EDISON

Sunesis Pharmaceuticals

Dosing update at ASH

Earnings and clinical update

Pharma & biotech

Sunesis released its abstracts for the upcoming American Society of Hematology (ASH) meeting, which included an update on the company's ongoing Phase Ib/II trial of vecabrutinib in hematologic cancers. The study is still in the dosing portion of the trial on the 50mg arm, but the data to date showed a safety and tolerability profile in line with expectations. The company will provide a complete update of the trial progress at ASH.

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	0.2	(28.8)	(0.81)	0.00	N/A	N/A
12/19e	0.0	(34.9)	(0.94)	0.00	N/A	N/A

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

The 50mg arm is continuing to enrol

Vecabrutinib is in the dosing portion of a dose escalation/expansion study in patients with chronic lymphocytic leukemia and other hematologic malignancies. The study hit a delay earlier this year when it encountered a dose-limiting toxicity (DLT) that triggered an expansion of the 50mg cohort. In the abstract, the company revealed that some of these patients progressed before completion of their first course, necessitating further enrolment. The 50mg dose is below the threshold of clinical activity, so it is simply an unfortunate risk they have encountered.

AE mostly hematologic; prior DLT due to ALT

The initial safety profile from the evaluation patients was predominantly hematologic, which is to be expected given the patient population and drug class. Additionally there were night sweats, back pain, pyrexia and elevated aminotransferase (ALT). The abstract also revealed that the previously reported DLT was caused by an ALT elevation that prevented complete dosing; although we need further data to fully assess this, it is less of a worry than many alternatives.

Increased evidence on BTK C481 mutations

One of the goals of vecabrutinib is to address the known mechanism of resistance to Imbruvica via mutation of cysteine 481 (C481) of Bruton's tyrosine kinase (BTK). However, real-world data on the prevalence of this mutation has been sparse. Sunesis participated in a collaborative study being presented at ASH in which patients were examined after three years of Imbruvica treatment, of which 57% had mutations at C481, most of which subsequently progressed. This provides increasing evidence this mechanism is central to Imbruvica resistance.

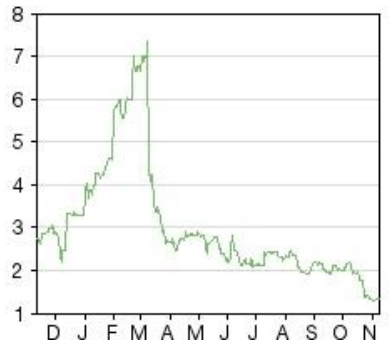
Valuation: $224m or $5.99 per basic share

Our valuation is negligibly changed at $224.0m (from $224.4m) although it is lower on a per basic-share basis ($5.99 from $6.21) due to an increase in shares outstanding. We have slightly delayed the commercialization of vecabrutinib by six months to 2023, although the impact of this is offset by advancing our NPVs.

9 November 2018

Price	**US$1.35**
Market cap	**US$51m**
Net cash ($m) at Q318	12.8
Shares in issue	37.4m
Free float	96%
Code	SNSS
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(38.9)	(42.3)	(49.6)
Rel (local)	(37.2)	(41.3)	(53.4)
52-week high/low	US$7.4		US$1.3

Business description

Sunesis Pharmaceuticals is a pharmaceutical company focused on oncology. Its lead asset is SNS-062, a Bruton's tyrosine kinase inhibitor for chronic lymphocytic leukemia 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

ASH update	1–4 December 2018
SNS-510 IND filing	2019

Analysts

Nathaniel Calloway +1 646 653 7036

Maxim Jacobs +1 646 653 7027

healthcare@edisongroup.com

Edison profile page

ASH abstracts out

On 1 November 2018, Sunesis announced three abstracts it would be presenting at the annual meeting of the ASH on 1–4 December.

- Preliminary safety, pharmacokinetic and pharmacodynamic results from a Phase Ib/II dose-escalation and cohort-expansion study of the noncovalent, reversible BTK inhibitor (BTKi), vecabrutinib, in B-lymphoid malignancies
- High prevalence of BTK mutations on ibrutinib therapy after three years of treatment in a real-life cohort of chronic lymphocytic leukemia (CLL) patients: a study from the French innovative leukemia organization group
- Vecabrutinib is efficacious in vivo in a preclinical CLL adoptive transfer model

We expect to provide more thorough analysis of the data following the presentations, although we can provide some initial insights from the published abstracts.

Phase Ib/II continues to enrol 50mg, no safety surprises

The most immediately important news from the abstracts was the update on the ongoing Phase Ib/II study of vecabrutinib in patients with CLL and other hematologic malignancies. The study is in the dose-ranging phase and the abstract provided the information that enrolment was continuing with the second (50mg twice daily) dosing cohort. Three of the six patients enrolled in the cohort had disease progression before completion of their first treatment cycle, and therefore additional patients will need to be enrolled to complete the cohort. The 50mg dose is below the expected range in which we would expect to see clinical activity, so we do not consider these progressions indicative of issues with the drug, simply an unavoidable risk intrinsic to the study protocol.

The abstract provided an update of the observed adverse events (AEs) to date, which were in line with expectations. Most of the treatment emergent AEs in the study were hematologic (anemia, leukopenia, etc), which can be caused by either these disease or the treatment effect of the drug (although it is too early to draw conclusions in this regard). Night sweats, back pain, pyrexia and elevated ALT were also reported. The company previously expanded the 50mg cohort (per the 3+3 dose escalation protocol) following a DLT, which this abstract revealed was because a patient failed to receive an adequate number of doses in the first cycle due to elevated ALT. We consider the revelation that the DLT was caused by elevated ALT to be preferable to the alternatives. It is still too early to conclude if hepatotoxicity is tied to administration of the drug, but even if it is, it is an AE that can generally be managed. This is a better case than the other events that could be imagined, but continued safety data will be needed to draw any lasting conclusions.

More evidence of the importance of BTK C481

One of the uncertainties regarding vecabrutinib has been a precise understanding of Imbruvica resistance. A mechanism of Imbruvica resistance has been the mutation of C481 in the drug's target, BTK. Vecabrutinib is a non-covalent inhibitor of BTK and can efficiently bind and inhibit BTK C481 mutants, positioning it as an effective treatment in these patients. However, there has been limited data gathered regarding the frequency of C481 mutations in this population to date. To hopefully illuminate this, Sunesis participated in a study along with a number of French academic institutions to determine the prevalence of various resistance mutations, the data from which will be presented at ASH.

The study examined blood samples from 57 individuals with CLL that had been on Imbruvica treatment for at least three years. Of these, 30 were evaluable for mutations, of which 17 (57%) had C481 mutations (a majority of which were to serine, C418S). A minority (four of 30) had mutation in

PLCγ2, which is another known resistance mechanism for Imbruvica. In total, 12 patients on the study progressed within six months of blood-sample collection, 11 of which harboured BTK C481 mutations (and two of which had PLCγ2 mutations). These data are encouraging because it provides additional evidence that C481 is the primary resistance mechanism for Imbruvica.

Vecabrutinib alters T-cell populations in mice

The third presentation that Sunesis will have at ASH regards a preclinical mouse model study in which the impact of vecabrutinib on T-cells is studied. It was found that the drug significantly altered the composition of T-cell subpopulations without changing the ratio of CD4 (helper) to CD8 (killer cells). There was a decrease in regulatory CD4 T-cells, which should result in more immune activation, but this was balanced by a shift in CD8 cells toward naïve cells from memory and effector cells, so the net impact on immune activation is unclear. Other studies have reported similar shifts in T-cell populations in patients on Imbruvica.[1] However, the current study also included survival data from mice showing a significant increase in survival (35 days vs 28 days $p<0.001$), confirming the drug's activity in this model. We will need further data to fully appreciate what impact, if any, these results indicate.

Valuation

Our valuation is negligibly changed at $224.0m (from $224.4m) although is lower on a per basic-share basis ($5.99 from $6.21) due to an increase in shares outstanding. We have delayed the expected commercialization of vecabrutinib by approximately six months to account for the increased time to complete the dosing study, which has moved our initial launch date into 2023 (from 2022). However, the impact of this adjustment is offset by advancing our NPVs. We may update our valuation of vecabrutinib in the future following more data from the ongoing study at ASH.

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 Takeda	10%	2025	500,000	603	2032	15%	$19
Vecabrutinib	Phase Ib/II	Proprietary	20%	2023	152,000	666	2034	56%	$187
SNS-510	IND ready	Proprietary	10%	2024	130,000	361	2031	51%	$25
Unallocated costs (discovery programs, administrative costs, etc.)									($20)
Total									$211
Net cash and equivalents (Q318) ($m)									$12.8
Total firm value ($m)									$224.0
Total basic shares (m)									37.4
Value per basic share ($)									$5.99
Convertible pref stock (m)									6.3
Warrants and options									8.7
Total diluted shares									52.4
Value per diluted share									$4.98

Source: Sunesis reports, Edison Investment Research

Financials

Losses for Q318 were lower than expected at $6.3m due to the continued enrolment into the dosing portion of the vecabrutinib clinical study. We expect R&D expenses to increase when the study

[1] Podhorecka M, et al. (2017) Changes in T-cell subpopulations and cytokine network during early period of ibrutinib therapy in chronic lymphocytic leukemia patients: the significant decrease in T regulatory cells number. *Oncotarget* 23, 34661-34669.

enrols a wider number of patients, which we now predict in 2019. This has reduced our expected R&D spending for 2018 to $15.1m from $18.0m. Our financing schedule remains unchanged, however. 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 2: Financial summary

$'000s	2016	2017	2018e	2019e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS				
Revenue	2,536	669	237	0
Cost of Sales	0	0	0	0
Gross Profit	2,536	669	237	0
Research and development	(22,881)	(21,540)	(15,123)	(17,485)
Selling, general & administrative	(16,115)	(13,548)	(12,575)	(12,952)
EBITDA	(36,313)	(34,428)	(27,470)	(30,447)
Operating Profit (before GW and except.)	(36,302)	(34,419)	(27,461)	(30,438)
Intangible Amortisation	0	0	0	0
Exceptionals/Other	0	0	0	0
Operating Profit	(36,302)	(34,419)	(27,461)	(30,438)
Net Interest	(1,721)	(1,039)	(1,360)	(4,475)
Other (change in fair value of warrants)	0	0	0	0
Profit Before Tax (norm)	(38,023)	(35,458)	(28,821)	(34,912)
Profit Before Tax (IFRS)	(38,023)	(35,458)	(28,821)	(34,912)
Tax	0	0	0	0
Deferred tax	0	0	0	0
Profit After Tax (norm)	(38,023)	(35,458)	(28,821)	(34,912)
Profit After Tax (IFRS)	(38,023)	(35,458)	(28,821)	(34,912)
Average Number of Shares Outstanding (m)	15.7	24.5	35.6	37.2
EPS - normalised ($)	(2.42)	(1.45)	(0.81)	(0.94)
EPS - IFRS ($)	(2.42)	(1.45)	(0.81)	(0.94)
Dividend per share ($)	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	38,989	28,318
Stocks	0	0	0	0
Debtors	0	0	0	0
Cash	42,588	31,750	37,687	27,016
Other	643	1,183	1,302	1,302
Current Liabilities	(5,814)	(8,901)	(1,414)	(1,554)
Creditors	(2,481)	(1,697)	(1,414)	(1,554)
Short term borrowings	(3,333)	(7,204)	0	0
Long Term Liabilities	(11,271)	(112)	(32,400)	(52,400)
Long term borrowings	(11,102)	0	(32,396)	(52,396)
Other long term liabilities	(169)	(112)	(4)	(4)
Net Assets	26,149	25,321	5,186	(25,634)
CASH FLOW				
Operating Cash Flow	(36,962)	(36,142)	(25,373)	(30,671)
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	6,303	0
Dividends	0	0	0	0
Other	0	0	0	0
Net Cash Flow	(10,851)	(3,238)	(19,070)	(30,671)
Opening net debt/(cash)	(38,596)	(28,153)	(24,546)	(5,291)
HP finance leases initiated	0	0	0	0
Exchange rate movements	0	0	0	0
Other	408	(369)	(185)	0
Closing net debt/(cash)	(28,153)	(24,546)	(5,291)	25,380

Source: Sunesis reports, Edison Investment Research

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
295 Madison Avenue, 18th Floor
10017, New York
US

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia