently transferred to The CIT Group/Equity Investments, Inc.)
4.7(1)	Transfer of Warrant dated March 24, 2009 from CIT Healthcare LLC to The CIT Group/Equity Investments, Inc.
4.8(1)	Warrant dated July 1, 2010 issued by the Registrant to Oxford Finance Corporation
4.9(1)	Warrant dated July 1, 2010 issued by the Registrant to Silicon Valley Bank
4.10	Warrant dated June 30, 2011 issued by the Registrant to Oxford Finance LLC
4.11	Warrant dated June 30, 2011 issued by the Registrant to Silicon Valley Bank
4.12	Warrant dated July 18, 2011 issued by the Registrant to Cowen Healthcare Royalty Partners II, L.P.
4.13	Second Amendment to Third Amended and Restated Investors Rights Agreement dated as of June 30, 2011
10.1	First Amendment to Second Amended and Restated Loan and Security Agreement dated as of June 30, 2011 among the Registrant and Oxford Finance LLC
10.2	Financing Agreement dated as of June 30, 2011 between the Registrant and Cowen Royalty Healthcare Partners II, L.P.
10.3	Stock and Warrant Purchase Agreement dated as of June 30, 2011 between the Registrant and Cowen Royalty Healthcare Partners II, L.P.
10.4	Development and License Agreement dated as of July 11, 2011 between the Registrant and Durect Corporation
10.5#	Annual Incentive Plan
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
32.1	Certification of Chief Executive Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
32.2	Certification of Chief Financial Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
101	The following financial statements from Zogenix, Inc. s Quarterly Report on form 10-Q for the quarter ended June 30, 2011, filed on August 11, 2011, formatted in XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of

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Exhibit Number	Description
	Operations, (iii) Consolidated Statements of Cash Flows, and (iv) the Notes to Consolidated Financial Statements, tagged as blocks of text.

(1) Filed with the Registrant s Registration Statement on Form S-1 on September 3, 2010.
(2) Filed with Amendment No. 2 to Registrant s Registration Statement on Form S-1 on October 27, 2010.
(3) Filed with Amendment No. 3 to the Registrant s Registration Statement on Form S-1 on November 4, 2010.
Application has been made to the Securities and Exchange Commission to seek confidential treatment of certain provisions. Omitted material for which confidential treatment has been requested has been filed separately with the Securities and Exchange Commission.
# Indicates management contract or compensatory plan.