EDISON

Sunesis Pharmaceuticals

Earnings update

A slight delay

Pharma & biotech

On the YE FY17 conference call, the company provided revised guidance on the dosing portion of its ongoing Phase Ib/II study of vecabrutinib (SNS-062) in chronic lymphocytic leukemia (CLL) and other B-cell cancers. The final dose is expected to be reached in fall 2018 (revised from mid-2018) due to an on-protocol expansion of the second (50mg) dosing cohort because of a dose-limiting adverse event (AE). At this time we do not consider this delay or the AE to be material to the success of the program.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/16	2.5	(38.0)	(2.42)	0.00	N/A	N/A
12/17	0.7	(35.5)	(1.45)	0.00	N/A	N/A
12/18e	0.0	(36.8)	(1.02)	0.00	N/A	N/A
12/19e	0.0	(38.4)	(1.02)	0.00	N/A	N/A

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

Cohort expansion triggered for 50mg dose

The dose escalation is of a traditional 3+3 design, in which an additional three patients are enrolled if a dose-limiting toxicity (DLT) is observed in the initial three person cohort. A DLT is defined as an AE that prevents the patient from continuing dosing, although this may be an isolated event. The 3+3 design is structured to adapt to such unforeseen events to find the true maximum tolerated dose, although it does trigger a delay before higher doses can be assessed.

Enrolment expanded to include DLBCL and FL

In January, the company expanded the enrolment criteria for the Phase Ib/II trial to also include diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL), two other B-cell cancers. The addition of these indications was made to ensure the timely enrolment of the dosing portion of the trial, although we expect it to complicate the interpretation of the efficacy of the drug in C481S mutants as BTK inhibitors are not currently approved for these indications.

Early dosing data show a cumulative dose response

The company presented data on patients from the first dosing cohort (25mg twice a day) of its ongoing Phase Ib/II trial of vecabrutinib (SNS-062). Two out of the three patients examined had the C481S mutation, confirming in practice data from independent studies. Two of the patients were evaluable for pharmacology and saw potent inhibitions of phosphorylated BTK that increased with repeated dosing, even at this low concentration, further supporting the clinical activity of this drug.

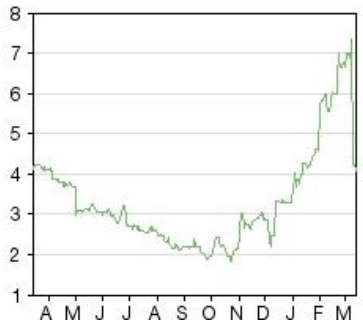
Valuation: $237.8m or $6.92 per basic share

We have increased our valuation of Sunesis to $237.8m or $6.92 per basic share from $125.9m or $3.68. This is driven by adjustments in our pricing assumptions to maintain consistency with current trends, as well as decreasing the corporate tax rate in line with US tax reform and advancing our NPVs. We believe it is premature to draw any conclusions regarding vecabrutinib from the recent announcement.

13 March 2018

Price	**US$4.07**
Market cap	**US$139m**
Net cash ($m) at 31 December 2017	24.5
Shares in issue	34.2m
Free float	56%
Code	SNSS
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(29.1)	22.1	(1.6)
Rel (local)	(32.3)	16.9	(16.1)
52-week high/low	US$7.4	US$1.8	

Business description

Sunesis Pharmaceuticals is a pharmaceutical company focused on oncology. Its lead asset is SNS-062, a BTK inhibitor for CLL for Imbruvica refractory patients. The program is entering a dose escalation Phase Ib/II. It has also developed TAK-580 with partner Takeda, and the preclinical PDK1 inhibitor SNS-510.

Next events

Vecabrutinib Phase II dose announced	Fall 2018
TAK-580 option decision	Mid/late 2018

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Edison profile page

Vecabrutinib Phase Ib hits a snag

The company provided an update of its ongoing Phase Ib/II clinical trial of vecabrutinib on its year-end FY17 conference call. The trial is currently in the dose escalation portion, examining between 25mg and 500mg twice a day, with plans to expand the study into Phase II once the appropriate dose is found. Progression may be triggered either when the maximum tolerated dose (MTD) or another lower dose with sufficient efficacy is found.

The company announced that in the second dosing cohort (50mg) a patient was unable to proceed due to an adverse event (AE). Whenever a patient is unable to continue treatment due to an AE that cannot be ruled out as non-drug related, this is counted as a dose-limiting toxicity (DLT). As a result, the 50mg cohort was expanded with three additional patients (the standard '3+3' dose escalation trial protocol). Per the protocol, if an additional DLT is observed, 50mg will be considered above the MTD.

The company did not provide any additional detail on the nature or severity of the AE that triggered the withdrawal. We believe that it is premature to draw conclusions regarding the tolerability of the drug as the 3+3 trial design is crafted to adapt to unforeseen terminations of treatment. However, because additional patients will need to be enrolled in this arm, the company has delayed its guidance for completion of the dosing study to fall 2018 from mid-2018.

The company also mentioned that one patient in the 50mg cohort progressed before he or she could complete the study. This detail is not surprising given the severity of these patients and the fact that the 50mg dose is below the expected effective dose (100-300mg).

The company has also added additional clinical sites to the trial and expanded the enrolment criteria to include diffuse large B-cell lymphoma of the activated B-cell subtype (DLBCL-ABC) and follicular lymphoma (FL). This amendment was made to the clinical trial protocol in January 2018. The inclusion of these other indications should speed trial enrolment to help the company maintain the guidance toward completion in fall 2018. However, it may potentially complicate the evaluation of efficacy. Imbruvica is not currently approved for either of these cancers and it is therefore unlikely that these patients will harbour the C481S resistance mutation. This being said, Imbruvica has shown activity in the ABC subtype of DLBCL.[1] Likewise, there are signals of activity in FL, but limited to particular genetic subtypes.[2] The inclusion of these indications should not affect the interpretation of the dosing data and it should therefore increase the likelihood of delivering the Phase II dose on time. The main focus of the program is on patients with the C841S mutation, but vecabrutinib also has potential activity and is planned to also be examined in unmutated individuals. In addition, if any efficacy is seen in these new indications, the company could potentially include them in the expansion portion of the study.

Preliminary data from first dosing cohort

At the American Society of Hematology annual meeting in December 2017, Sunesis presented some preliminary data from its first dosing cohort in the Phase Ib/II trial. It should be noted that the dose examined in the data (25mg twice a day) is 20 times lower than the maximum that will be examined on the study (500mg twice a day) and we expect a dose well below this will be moved

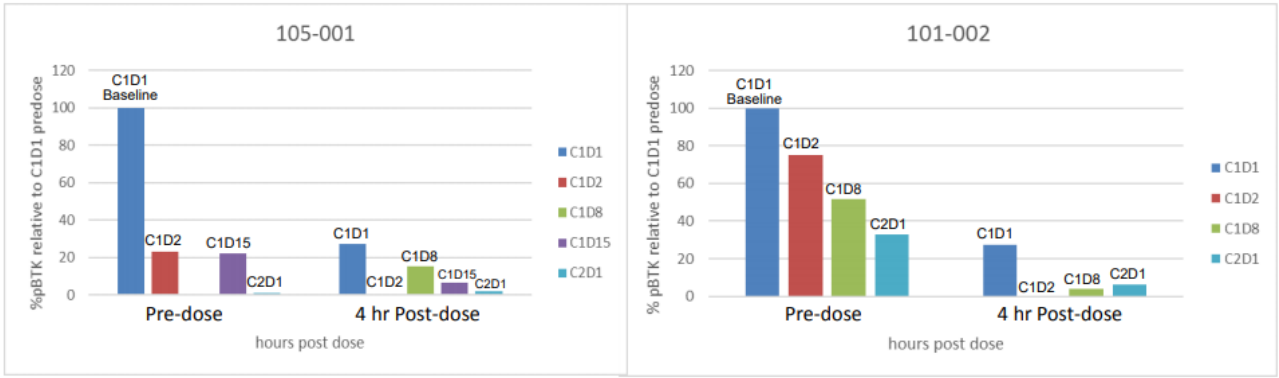
[1] Wilson WH (2014) Targeting B cell receptor signaling with ibrutinib in diffuse large B cell lymphoma. *Nature Med* 21, 922-926.

[2] Bartlett NL (2018) Single-Agent Ibrutinib in Relapsed or Refractory Follicular Lymphoma: A Phase 2 Consortium Trial. *Blood* 131, 182-190.

forward. Of the three patients examined, two had C481S mutations. This is important because it provides additional confirmation in practice that a large fraction of patients developing Imbruvica resistance via this mechanism. This is in line with results obtained in other independent studies.[3]

These results did not provide any efficacy data, given its preliminary nature. However, the company was able to provide some pharmacologic data demonstrating that the drug was well absorbed and inhibited the generation of phosphorylated BTK (pBTK), the core mechanism of BTK inhibitors. It was found that even at this low dose, the drug effectively inhibited the enzyme and that this inhibition became more pronounced with repeated dosing (Exhibit 1). This provides additional evidence that the drug is working as designed, and is potent, even at this low dose. 85% inhibition of BTK has previously been identified as sufficient for clinical activity during studies of AstraZeneca's BTK inhibitor Calquence (acalabrutinib).[4]

Exhibit 1: Inhibition of pBTK formation in two patients



Source: Sunesis

The study also provided some safety data: AEs included low grade headache, back pain, cytopenias and infection. It is hard to draw any conclusions regarding the safety of the drug at this point given the low dose. Cytopenias and infection are on-target AEs for this class and were common in trials of Imbruvica.

Valuation

We have increased our valuation of Sunesis to $237.8m or $6.92 per basic share from $125.9m or $3.68 per basic share. We have decreased the federal corporate tax rate to 20% in accordance with the new US legislation. We have updated our launch pricing assumptions for SNS-510 from $101,000 to $130,000 and for TAK-580 to $146,000 from $138,000 to bring them in line with recent pricing trends for Zydelig (idelalisib, Gilead) and Tafinlar (dabrafinib, GSK) respectively. As previously, our pricing assumes a further 2% yearly growth in prices until launch. We have decreased our gross/net discount for vecabrutinib to 20% (from 30%) to bring it in line with our estimates for Imbruvica (ibrutinib, AbbVie/Janssen). Another factor affecting our valuation is the continued strong growth in Imbruvica market share, which has limited impact on our peak sales estimates but has lifted near-term sales estimates of Imbruvica-resistant patients. We have also advanced our NPVs to the most recent period and adjusted for new net cash. These effects are partially offset by a delay in our expected commercialization of SNS-510 given the company guidance to an IND filing in 2019.

[3] Woyach JA (2017) BTKC481S-Mediated Resistance to Ibrutinib in Chronic Lymphocytic Leukemia. *J Clin Oncol* 35, 1437-1443.

[4] Byrd JC, et al. (2016) Acalabrutinib (ACP-196) in Relapsed Chronic Lymphocytic Leukemia. *N Engl J Med.* 374, 323-32

Exhibit 2: 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 Ib	Licensed to Takeda	15%	2021	146,000	777	2032	15%	$38
Vecabrutinib	Phase Ib/II	Proprietary	20%	2022	152,000	666	2034	56%	$176
SNS-510	IND ready	Proprietary	10%	2023	130,000	380	2031	51%	$24
Unallocated costs (discovery programs, administrative costs etc)									($25)
Total									$213
Net cash and equivalents (YE FY17) ($m)									$24.5
Total firm value ($m)									$237.8
Total basic shares (m)									34.3
Value per basic share ($)									**$6.92**
Convertible pref stock (m)									6.3
Warrants and options									8.7
Total diluted shares									49.4
Value per diluted share ($)									$5.57

Source: Sunesis reports, Edison Investment Research.

Financials

The company reported results for year-end FY17 on 8 March 2018 and results were largely within our expectations. The company reported losses of $35.5m for the year, driven largely by $21.5m in R&D spending. This spending was slightly lower than previous years ($22.9m in 2016, $23.7m in 2015) largely because of the deprioritization of vosaroxin. We expect R&D spending to remain relatively steady ($20m in 2018) in the near term as the company progresses the ongoing vecabrutinib Phase Ib/II study. The company paid down and refinanced its debt, leaving $7.2m in notes payable (at 8.54%+LIBOR). Principal payments will start in October 2018, unless the company can raise at least $6.5m in additional capital from equity (which will delay principal payments until January 2019). We expect the company to require at least $135m in additional financing before profitability in 2023, which we record as illustrative debt ($25m, $20m, $30m, $40m and $20m in 2018-2022 respectively).

Exhibit 3: Financial summary

$'000s	2016	2017	2018e	2019e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS				
Revenue	2,536	669	0	0
Cost of Sales	0	0	0	0
Gross Profit	2,536	669	0	0
Research and development	(22,881)	(21,540)	(19,824)	(19,333)
Selling, general & administrative	(16,115)	(13,548)	(13,634)	(14,043)
EBITDA	(36,313)	(34,428)	(33,467)	(33,385)
Operating Profit (before GW and except.)	(36,302)	(34,419)	(33,458)	(33,376)
Intangible Amortisation	0	0	0	0
Exceptionals/Other	0	0	0	0
Operating Profit	(36,302)	(34,419)	(33,458)	(33,376)
Net Interest	(1,721)	(1,039)	(3,365)	(5,073)
Other (change in fair value of warrants)	0	0	0	0
Profit Before Tax (norm)	(38,023)	(35,458)	(36,824)	(38,449)
Profit Before Tax (IFRS)	(38,023)	(35,458)	(36,824)	(38,449)
Tax	0	0	0	0
Deferred tax	0	0	0	0
Profit After Tax (norm)	(38,023)	(35,458)	(36,824)	(38,449)
Profit After Tax (IFRS)	(38,023)	(35,458)	(36,824)	(38,449)
Average Number of Shares Outstanding (m)	15.7	24.5	36.0	37.6
EPS - normalised ($)	(2.42)	(1.45)	(1.02)	(1.02)
EPS - IFRS ($)	(2.42)	(1.45)	(1.02)	(1.02)
Dividend per share ($)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	3	1,401	11	2
Intangible Assets	0	0	0	0
Tangible Assets	3	20	11	2
Other	0	1,381	0	0
Current Assets	43,231	32,933	34,085	19,644
Stocks	0	0	0	0
Debtors	0	0	0	0
Cash	42,588	31,750	32,902	18,461
Other	643	1,183	1,183	1,183
Current Liabilities	(5,814)	(8,901)	(1,708)	(1,704)
Creditors	(2,481)	(1,697)	(1,708)	(1,704)
Short term borrowings	(3,333)	(7,204)	0	0
Long Term Liabilities	(11,271)	(112)	(39,520)	(59,520)
Long term borrowings	(11,102)	0	(39,408)	(59,408)
Other long term liabilities	(169)	(112)	(112)	(112)
Net Assets	26,149	25,321	(7,132)	(41,578)
CASH FLOW				
Operating Cash Flow	(36,962)	(36,142)	(31,052)	(34,441)
Net Interest	0	0	0	0
Tax	0	0	0	0
Capex	0	(26)	0	0
Acquisitions/disposals	0	0	0	0
Financing	26,111	32,930	0	0
Dividends	0	0	0	0
Other	0	0	0	0
Net Cash Flow	(10,851)	(3,238)	(31,052)	(34,441)
Opening net debt/(cash)	(38,596)	(28,153)	(24,546)	6,506
HP finance leases initiated	0	0	0	0
Exchange rate movements	0	0	0	0
Other	408	(369)	0	0
Closing net debt/(cash)	(28,153)	(24,546)	6,506	40,947

Source: Company data; Edison Investment Research estimates

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