EDISON

Sunesis Pharmaceuticals

A new BTK for a new day

Company outlook

Pharma & biotech

Sunesis remains on track to complete the dose-escalation portion of its Phase Ib/II clinical trial for lead compound SNS-062, an oral Bruton's tyrosine kinase (BTK) inhibitor, in patients with confirmed Imbruvica resistance in mid-2018, and present initial safety and efficacy interim data in Q218. In addition, Sunesis is moving forward with SNS-510, a PDK1 inhibitor with potential activity across multiple tumor types, and we expect a decision from Takeda on the advancement of pan-Raf inhibitor TAK-580 by mid- to late 2018. Sunesis completed a $20m offering of common and preferred stock in October 2017. We value Sunesis at $125.9m or $3.68.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/15	3.1	(36.7)	(3.02)	0.0	N/A	N/A
12/16	2.5	(38.0)	(2.42)	0.0	N/A	N/A
12/17e	0.7	(35.9)	(1.48)	0.0	N/A	N/A
12/18e	0.0	(34.6)	(0.96)	0.0	N/A	N/A

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

SNS-062 Phase Ib/II readout approaching

The first data on the efficacy of SNS-062 is expected as part of the interim readout from the dosing portion of the Phase Ib/II trial. The data are planned to be presented at a major conference in mid-2018. Sunesis will also provide an update on the program at the American Society of Hematology (ASH) conference in December 2017.

Growing market for BTK inhibitors

The FDA recently approved AstraZeneca's Calquence (acalabrutinib), a covalent BTK inhibitor for the treatment of mantle cell lymphoma (MCL), and only the second BTK inhibitor to receive approval. Similar to Imbruvica, Calquence forms a covalent bond that causes the same C481S mutation that can render the drug ineffective. In preclinical studies, SNS-062 maintained potent inhibitory activity against C481S BTK mutations resistant to inhibition by Imbruvica and Calquence.

SNS-510 is a "go"

The company announced on its Q317 call that it will be moving forward with SNS-510 to IND enabling studies, as opposed to SNS-229 as we previously modeled. This decision was made on the basis of a more favorable therapeutic index and toxicology, according to the company. We have increased our probability of success to 10% (from 5%) to reflect the advancement of this program.

Valuation: Increased to $125.9m or $3.68/basic share

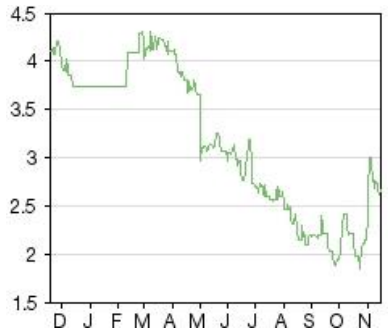
We have increased our valuation to $125.9m, from $93.0m, although it is reduced on a per-share basis to $3.68 ($3.06 diluted) from $3.96 ($2.33 diluted). This is driven by rolling forward our NPVs, the increase in the probability of success of SNS-510, and recent offerings to the effect of $24.6m (17m new shares fully diluted since last report). We forecast $135m in capital will be needed before profitability in 2023. We expect to provide an update to our valuation following Takeda's option on TAK-580 and SNS-062 Phase Ib results in 2018.

16 November 2017

Price	**US$2.67**
Market cap	**US$91m**

Net cash ($m) at 30 September 2017	5.3
Shares in issue	34.2m
Free float (%)	95%
Code	SNSS
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	20.3	17.6	(36.4)
Rel (local)	19.7	13.0	(46.0)

52-week high/low	US$4.3 / 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

Presentation at ASH	December 2017
SNS-062 dosing update	Mid-2018
TAK-580 option decision	Mid/late 2018

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Edison profile page

Investment summary

Company description: Cancer- focused biotech

Sunesis Pharmaceuticals is an oncology company focused on the development of novel small molecule therapeutics. It was incorporated in 1998 and has been public since 2005, although since this time it has shifted away from drug discovery purely to development. In 2017, Sunesis refocused its efforts from vosaroxin (Qinprezo), after withdrawing its EMA marking application, to its new lead asset SNS-062, an oral non-covalent inhibitor of Bruton's tyrosine kinase (BTK) that binds with potential efficacy in Imbruvica-resistant chronic leukemia (CLL) patients. Approximately 25% or more of those treated with Imbruvica develop resistance and this number is expected to increase with more patients on the drug for an extended amount of time. Recently, the company initiated a Phase Ib/II dose escalation clinical trial with seven planned cohorts in patients with confirmed Imbruvica-resistance. The target completion date for the dose escalation portion is mid-2018. Sunesis is also developing SNS-510, a preclinical pan-cancer inhibitor of PDK1 that may work in resistant populations, and has licensed TAK-580, a pan-Raf inhibitor for solid tumors, to Takeda.

Valuation: $125.9m or $3.68 per basic share

We have increased our valuation of Sunesis to $125.9m up from $93.0m, although it has reduced on a per-share basis to $3.68 ($3.06 diluted) from $3.96 ($2.33 diluted) as a result of the October offering. This increase in total value is driven by rolling forward our NPVs to the most recent quarter as well as the increase in the probability of success (to 10% from 5%) of the SNS-510 program to reflect clinical progress. The increase in share counts represents dilution from recent offerings.

Financials: Estimated $37m in cash

Sunesis reported an operational loss of $9.9m for Q317, up from $8.5m for Q316, primarily due to the continuation of the SNS-062 clinical trial and a one-time milestone payment to Biogen of $2.5m. The company completed a secondary offering of common and preferred stock (worth $20m gross) in October 2017 as well as continuing its at-the-market facility for a total of $24.6m net proceeds. This has reduced our expected financing requirement to $135m (from $155m) before profitability in 2023. A portion of this financing need should be provided by milestone and upfront payments associated with the development of TAK-580. We predict significant future increases in cash burn with the advancement of the SNS-062 and SNS-510 clinical programs, although we expect decreases in 2018 due to the discontinuation of spending on vosaroxin.

Sensitivities: Early stage development risks

Sunesis has a set of sensitivities indicative of the combination of risks due to its very early stage development pipeline and its potential near-term commercialization. We believe the company's new lead therapeutic, SNS-062, has significant profit potential because it is wholly owned by Sunesis, it is based on a mechanism with established efficacy, and it is substantially differentiated from competitors. However, even with the established mechanism of action, we predict a 20% probability of approval considering the exceptionally low success rate for development of small molecule targeted oncology drugs and the lack of efficacy data in humans. Moreover, there is a high degree of uncertainty surrounding the market of Imbruvica refractory patients, considering the eventual size of this population is largely unknown at this point. Additionally, the survival for these patients is typically measured in months, presenting issues initiating them on a new therapy. The remainder of the Sunesis pipeline is very early stage, and carries the associated clinical risk. We assign probabilities of approval of 15% and 10% for the TAK-580 and SNS-510 programs, respectively, neither of which have established in-human efficacy.

A BTK on the path of least resistance

Sunesis is a clinical-stage biopharmaceutical company developing oncology therapeutics. The company is advancing its kinase-inhibitor pipeline, with an emphasis on establishing its lead therapeutic, SNS-062, an oral non-covalent inhibitor of Bruton's tyrosine kinase (BTK) for the treatment of chronic lymphocytic leukemia (CLL) and other B-cell cancers. In January of this year, the US FDA accepted the Investigational New Drug (IND) application for SNS-062. The company expects to present safety and efficacy data from the dose escalation portion of its Phase Ib/II trial in patients with confirmed Imbruvica-resistance in mid-2018. Sunesis has two additional early stage programs. SNS-510 is a preclinical phosphoinositide dependent protein kinase 1 (PDK1) inhibitor being investigated for solid and hematological tumors. PDK1 is a novel target that could have improved efficacy in tumors with PI3K and PTEN mutations, which are exceptionally common (30-50% of certain cancers). We previously reported on the preclinical molecule SNS-229 from the PDK1 inhibitor program, although SNS-510 has supplanted the earlier compound as the lead due to an improved profile. Lastly, Sunesis has out-licensed the Phase Ib/II pan-Raf inhibitor TAK-580 to Takeda. Pan-Raf inhibitors are a new class of drug that avoids the paradoxical enhancement of tumor growth in some patients that take B-Raf inhibitors.

Exhibit 1: Sunesis pipeline

Product	Indication	Class	Phase	Catalyst	Timing	Commercial advantage
SNS-062	CLL	BTK inhibitor	Phase I/II	Phase Ib data	2018	Non-covalent inhibitor effective in Imbruvica resistant tumors
SNS-510	Pan cancer	PDK1 inhibitor	Preclinical	IND preparation	2018	Potential efficacy similar to PI3K inhibitors, resistant to PI3K, PTEN mutations
TAK-580	Solid tumors/melanoma	Pan-Raf inhibitor	Phase I	Phase Ib data	2018	Avoids "paradoxical activation" present in B-Raf inhibitors, effective in Ras mutants

Source: Sunesis Pharmaceuticals

SNS-062: The lead development program

Sunesis is developing SNS-062 as a treatment for CLL, in particular for patients refractory to Imbruvica (ibrutinib; AbbVie, Janssen). CLL is a hematologic malignancy indicated by the proliferation of mature B-cell lymphocytes and the clinical course of CLL can vary from indolence with a relatively normal life expectancy to a rapidly progressive disease leading to an early death. There are an estimated 20,110 new patients in the US in 2017 (4.7 per 100,000 on an age-adjusted basis).[1] The treatment of B-cell malignancies has been an area of substantial investment and it has been transformed over the past decade by the development of new, targeted drugs for these diseases. One of the greatest successes in this field was the development of Imbruvica by Pharmacyclics (acquired by AbbVie in May 2015, partnered with Janssen). The drug was approved in 2013 with accelerated approval following a three-year Phase III trial and it retails for approximately $130,000. Imbruvica substantially improved the standard of care for relapsed and refractory CLL by more than doubling the survival rate for these patients (HR=0.43 vs ofatumumab at 18 months). Imbruvica is also approved in mantle cell lymphoma (MCL) and Waldenström's macroglobulinemia (WM). In 2016, sales more than doubled following approval of label expansion to front-line CLL treatment and worldwide sales are approximately $2.2bn.

Imbruvica was the first marketed drug to target Bruton's tyrosine kinase (BTK), a protein expressed in B-cells, and important for their activation and maturation in response to antigen binding. When the antibody being expressed by a particular B-cell binds to a pathogen or foreign substance, this triggers the cell to continue expressing this antibody and multiply, such that sufficient antibodies are present to fight the invader. This pathway is frequently mutated in B-cell malignancies leading to the out-of-control proliferation of these cells. However, an interesting facet of BTK is that because it is

[1] National Cancer Institute.

present solely in leukocytes, it can be inhibited (or functionally absent as in the case of X-linked agammaglobulinemia) and patients are immune suppressed but otherwise phenotypically normal.

Imbruvica has only been approved as a first-line indication for CLL since March 2016, and therefore the degree of patient exposure to the drug has been limited. 25% of patients developed resistance to the drug at 26 months in early trials, and this number is expected to increase the longer it is in use.[2] The precise mechanism of this resistance is an area of active investigation, and a recent report identified a particular mutation to BTK (cysteine-481 to serine) is frequently present in resistant individuals.[3] This particular amino acid residue is critical because it forms an irreversible covalent bond with Imbruvica and is essential for the drug's potency. It is the position at which Imbruvica forms a covalent bond to BTK, and its mutation dramatically affect the potency of the drug (Exhibit 2). There is also increasing evidence that the vast majority of these resistant patients, up to 80%, harbor the C481S mutation that SNS-062 can address.

Exhibit 2: Comparison of Imbruvica and SNS-062 binding to wild type and mutant BTK

	Kinase inhibition			Inhibition of activated BTK formation		
IC50 (nM)	BTK	Mutant BTK	Fold change	BTK	Mutant BTK	Fold change
Imbruvica	0.58	25.2	43.4	0.016	25.5	>1,000
SNS-062	2.9	4.5	1.6	0.57	0.8	1.4

Source: Sunesis

Sunesis has developed a next-generation BTK inhibitor, SNS-062. Unlike Imbruvica, SNS-062 does not form a covalent bond with cysteine-481 of BTK, but retains significant binding affinity to both native and mutant forms of the enzyme. Moreover, it prevents the generation of activated BTK (auto-phosphorylated BTK, pBTK) in the presence of the mutant, whereas this effect is completely lost by Imbruvica. This positions SNS-062 as a potential treatment for Imbruvica resistant forms of the disease. The most recent report suggests the cysteine-481 mutation is present in approximately 80% of these remissions (leaving 20% of Imbruvica patients appropriate for SNS-062).[4]

Phase Ia results

Sunesis presented the results of a Phase Ia healthy volunteer study of SNS-062 via a poster at the Second International Conference on New Concepts in B-Cell Malignancies in September 2016. The clinical trial examined the pharmacokinetic and pharmacodynamic profile and adverse events in volunteers following a single dose of the drug at four different dosing levels (from 50mg to 300mg) or with placebo. Six volunteers received drug for each active arm (n=24 total for SNS-062) and eight received placebo. Although these results are from a small set of healthy volunteers, we consider them very important for evaluating the viability of this drug, because the mechanism of action has already been validated and the unknowns are largely associated with the pharmacokinetic, pharmacodynamic and safety profile of the molecule.

The primary endpoint of the trial was safety, and in general, the adverse event (AE) profile was similar between patients who received drug and those who received placebo (Exhibit 3). 33% of patients who received active drug had an AE, compared to 38% in the placebo arm. The adverse events observed in the trial were all mild (grade 1) except for a single patient on the 300mg arm who reported grade 2 fatigue and headache. Also, an important AE to note is that a single patient reported supraventricular tachycardia (racing heart) on the 300mg arm. Although the event was asymptomatic and resolved in 20 seconds, adverse events related to heart rhythm have been associated with BTK inhibitors in the past and patients receiving Imbruvica experience atrial

[2] Byrd JC, et al. (2013) Targeting BTK with ibrutinib in relapsed chronic lymphocytic leukemia. *N. Engl. J.* Med. 369, 32-42.

[3] JA Woyach, RR Furman (2014) Resistance mechanisms for the Bruton's tyrosine kinase inhibitor ibrutinib. *NEJM*. 370;24, 2286-94.

[4] Kami J. Maddocks, MD1; Amy S. Ruppert (2015) Etiology of Ibrutinib Therapy Discontinuation and Outcomes in Patients With Chronic Lymphocytic Leukemia. JAMA Oncol. 1(1): 80-87.

fibrillation at a rate of 6% to 9%, typically after prolonged exposure. Importantly, the trial also monitored patients via laboratory blood testing and via electrocardiogram, and no other abnormalities were found. We expect hematological AEs to emerge with repeated dosing, consistent with molecules of this class and the drug's mechanism of action. Additionally, we expect the differences in AEs between SNS-062 and other drugs of this class to become clearer with repeated dosing. In fact, Imbruvica has off-target epidermal growth factor (EGFR) activity, and drugs that primarily target EGFR such as Tarceva (erlotinib, Roche) and Iressa (gefitinib, AstraZeneca) are associated with gastrointestinal and dermatological AEs, not unlike Imbruvica.

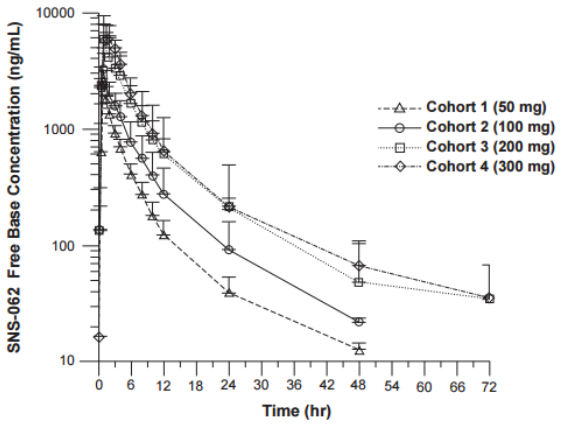
Exhibit 3: Adverse event profile of SNS-062

	SNS-062										Placebo (n=8)	
	50mg (n=6)		100mg n=6)		200mg (n=6)		300mg (n=6)		All active (n=24)			
Headache	4	67%	0	0%	0	0%	1	17%	5	21%	2	25%
Supraventricular tachycardia	0	0%	0	0%	0	0%	1	17%	1	4%	0	0%
Constipation	0	0%	1	17%	0	0%	0	0%	1	4%	0	0%
Nausea	0	0%	0	0%	1	17%	0	0%	1	4%	2	25%
Diarrhea	0	0%	0	0%	0	0%	0	0%	0	0%	1	13%
Fatigue	0	0%	0	0%	0	0%	1	17%	1	4%	0	0%
Bronchitis	0	0%	0	0%	0	0%	1	17%	1	4%	0	0%
Orthostatic hypotension	0	0%	0	0%	0	0%	1	17%	1	4%	0	0%
Total patients with AE	4	67%	1	17%	1	17%	2	33%	8	33%	3	38%

Source: Sunesis

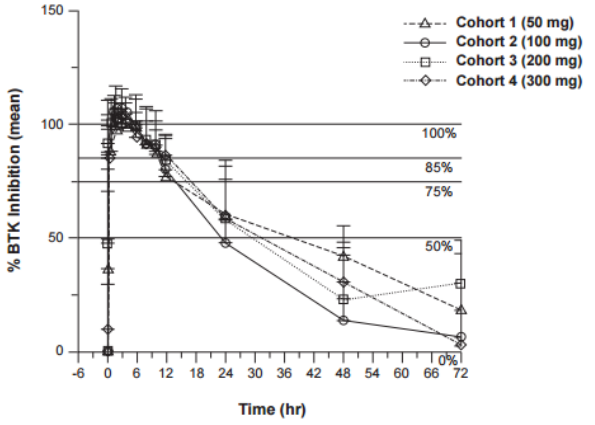
Sunesis also reported initial pharmacokinetic and pharmacodynamic data from the active arms of the trial, which included both blood concentrations (Exhibit 4) and the degree of BTK inhibition (Exhibit 5) following dosing. Patients were followed for up to 72 hours and the results showed that the molecule had a long half-life in humans (eight to 17 hours depending on dose), and that at the plasma levels observed in this study, BTK inhibition of 85% or more was seen for approximately 12 hours for all the doses studied. 85% inhibition of BTK has previously been identified as sufficient for clinical activity during studies of AstraZeneca's BTK inhibitor Calquence (acalabrutinib), which received FDA approval in October 2017 for the treatment of mantle cell lymphoma (MCL).[5] This profile presents the possibility of a twice-a-day dosing regimen, which the company has proposed using when moving forward with clinical trials.

Exhibit 4: Plasma concentrations of SNS-062



Source: Sunesis

Exhibit 5: BTK inhibition by SNS-062



Source: Sunesis

Preclinical results presented in April 2017 further demonstrate that SNS-062 inhibits BTK signaling in primary chronic lymphocytic leukemia (CLL) cell lines and remains unaffected by the C481S

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

mutation. Sunesis announced in July 2017 that the first patient had been dosed in the Phase Ib/II clinical trial of SNS-062 in patients with relapsed and refractory chronic lymphocytic leukemia (CLL) and other B-cell malignancies (Waldenstrom's macroglobulinemia and mantle cell lymphoma). The current Phase Ib/II study is a dose escalation trial with seven planned dosing cohorts, and once the maximum tolerated dose is found, it will expand into a total estimated enrolment of 124 patients. The study will enroll patients who have progressed and have documented C481S mutations. The program is taking place at some of the leading cancer institutes in the US: U.C. Irvine Cancer Center, the Ohio State University Comprehensive Cancer Center, Dana-Faber Cancer Institute, MD Anderson Cancer Center and Weill Cornell Cancer Center. The company has announced that it will provide a program update at the American Society of Hematology (ASH) Conference in December, and will present data from the Phase Ib dosing portion of the trial in mid-2018.

Market and competitive environment

Imbruvica was approved for the first-line treatment of CLL in March 2016, expanding its previous label for relapsed and refractory CLL or those patients carrying the 17p chromosomal deletion. This development substantially increased the number of patients on the drug (increasing US sales from $659m in 2015 to $1.6bn in 2017) and consequently we expect the number of resistant patients to increase. Additionally, patients who become resistant to Imbruvica during front-line treatment should be healthier and more fit to receive follow-up treatments. AstraZeneca's Calquence, approved for the treatment of MCL in October 2017, will directly rival Imbruvica, and we expect it to expand into the CLL indication. Phase III results of Calquence in CLL are expected in the 2019-20 time frame.

Assuming that 20% of new CLL patients will develop a cysteine-481 mutation, this corresponds to a present day market of approximately $400m in the US per year that patients remain on the drug. We currently assume that patients will remain on the drug for approximately 18 months, although at the moment, there is little insight into this number, as it is highly dependent on efficacy. With the current standard of care, survival times are very short following Imbruvica resistance.[6]

There are at least 14 other BTK inhibitors in clinical development. Ten of these inhibitors form covalent bonds to BTK similar to Imbruvica, and therefore are susceptible to the same cysteine-481 mutation that leads to Imbruvica resistance. Potential competitors in the Imbruvica resistance space include non-covalent BTK inhibitors such as Genentech's GDC-0853, Loxo's LOXO-305 and ArQule's ARQ-531. In contrast, entrance of irreversible BTK inhibitors, such as the recent approval of Calquence from AstraZeneca, could drive an expansion of the market and therefore more resistant individuals. Because they share the same cysteine-481 dependent mechanism, they should induce the same resistance as Imbruvica. We expect the drug's composition of matter patent (9,029,359) to provide market exclusivity through the early 2030s (2034 in our model, based on a five-year Hatch-Waxman extension).

[6] Kami J. Maddocks, MD1; Amy S. Ruppert (2015) Etiology of Ibrutinib Therapy Discontinuation and Outcomes in Patients With Chronic Lymphocytic Leukemia. JAMA Oncol. 1(1): 80-87.

Exhibit 6: BTK inhibitors

Drug	Company	Status	Lead indication	Binding mode
Imbruvica	AbbVie	Approved	CLL, MCL, WM	Covalent
Calquence	AstraZeneca	Approved	MCL	Covalent
BGB-3111	BeiGene	Phase III	WM	Covalent
Spebrutinib	Celgene	Phase II	RA	Covalent
PRN1008	Principia	Phase II	Pemphigus vulgaris	Covalent
BMS-986142	Bristol-Myers Squibb	Phase II	RA	Non-covalent
Evobrutinib	Merck KGaA	Phase II	RA	Covalent
ONO/GS-4059	Ono/Gilead	Phase II	CLL, Sjogren's	Covalent
SNS-062	Sunesis	Phase I/II	CLL, MCL, WM	Non-covalent
GDC-0853/ (RG7845)	Genentech/Roche	Phase I/II	RA, lupus	Non-covalent
HM71224	Lilly/Hanmi	Phase I	RA	Covalent
ARQ-531	ArQule	Phase I	CLL, DBCL, MCL, WM	Non-covalent
TAK-020	Takeda	Phase I	RA	Covalent
PRN2246	Principia	Preclinical	CNS	Covalent
LSK9985	LSK BioPharma	Preclinical	RA; BTK & Jak3 inhibitor	Covalent
LOXO-305	Loxo Oncology	Preclinical	B cell lymphoma	Non- covalent
BTKwt	X-Rx	Preclinical	Inflammation	Covalent

Source: BioCentury, ClinicalTrials.gov, Edison Investment Research

Pipeline decisions

Sunesis has two additional early stage programs: a phosphoinositide dependent protein kinase 1 (PDK1) inhibitor program comprised of two drug candidates, SNS-510 and SNS-229, that target hematological and solid tumors by way of the same mechanism of action; and TAK-580, a pan-Raf inhibitor program. The company announced on its Q317 call that it will be moving forward with SNS-510 as it planned to take only one PDK1 inhibitor to clinic and in preclinical studies SNS-510 demonstrated a favorable therapeutic index and toxicology over SNS-229, although it has released no data. Our previous reports focused on SNS-229, but this information should apply equally to SNS-510 as both share a mechanism of action, which is the extent of our knowledge of the compounds.

SNS-510

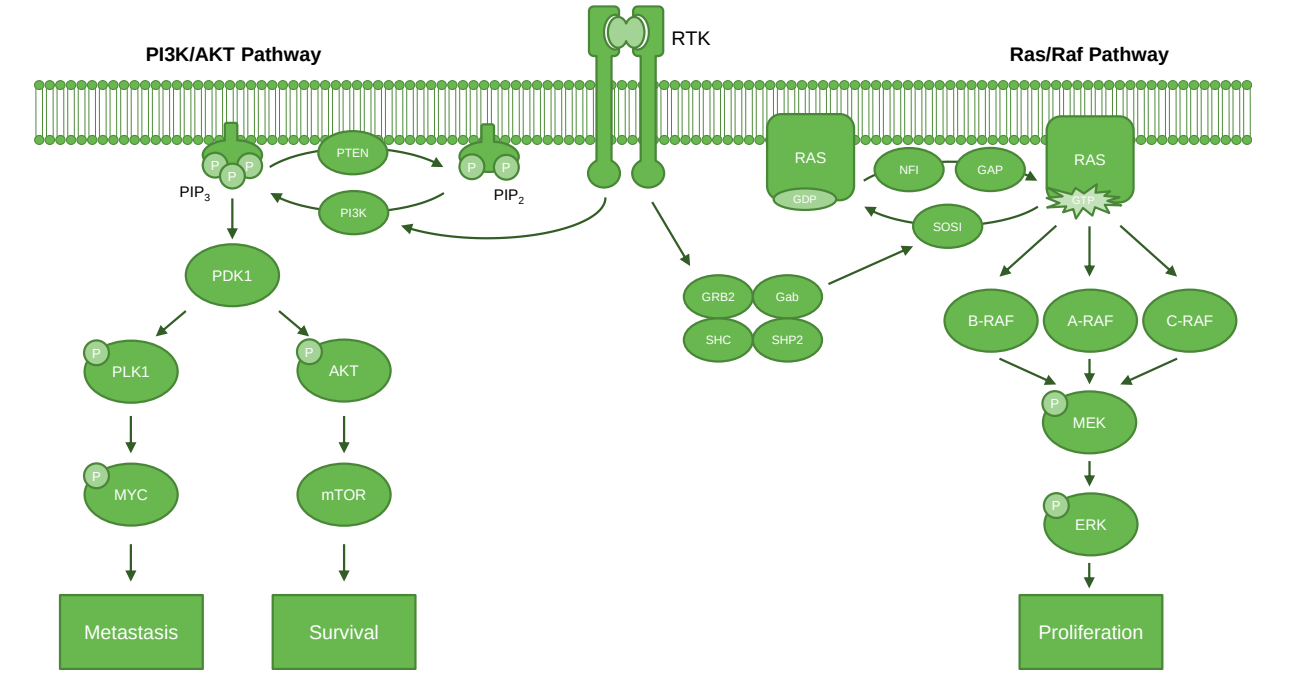
The receptor tyrosine kinase (RTK) signaling pathway has been central to the development of targeted cancer therapies for the past two decades. RTKs are a class of protein that respond to signals from growth factors and other signaling molecules, but mutations in this pathway can lead to a constitutive growth signal that is characteristic of cancer. Drugs have been developed targeting the receptor itself (for instance Herceptin targeting HER2), as well as the downstream effectors of RTKs in the so-called PI3K/AKT pathway, for instance PI3K (Gilead's Zydelig) and mTOR (Pfizer's Torisel). The RTK pathway is central to the pathology of a wide array of different cancer types, as evidenced by the indications this class of drug has been approved for in both solid tumor and hematologic malignancies. One of the multiple downstream pathways from RTK is the PI3K/AKT pathway, which has been a topic of considerable development interest due to its role in promoting cancer cell survival and metastasis.

Sunesis has developed SNS-510 as an inhibitor of PDK1, a previously unstudied target in the PI3K/AKT pathway. PDK1 is an effector of PI3K, and therefore it is reasonable to expect an efficacy profile similar to PI3K inhibitors like Zydelig (idelalisib, Gilead). Zydelig was approved for the treatment of B-cell malignancies such as CLL and non-Hodgkin lymphoma. Because the RTK pathway is implicated in such a broad array of cancers, SNS-510 could potentially have many applications. However, the drug would be uniquely effective in malignancies where PI3K or PTEN is frequently mutated such as breast cancer (27% PI3K mutation frequency), or endometrial cancer (38% PTEN mutation frequency). In these cases a PDK inhibitor could potentially limit the effect of these mutations as it is the immediate downstream effector of these proteins. A potential risk to this

program is opportunistic infections among patients, considering that inhibition of this pathway by Zydelig is associated with this risk. In early 2016, a series of deaths in clinical trials involving Zydelig prompted Gilead to terminate further clinical development. In spite of this, the drug had sales of $168m for 2016.

There are no other PDK1 inhibitors in development to our knowledge. Sunesis has completed SNS-510 non-GLP toxicology studies, and is currently engaged in IND enabling studies. The drug was initially developed in a collaboration with Biogen Idec, whose rights were acquired by Takeda. Sunesis will owe royalties and $9.2m in development milestones to Takeda for these rights. It is protected by composition of matter patent 8,778,977.

Exhibit 7:PI3K/AKT and Ras/Raf pathways



Source: Edison Investment Research

TAK-580

There has been substantial success recently developing and getting approval for inhibitors of the oncogene B-Raf. There are currently three B-Raf targeted medications approved in the US (Nexavar, Bayer, €870m worldwide sales in 2016; Zelboraf, Roche, CHF213m; Tafinlar, Novartis, $672m) and at least four others in development. B-Raf is a very common oncogene that is mutated in 20% of cancers. When mutated it activates a pathway that triggers uncontrolled growth of cells.

However, a major limiting factor in the efficacy of B-Raf inhibitors is that they can have a detrimental effect when a mutation in the upstream signaling protein Ras is mutated. Cancers with a Ras mutation have a very similar phenotype to B-Raf mutations and activate the same pathway, but the signal is transduced through all three Raf isoforms (A-Raf, B-Raf, and C-Raf aka Raf1). The presence of a B-Raf inhibitor paradoxically enhances this response by encouraging the association of B-Raf with other isoforms. Because Ras mutations are exceptionally common in certain cancers (eg 34% of colon cancer, 57% of pancreatic cancer), the potential application for B-Raf inhibitors is limited to only certain cancer indications where paradoxical activation is not an issue.

TAK-580 was developed as a pan-Raf inhibitor by Sunesis and inhibits all Raf isoforms, therefore preventing the activation of the pathway even in the presence of Ras mutations. The drug was developed in collaboration with Biogen Idec and is out-licensed to Takeda, which is investigating the drug for a range of tumors in Phase Ib in six different drug combinations. Sunesis stated that it expects a go or no-go decision from Takeda regarding the program by mid- to late 2018. Sunesis is

entitled to up to $57.5m in development milestones from the collaboration, of which some undisclosed portion would be triggered upon the initiation of a registration trial. Eli Lilly is currently the only other major pharmaceutical company with a pan-Raf in clinical trials (Phase I). It is protected by composition of matter patent 8,802,657.

Sensitivities

Sunesis has a set of sensitivities indicative of the combination of risks due to its very early stage development pipeline and its potential near-term commercialization. We believe the company's new lead therapeutic, SNS-062, has significant potential because it is based on a mechanism with established efficacy and is differentiated from competitors. However, even with the established mechanism of action, we predict a 20% probability of approval considering the exceptionally low success rate for development of small molecule targeted oncology drugs and the lack of efficacy data in humans. Moreover, there is a high degree of uncertainty surrounding the market of Imbruvica refractory patients, considering the eventual size of this population is largely unknown at this point. Additionally, the survival for these patients is typically measured in months, presenting issues initiating them on a new therapy. The remainder of the Sunesis pipeline is very early stage, and carries the associated clinical risk. The TAK-580 and SNS-510 programs, while principled in design, are largely untested, and we assign probabilities of approval of 15% and 10% respectively.

Although Sunesis voluntarily recalled the EMA application for vosaroxin for the treatment of AML, there remains some possibility that the drug could be approved with new data, although the company has stepped away from internal development of the drug for the time being. There are two ongoing investigator-sponsored trials (at Vanderbilt-Ingram Cancer Center and University Hospital, Angers) that will continue as planned and could build a future value proposition for the asset. However, company investment into the program will be purely supportive to these investigator-sponsored studies in the future.

Sunesis also has risks associated with the continuing financing of the company. We predict that it will need an additional $135m to reach profitability in 2023, which may result in significant dilution, unless the company institutes significant cost reductions. The company spent $6.8m on R&D and $3.2m on SG&A in Q317, both of which figures are high for a company at this development stage.

Valuation

We have increased our valuation of Sunesis to $125.9m up from $93.0m, although it has reduced on a per share basis to $3.68 ($3.06 diluted) from $3.96 ($2.33 diluted) as a result of the October offering. This increase in valuation is driven by rolling forward our NPVs to the most recent quarter, an increase in net cash, and the increase in the probability of success of the SNS-510 program to 10% from 5%, following the company's decision to move forward with the drug candidate. The reduction in basic share value is due to an increased share count following the October offering, bringing the total estimated number of shares to 34.2m (45.5m diluted).

We estimate peak sales of $604m for SNS-062, which represents 50% penetration into the US and European market of BTK inhibitor refractory patients with a C481S mutation. We currently assume pricing on par with Imbruvica ($130,000 per year on drug, adjusted for future growth of 2% per year), with a net sales discount of 30%, and an expected time on drug of 18 months, although these values are subject to change based on efficacy. Although a lead indication has not been announced for SNS-510, and the potential indications for this drug are wide (both solid and hematologic tumors) we currently use breast cancer as our target market. We include only metastatic patients with PI3K mutations, which corresponds to approximately 7% of patients. Our launch pricing is $101,000 based on Zydelig and adjusted for price growth to launch in 2022. We model TAK-580

achieving 10% penetration into the melanoma market. We assume a launch pricing of $138,000 for a one-year course of treatment, which is in line with other Raf inhibitors (adjusted for price growth).

Exhibit 8: Sunesis valuation

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	138,000	727	2032	15%	$24
SNS-062	Phase Ib/II	Proprietary	20%	2022	152,000	604	2034	45%	$91
SNS-510	IND ready	Proprietary	10%	2022	101,000	320	2031	44%	$16
Unallocated costs (discovery programs, administrative costs, etc.)									($35)
Total									$96
Net cash and equivalents (Q317 + offering + ATM) ($m)									$29.9
Total firm value ($m)									$125.9
Total basic shares (m)									34.2
Value per basic share ($)									$3.68
Convertible Pref stock (m)									6.8
Warrants and Options									4.5
Total diluted shares									45.5
Value per diluted share									$3.06

Source: Sunesis reports, Edison Investment Research

Financials

Sunesis reported an operational loss of $9.9m for Q317. This is up from $8.6m during the previous period, primarily due to the continuation of the SNS-062 clinical trial, as well as a one-time milestone payment of $2.5m to Biogen associated with the initiation of the Phase Ib/II clinical trial of SNS-062. Our R&D spending estimates have increased from our last report ($22.3m for 2017 from $19.7m) based on higher than expected development spending in Q317. We expect spending to further increase in coming quarters associated with the SNS-062 Phase Ib/II dose escalation trial as well advancement of SNS-510 molecule in IND enabling studies, although we expect slightly lower spending in 2018 R&D overall ($19.4m) from ending spending on vosaroxin.

The company completed a $20m financing in October 2017 of common and preferred stock (10m fully converted at $2.00) and 5m warrants (at $3.00). Combined with an ongoing at-the-market facility, the company raised a net $24.6m since the end of Q317, bringing estimated cash to $37.1m. This corresponds to $29.9m in net cash after deducting the company's $7.2m in notes payable (due between 2017 and 2020). We currently project that the company will require $135m in additional funding (down from $155m in previous estimates) to reach profitability in 2023. This is in addition to the Takeda milestones ($57.5m), which we may integrate into our estimates following a decision from Takeda on the option to progress with the asset. Management has stated that the current cash should provide a runway into 2019, although we model a raise following the results from the SNS-062 trial in mid-2018 ($15m) to remove any overhangs.

Exhibit 9: Financial summary

$'000s	2013	2014	2015	2016	2017e	2018e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS						
Revenue	7,956	5,734	3,061	2,536	669	0
Cost of Sales	0	0	0	0	0	0
Gross Profit	7,956	5,734	3,061	2,536	669	0
Research and development	(28,891)	(27,665)	(23,701)	(22,881)	(22,293)	(19,447)
Selling, general & administrative	(10,838)	(23,112)	(18,662)	(16,115)	(13,237)	(13,634)
EBITDA	(31,701)	(41,312)	(35,764)	(36,313)	(34,871)	(33,091)
Operating Profit (before GW and except.)	(31,681)	(41,283)	(35,737)	(36,302)	(34,861)	(33,081)
Intangible Amortisation	0	0	0	0	0	0
Exceptionals/Other	0	0	0	0	0	0
Operating Profit	(31,681)	(41,283)	(35,737)	(36,302)	(34,861)	(33,081)
Net Interest	(2,917)	(1,719)	(939)	(1,721)	(995)	(1,564)
Other (change in fair value of warrants)	0	0	0	0	0	0
Profit Before Tax (norm)	(34,598)	(43,002)	(36,676)	(38,023)	(35,855)	(34,645)
Profit Before Tax (IFRS)	(34,598)	(43,002)	(36,676)	(38,023)	(35,855)	(34,645)
Tax	0	0	0	0	0	0
Deferred tax	0	0	0	0	0	0
Profit After Tax (norm)	(34,598)	(43,002)	(36,676)	(38,023)	(35,855)	(34,645)
Profit After Tax (IFRS)	(34,598)	(43,002)	(36,676)	(38,023)	(35,855)	(34,645)
Average Number of Shares Outstanding (m)	8.7	10.0	12.2	15.7	24.2	36.0
EPS - normalised ($)	(3.97)	(4.30)	(3.02)	(2.42)	(1.48)	(0.96)
EPS - IFRS ($)	(3.97)	(4.30)	(3.02)	(2.42)	(1.48)	(0.96)
Dividend per share ($)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets	33	42	14	3	1,354	9
Intangible Assets	0	0	0	0	0	0
Tangible Assets	23	42	14	3	19	9
Other	10	0	0	0	1,335	0
Current Assets	40,492	44,204	46,988	43,231	31,919	15,205
Stocks	0	0	0	0	0	0
Debtors	0	0	0	0	0	0
Cash	39,293	42,981	46,430	42,588	30,661	13,947
Other	1,199	1,223	558	643	1,258	1,258
Current Liabilities	(25,858)	(19,395)	(12,728)	(5,814)	(4,972)	(5,280)
Creditors	(16,840)	(10,138)	(4,894)	(2,481)	(1,404)	(1,689)
Short term borrowings	(9,018)	(9,257)	(7,834)	(3,333)	(3,568)	(3,591)
Long Term Liabilities	(12,737)	(2,563)	(610)	(11,271)	(3,476)	(14,789)
Long term borrowings	(9,025)	0	0	(11,102)	(3,408)	(14,721)
Other long term liabilities	(3,712)	(2,563)	(610)	(169)	(68)	(68)
Net Assets	1,930	22,288	33,664	26,149	24,824	(4,855)
CASH FLOW						
Operating Cash Flow	(37,423)	(43,181)	(38,731)	(36,962)	(37,056)	(28,050)
Net Interest	0	0	0	0	0	0
Tax	0	0	0	0	0	0
Capex	0	(48)	0	0	(26)	0
Acquisitions/disposals	0	0	0	0	0	0
Financing	12,570	56,277	43,826	26,111	32,871	0
Dividends	0	0	0	0	0	0
Other	0	0	0	0	0	0
Net Cash Flow	(24,853)	13,048	5,095	(10,851)	(4,211)	(28,050)
Opening net debt/(cash)	(46,966)	(21,250)	(33,724)	(38,596)	(28,153)	(23,685)
HP finance leases initiated	0	0	0	0	0	0
Exchange rate movements	0	0	0	0	0	0
Other	(863)	(574)	(223)	408	(257)	0
Closing net debt/(cash)	(21,250)	(33,724)	(38,596)	(28,153)	(23,685)	4,365

Contact details	Revenue by geography
395 Oyster Point Boulevard Suite 400 South San Francisco, CA 94080 US +1 650 266-3500 www.sunesis.com	N/A

Management team

CEO: Daniel N Swisher, Jr	CSO: Judy A Fox, PhD
Since December 2003, Daniel Swisher has served as chief executive officer and a member of the Sunesis board of directors, and president since August 2005. He joined the company in 2001 and served as chief business officer and chief financial officer until 2003. Prior to joining Sunesis, Mr Swisher served in various management roles, including senior vice president of sales and marketing for ALZA Corporation from 1992 to 2001. He serves as chairman of the board of Cerus Corporation and as a member of the board of Corcept Therapeutics Inc.	Judy A Fox, PhD, rejoined Sunesis in 2017 as chief scientific officer where she previously served as vice president, product & preclinical development. Prior to joining Sunesis, she was senior director in translational sciences at Chiron Corporation and established the pharmacological sciences department at Genencor International. Dr Fox began her industry career at Genentech, Inc.
VP Global Oncology Operations: Parvinder S Hyare	**VP Technical Operations: Gene Jamieson**
Parvinder S Hyare joined Sunesis in 2014 as vice president of market access. Prior to joining Sunesis, Mr Hyare was executive director, managed markets & reimbursement at AMAG Pharmaceuticals, Inc. and previously served as national sales director for that company from 2008-14. Prior to AMAG, Mr Hyare was region business director and also served in various management roles across sales and managed markets for Ortho Biotech, a division of Johnson & Johnson, from 2000-08.	Gene C Jamieson joined Sunesis in December 2010 as executive director of CMC and is now vice president of technical operations. Mr Jamieson joined Sunesis from AllyCMC, a CMC consulting services company, where he served as principal partner from 2009-10. Previously, he was executive director of product development at Jazz Pharmaceuticals, Inc. and vice president, pharmaceutical sciences, at NeurogesX, Inc. Mr Jamieson has developed diverse products with such companies as Centaur Pharmaceuticals, Nycomed Salutar Inc. and Novartis.

Principal shareholders	(%)
BVF Inc.	7.18
Great Point Partners	7.17
NEA Management	6.05
Palo Alto Investors	5.42

Companies named in this report

AbbVie (ABBV), Janssen (JNJ), Celgene (CELG), Novartis (NVS), Bayer (BAYN), Roche (RHHBY), Genentech (DNA)

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