EDISON

Sunesis Pharmaceuticals

Clinical update

Vecabrutinib not to progress, SNS-510 elevated

Pharma & biotech

Sunesis announced on 23 June that it would not be advancing vecabrutinib to the Phase II portion of its Phase Ib/II study following the results from its highest dose (500mg) cohort. The cohort had three stable disease (SD) responses out of six patients enrolled in the cohort, and Sunesis determined that this level of activity was not sufficient to warrant advancing the program. The company will now refocus efforts on developing its PDK1 inhibitor SNS-510, for which it expects to file an IND by the end of 2020.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/18	0.2	(26.6)	(0.75)	0.0	N/A	N/A
12/19	2.1	(23.3)	(0.27)	0.0	N/A	N/A
12/20e	0.0	(16.6)	(0.14)	0.0	N/A	N/A
12/21e	0.0	(19.9)	(0.16)	0.0	N/A	N/A

Note: *PBT and EPS are normalized, excluding amortization of acquired intangibles, exceptional items and share-based payments.

An unfortunate event, but moving forward

Vecabrutinib is the company's non-covalent BTK inhibitor, which is being examined for the treatment of relapsed and refractory B-cell malignancies such as chronic lymphocytic leukemia (CLL). The aim was that the drug would show activity in patients who had progressed on previous covalent BTK therapy, such as Imbruvica (ibrutinib, AbbVie, Janssen). Three of six patients on the 500mg cohort had SD at the first response assessment (cycle 4), but one of these subsequently relapsed. In the end, one patient from the previous 300mg cohort developed a partial response (PR), but this was not sufficient to justify advancing the program to Phase II.

SNS-510 now on top

Sunesis will now refocus its efforts on the development of SNS-510, its PDK1 inhibitor currently in IND-enabling studies. PDK1 is an enzyme involved in the receptor tyrosine kinase (RTK) activation pathway and implicated in a range of solid and hematologic tumors. The company previously identified heightened activity in cancers with alterations in CDKN2A, which is common in breast and other cancers. Sunesis has been testing it in combination with CDK4/6 (in breast cancer cell lines), KRAS G12C (in KRAS-mutant cancer cells) and BCL-2 (in lymphoma cells).

Valuation: Lowered to $47.2m or $0.36 fully diluted

We have lowered our valuation of Sunesis to $47.2m or $0.36 per diluted share from $188.7m or $1.56 per diluted share. We have fully removed vecabrutinib from our models. This reduction is offset by lower unallocated costs going forward ($10m from $22m) to reflect reduced overhead in light of the discontinuation and other cost-cutting measures that we expect to be put in place. We model a loss of $16.6m for 2020, from $28.5m previously. We expect the company to have a cash runway into 2021, but to require an additional $60m (from $115m) to reach profitability.

26 June 2020

Price	**US$0.31**
Market cap	**US$35m**

Net cash ($m) at 31 March 2020	23.4
Shares in issue	111.4m
Free float	59%
Code	SNSS
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(28.2)	(31.4)	(51.0)
Rel (local)	(31.2)	(44.9)	(53.7)
52-week high/low	US$1.11		US$0.28

Business description

Sunesis Pharmaceuticals is a pharmaceutical company focused on oncology. Its lead asset is SNS-510, an inhibitor of PDK1 in preclinical studies for a range of solid and hematologic tumors. It recently discontinued the development program for its previous lead asset vecabrutinib. It has also developed pan-Raf inhibitor TAK-580, currently licensed to DOT Therapeutics.

Next events

SNS-510 IND filing	By year end FY20

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Edison profile page

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History of vecabrutinib

The goal with vecabrutinib was to develop an inhibitor of Bruton's tyrosine kinase (BTK) that would retain activity after progression on other BTK inhibitors such as Imbruvica. The drug non-covalently binds to BTK, and the company hoped that this would allow it to retain activity in patients with mutations in cysteine-481 (C481), a common resistance mechanism for approved covalent BTK inhibitors (including Imbruvica). It is one of several such non-covalent BTK inhibitors currently in clinical development, which include ARQ-531 (ArQule, Merck) and LOXO-305 (Loxo, Eli Lilly).

The drug previously showed BTK binding and inhibition in preclinical studies and in humans in a Phase Ia study of healthy volunteers. It has been in a Phase Ib/II dose escalation/expansion study since 2017, which showed indications of potential efficacy at some of the earlier tested dose levels, but the hope was that these would develop into robust responses in higher doses. Sunesis previously reported results from dosing cohorts ranging from 25mg to 400 mg, which showed nine SD responses from 18 evaluable patients, including multiple SD responses that were tantalizingly close to being PRs. In the most recent press release, the company announced that one of these patients from the 300mg cohort subsequently developed a PR by cycle 11.

The aim was that that these responses would continue to improve at higher doses and translate into more consistent responses. However, the data seen in the 500mg cohort were not sufficient to warrant advancing the program to Phase II. Three of the six patients enrolled in the cohort had an SD response, but none saw a reduction in tumor burden. Given the lack of improvement in responses at higher doses, Sunesis will complete the ongoing Phase Ib portion of the study, but not advance the drug further.

It is difficult to draw conclusions about the reasons why the drug underperformed. The clinical results from the Phase Ib study do not comport with the previous pharmacokinetics and biochemical activity seen in the Phase Ia healthy volunteer study, which showed inhibitions of phospho-BTK (pBTK) generation of up to 85% at concentrations above 100mg per patient. The number of patients with stable disease in the higher dose cohorts also suggests some degree of activity, but there was no clear dose response. We expect Sunesis to present a more complete picture of these data in the future at a medical conference, which may answer some of these questions.

Realigning efforts to advance SNS-510

The decision to discontinue the clinical program for vecabrutinib will free up resources to develop SNS-510, the company's inhibitor of phosphoinositide-dependent kinase 1 (PDK1). PDK1 is an enzyme central to the malignancy of a range of different cancers given its importance in many growth-signaling pathways. It serves as the junction between PI3K and AKT signaling pathways, both of which have been areas of intense drug development for cancer. Moreover, the company has indicated that the drug inhibits PIP3-independent pathways (outside of the PI3K axis) that may have implications for cancer treatment.

The drug has potential in a range of different solid and hematologic cancers, and Sunesis has invested recently in characterizing this activity profile. It presented results in autumn 2019 characterizing the activity in 320 cell lines in 20 tumor types (the OncoPanel).

The study identified 59 cell lines that were sensitive to the drug, with activity across a range of cancer types. Sunesis was able to correlate response to SNS-510 with mutational data from the OncoPanel, which pointed to the protein cyclin-dependent kinase inhibitor 2A (CDKN2A). 44% of cell lines where the drug was active harbored mutations or deletions in this protein. This is an

interesting new result, because it is currently unclear exactly why this particular protein would underpin activity of a PDK1 inhibitor as it is not part of the canonical pathway. CDKN2A is a protein important for regulating the cell cycle and division, a class of protein that is heavily implicated in cancer and cancer treatment. It has previously been identified as an oncogene, with a focus on familial melanoma.

The company also previously announced that it is investigating SNS-510 in combination with a series of different drugs for different cancer types. It has tested the drug in combination with inhibitors of CDK4/6, KRAS G12C, and BCL-2 in cell lines of breast cancer, KRAS-mutant cancer, and lymphoma respectively (although no data have been released yet). Sunesis stated that it intends to release more detailed preclinical information on these studies at a medical conference in H220, which we expect to inform the future direction that it takes with the drug. It expects to file an IND by the end of 2020 to support initiation of clinical studies in 2021.

Valuation

We have removed vecabrutinib from our model, which has reduced the valuation of Sunesis to $47.2m or $0.36 per diluted share from $188.7m or $1.56 per diluted share. This is partially offset by a reduction in unallocated costs ($10m from $22m) to reflect reduced overhead going forward to extend the cash runway (more details below). Sunesis ended Q120 with $23.4m in net cash, compared with $29.1m at end FY19. We currently model SNS-510 for breast cancer and assume an aggressive timeline, which is contingent on accelerated approval for a genetically defined subset of patients. We may adjust our assumptions for the program in the future when more information regarding its activity profile and future clinical plans become available.

Exhibit 1: Valuation of Sunesis

Development program	Clinical stage	Expected commercialization	Prob. of success	Launch year	Launch pricing ($)	Peak sales ($m)	Patent/exclusivity protection	Royalty/ margin	rNPV ($m)
TAK-580	Phase I/II	Licensed to DOT	5%	2025	500,000	600	2032	10%	$7
SNS-510	IND ready	Proprietary	10%	2025	130,000	344	2031	51%	$27
Unallocated costs (discovery programs, administrative costs, etc.)									($10)
Total									$24
Net cash and equivalents (Q120) ($m)									$23.4
Total firm value ($m)									$47.2
Total basic shares (m)									111.4
Value per basic share ($)									$0.42
Convertible Pref stock (m)									19.7
Total diluted shares									131.1
Value per diluted share									$0.36

Source: Sunesis reports, Edison Investment Research.

Financials

The company reported a net loss of $5.8m for Q120. Following the decision not to pursue a vecabrutinib Phase II study, we have significantly reduced our expected loss for 2020 to $16.6m from $28.5m. This reflects both the direct cost savings from not progressing vecabrutinib and other cost-cutting measures we expect to be put in place to reduce overhead and increase the cash runway. Sunesis ended Q120 with $23.4m net cash, which we model as sufficient to cover expenses into 2021. We expect the company to require an additional $60m in capital (from $115m previously) to bring SNS-510 to market, which we include on our balance sheet as illustrative debt ($30m in 2021 and $30m in 2023).

Exhibit 2: Financial summary

$'000s	2018	2019	2020e	2021e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS				
Revenue	237	2,073	0	0
Cost of Sales	0	0	0	0
Gross Profit	237	2,073	0	0
Research and development	(14,615)	(15,412)	(8,626)	(9,363)
Selling, general & administrative	(11,332)	(9,949)	(7,649)	(7,879)
EBITDA	(25,719)	(23,288)	(16,275)	(17,242)
Operating Profit (before GW and except.)	(25,710)	(23,288)	(16,275)	(17,242)
Intangible amortization	0	0	0	0
Exceptionals/Other	0	0	0	0
Operating Profit	(25,710)	(23,288)	(16,275)	(17,242)
Net Interest	(905)	(42)	(317)	(2,660)
Other (change in fair value of warrants)	0	0	0	0
Profit Before Tax (norm)	(26,615)	(23,330)	(16,592)	(19,901)
Profit Before Tax (IFRS)	(26,615)	(23,330)	(16,592)	(19,901)
Tax	0	0	0	0
Deferred tax	0	0	0	0
Profit After Tax (norm)	(26,615)	(23,330)	(16,592)	(19,901)
Profit After Tax (IFRS)	(26,615)	(23,330)	(16,592)	(19,901)
Average Number of Shares Outstanding (m)	35.6	87.1	117.0	122.2
EPS - normalized ($)	(0.75)	(0.27)	(0.14)	(0.16)
EPS - IFRS ($)	(0.75)	(0.27)	(0.14)	(0.16)
Dividend per share ($)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	124	918	787	19
Intangible Assets	0	0	0	0
Tangible Assets	11	3	10	19
Other	113	915	777	0
Current Assets	15,200	36,322	21,014	33,961
Stocks	0	0	0	0
Debtors	0	0	0	0
Cash	13,696	34,625	19,317	32,264
Other	1,504	1,697	1,697	1,697
Current Liabilities	(11,323)	(9,416)	(3,397)	(3,574)
Creditors	(3,927)	(3,951)	(3,397)	(3,574)
Short term borrowings	(7,396)	(5,465)	0	0
Long Term Liabilities	(8)	(281)	(5,605)	(35,605)
Long term borrowings	0	0	(5,465)	(35,465)
Other long term liabilities	(8)	(281)	(140)	(140)
Net Assets	3,993	27,543	12,799	(5,199)
CASH FLOW				
Operating Cash Flow	(24,404)	(22,185)	(15,301)	(17,043)
Net Interest	0	0	0	0
Tax	0	0	0	0
Capex	0	0	(7)	(9)
Acquisitions/disposals	0	0	0	0
Financing	6,343	45,082	0	0
Dividends	0	0	0	0
Other	0	0	0	0
Net Cash Flow	(18,061)	22,897	(15,308)	(17,052)
Opening net debt/(cash)	(24,546)	(6,300)	(29,160)	(13,852)
HP finance leases initiated	0	0	0	0
Exchange rate movements	0	0	0	0
Other	(185)	(37)	0	0
Closing net debt/(cash)	(6,300)	(29,160)	(13,852)	3,201

Source: Sunesis reports, Edison Investment Research.

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