EDISON

Sunesis Pharmaceuticals

Clinical update

ASH 2018: 50mg cohort on last patient

Pharma & biotech

The company provided an update at the American Society of Hematology (ASH) 2018 meeting in December on its ongoing dose-escalation study of vecabrutinib for B-cell malignancies. Four new patients have been enrolled in the past month and the 50 mg cohort is now overenrolled. Safety data is only needed from a single patient, so barring any issues, the trial should progress to 100mg soon, where we may see the first signs of efficacy.

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.

Signs of forward progress

The dosing study has struggled to progress past the 50mg cohort with delays due to a cohort expansion and patients that progressed before safety could be evaluated. However, following these most recent results it may soon be in the rear view. Enrolment appears to progressing steadily across the eight open clinical sites, and there are four patients on the drug after the enrolment, including two new patients in the 50mg cohort (although only one is needed to progress).

AEs in line, GI effects limited to date

The company presented the most detailed data so far on adverse events (AEs) from the 10 patients that were evaluable for safety. The most common continue to be hematological, which is normal for this drug class and patient population. Interestingly, there have been few gastrointestinal (GI) AEs, which is unlike what has been previously seen with Imbruvica and Calquence. It remains too early to draw definitive conclusions, but it would be a substantial benefit if vecabrutinib lacked the GI effects of these other drugs.

Vecabrutinib inhibits pBTK and downstream effects

The company also provided new data on the pharmacokinetics (PK) and pharmacodynamics of the drug in the patients it examined. PK remains consistent with previous results and in line with twice a day (BID) dosing. The company also provide data demonstrating that the drug inhibited the generation of phosphorylated Bruton's tyrosine kinase (pBTK), which is the mechanism of action of this class. Finally, the company showed that the drug inhibited the generation of cytokines in these patients, which is the downstream effect of BTK inhibition. This provides evidence indicating a definitive drug effect in these patients.

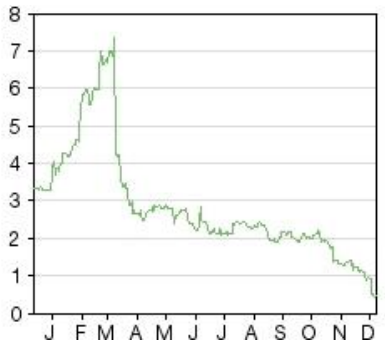
Valuation: Unchanged at $224m or $5.99 per share

Our valuation remains unchanged at $224m or $5.99 fper basic share. We expect to update this following additional data from the ongoing study. We expect the company to require at $135m in financing before profitability in 2023.

10 December 2018

Price	**US$0.46**
Market cap	**US$17m**
Net cash ($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	(66.0)	(78.8)	(78.9)
Rel (local)	(63.7)	(76.8)	(78.9)
52-week high/low	US$7.4	US$0.4	

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

Progress to 100mg cohort	Upcoming
SNS-510 IND filing	2019

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Edison profile page

The 50mg cohort overenrolled at ASH 2018

Sunesis presented a poster at ASH (followed up with a detailed presentation) on 2 December 2018 that provided an update on the progress of the company in its Phase Ib/II trial of vecabrutinib. The drug is an oral non-covalent BTK inhibitor being examined for chronic lymphocytic leukemia (CLL) and other B-cell malignancies. The data in the poster and presentation is consistent with the previous data provided in the abstract, but provides a to-the-minute look into the progress of the trial and an additional level of detail.

Importantly, the company announced it recently enrolled two additional patients into its 50mg BID dosing arm since the poster went to press, overenrolling it. Five of the six required patients have completed their safety evaluation, so only a single additional safety readout is needed before advancing to the next dose. A total of 13 patients have been enrolled to date, an increase of four since the abstract of the poster was presented. The company has faced a series of events that stalled completion of this cohort, so it is good to see progress continuing. Previously, an ALT elevation prevented a patient from receiving a number of doses, triggering a cohort expansion to six patients (per the standard 3+3 dose escalation protocol). Of the new patients, three progressed before they could be evaluated. We view these events as unfortunate and not necessarily indicative of any issues with the drug. The 50mg cohort is below the expected efficacy threshold at 100mg BID or higher, so we expect future cohorts to provide a clearer picture of the drug's safety and efficacy profile. For the current report, 11 patients were evaluable in some fashion.

The company provided a detailed breakdown of the AE profile from the 10 patients with data available (Exhibit 1). As previously described, hematologic AEs were common but are not unusual for this class of drug or this patient population. Four grade three events that were potentially related to drug were observed, three hematologic and the third being the previously mentioned ALT elevation. Of note in this profile is that the rate of GI events is low. This is in contrast to Imbruvica, which has high rates of GI effects (51% diarrhea, 31% nausea, 25% constipation, etc). Calquence also has high rates of reported GI effects, albeit at lower levels than Imbruvica. This indicates that the AE profile of vecabrutinib may be significantly different than these drugs, although higher doses will need to be evaluated before drawing any definitive conclusions.

Exhibit 1: Vecabrutinib dose-escalation safety

Adverse Event	All Grades >15% N(%)[a]	Grade ≥ 3 N	Related, Grade ≥ 3 N	Adverse Event	All Grades >15% N(%)[a]	Grade ≥ 3 N	Related, Grade ≥ 3 N
Anaemia	7 (70)	6	1	Constipation	2 (20)		
Neutropenia	5 (50)	5	1	Cough	2 (20)		
Night sweats	5 (50)			Diarrhea	2 (20)		
AST increased	4 (40)	1		Dyspepsia	2 (20)		
Thrombocytopenia	4 (40)	4		Dyspnoea	2 (20)		
Hypoalbuminaemia	3 (30)			Fatigue	2 (20)	1	
Hypocalcaemia	3 (30)	1		Haematuria	2 (20)		
Pyrexia	3 (30)			Headache	2 (20)		
Abdominal distension	2 (20)			Hyperglycaemia	2 (20)	1	
ALT increased	2 (20)	1	1[b]	Hyperkalaemia	2 (20)		
Back pain	2 (20)			Hypermagnesemia	2 (20)		
Alk phos increased	2 (20)	1		Hyponatremia	2 (20)	1	
Cellulitis	2 (20)	1		Leukopenia	2 (20)	2	
Chills	2 (20)			Lymphopenia	2 (20)	2	

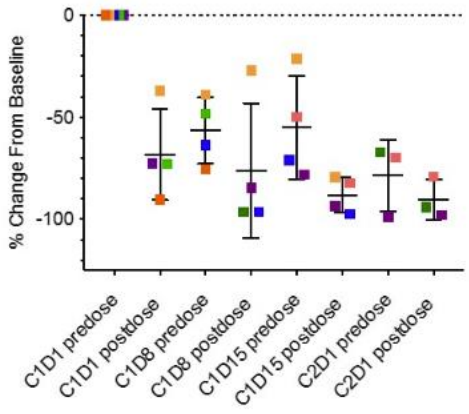
Additional Grade ≥3, N=1: Blood bilirubin increased, Hyperuricaemia, Hypophosphataemia, Intestinal perforation, Leukocytosis (related), Neutrophil count decreased, Pneumonia, Platelet count decreased.

[a]Preliminary safety data available for 10 of 13 treated subjects
[b]One patient in Cohort 2 experienced a DLT of an inadequate number of Cycle 1 doses administered due to a related grade 3 ALT increase

Source: Sunesis

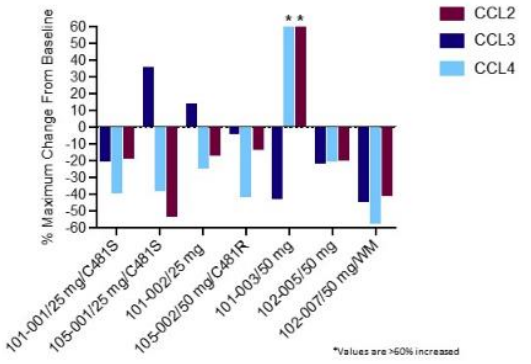
The company also provided additional PK and pharmacodynamic data to support the proposition of vecabrutinib. The PKs in the trial appear similar to previous *in vivo* measurements. The company also provided a breakdown of the impact of vecabrutinib on the concentrations of pBTK (Exhibit 2). pBTK is the active form of the enzyme and the efficacy of BTK inhibitors is effected by reductions in its concentration. These data also include patients with a C481 mutation, which is inadequately treated by Imbruvica. Moreover, the company provided evidence that the drug was having an impact on B-cell function, as indicated by a reduction in cytokines measured in a selection of patients (Exhibit 3). These data provide evidence that the drug is working as intended, and having a physiological impact.

Exhibit 2: Inhibition of pBTK production



Source: Sunesis

Exhibit 3: Reduction in cytokines



Source: Sunesis

Based on these data we expect the upcoming cohorts to provide data on the efficacy of the drug. The company noted that early indications of drug effect were seen but it did not report any measures of efficacy in this data. There are eight sites enrolling patients, and the company signalled that it believed these would be sufficient. Of the 13 patients enrolled to date, the majority (nine) had CLL. Patients with mantle cell lymphoma and Waldenstrom macroglobulinemia have also been enrolled in the trial, and earlier this year the company expanded enrolment to include

other B-cell malignancies such as diffuse large B-cell lymphoma and follicular lymphoma (although the company did not report any of these patients in the 11 that were evaluable). The company also announced in its presentation that it would be further expanding its enrolment to include marginal zone lymphoma in the near future. Marginal zone lymphoma is the third most common form of non-Hodgkin lymphoma (NHL), and data in this population could provide increasing evidence of utility in the NHL population, as well as potentially improve enrolment.

In other ASH news

Arqule is also developing a non-covalent BTK inhibitor ARQ-531, on which it presented data at ASH. ARQ-531 is also in a dose escalation study and is enrolling its seventh cohort. The main insight from the company's poster is that it observed its first partial response (PR) in a patient with follicular lymphoma. It is worth noting the study is in a dosing range where responses are expected (according to management), but the PR in question occurred after a patient had an unexpected response to much lower doses. Additionally, no PRs have been observed yet in the main indication of CLL.

Aptose Biosciences provided some initial preclinical data on its non-covalent FLT3/BTK inhibitor CG'806. FLT3 is a protein frequently mutated in B-cell malignancies, and the idea of this program is that the combined inhibition of both FLT3 and BTK will provide more potent effects. The drug was compared to Imbruvica in a range of cell lines and primary tumor cells, where is significantly higher cytostatic and cytotoxic potency shown. We plan to see in the future if this drug has the other properties besides potency necessary for effective treatment. Aptose has said it plans to file an IND in 2019.

Valuation

Our valuation remains unchanged at $224m or $5.99 per basic share and we have not updated our model. The timing for the progression through the 50mg cohort is in line with our expectations. We may update the valuation in future when further data are released from the ongoing clinical study.

Exhibit 4: 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 (m)									52.4
Value per diluted share ($)									4.98

Source: Sunesis reports, Edison Investment Research

Financials

Our financial projections also remain unchanged. The company ended Q318 with $20m in cash (and $7.3m in debt). Burn rates have historically been between $5m and $7m per quarter, so we expect the company to need additional financing in the near term. We currently model $25m in financing (as illustrative debt) in 2018, although we may move this into early 2019 depending on internal timelines. We expect the company to require a total of $135m in financing before profitability in 2023 ($25m, $20m, $30m, $40m and $20m in 2018–2022 respectively).

Exhibit 5: 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

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