EDISON

ASLAN Pharmaceuticals

ASLAN004 a go for atopic dermatitis

Clinical update

Pharma & biotech

ASLAN announced in July 2018 that it has received clinical trial authorisation in Singapore to conduct a Phase I study of ASLAN004 for the treatment of atopic dermatitis (AD). The product is a monoclonal antibody targeting interleukin 13 receptor α 1 (IL13Rα1). The Phase I dosing study will consist of a single dose escalation in healthy volunteers and a multiple dose escalation in AD patients.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/16	11.5	(7.6)	(0.07)	0.0	N/A	N/A
12/17	0.0	(38.8)	(0.31)	0.0	N/A	N/A
12/18e	0.0	(38.9)	(0.25)	0.0	N/A	N/A
12/19e	0.7	(62.5)	(0.36)	0.0	N/A	N/A

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

ASLAN004 mechanism previously validated

The target of ASLAN004 IL13Rα1 is a subunit of an interleukin receptor on the surface of macrophages that regulates their inflammatory and anti-inflammatory properties. The principle of targeting this receptor has already been tested in the form of the drug Dupixent (dupilumab, Regeneron/Sanofi), which inhibits the receptor's other subunit IL4Rα1. The drug was approved in March 2017 for atopic dermatitis and had revenues of €219m that year.

Atopic dermatitis: 18m adults affected in the US

AD is the most common form of eczema, affecting c 18 million adults in the US. Of these, 20% have moderate to severe disease and 4% have chronic forms, and we expect these patients to form the target market for the drug. The first-line treatment is typically topical steroids, although approximately half of patients with severe disease become refractory and require non-steroid treatments.

A competitive market

There are a number of options available for patients with steroid refractory AD both on the market and in development. Patients can be treated with PDE4 inhibitors such as Eucrisa (crisaborole, Pfizer) and calcineurin inhibitors such as Elidel (pimecrolimus, Valeant). In addition to Dupixent and ASLAN004, there are other drugs under development targeting the IL-4/IL-13 pathway such as tralokinumab (AstraZeneca) in Phase III and lebrikizumab (Dermira) in Phase 2b.

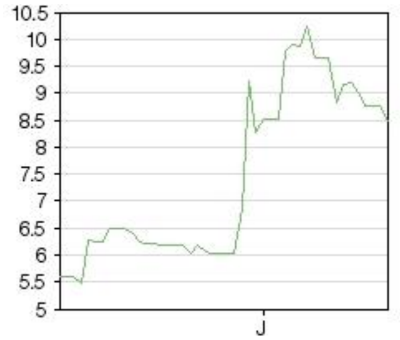
Valuation: Increased to $399m or $12.13 per ADS

We have increased our valuation to $399m or $12.13 per ADS from $364m or $11.04 per ADS due to the inclusion of ASLAN004. We arrive at a peak sales forecast of $587m based on conservative estimates of future market share (2%). The inclusion of the programme in our forecasts has increased our financing requirement by $22m to $82m, although we expect this to be offset by the out-licensing of assets.

9 July 2018

Price	**US$8.3**
Market cap	**US$273m**
	NT$30.06/US$
Net cash ($m) at 31 March 2018 + IPO + greenshoe	70.2
ADS in issue	32.9m
Free float	67%
Code	ASLN
Primary exchange	Taipei
Secondary exchange	NASDAQ

Share price performance



%	1m	3m	12m
Abs	(15.8)	N/A	N/A
Rel (local)	(15.4)	N/A	N/A
52-week high/low		US$10.24	US$5.48

Business description

ASLAN Pharmaceuticals is a Singapore-based drug developer targeting Asia-prevalent diseases. It has varlitinib in pivotal clinical trials for biliary tract cancer and gastric cancer, and will be advancing ASLAN003 to Phase II trials for acute myeloid leukaemia and ASLAN004 to Phase I for atopic dermatitis.

Next events

Varlitinib first-line BTC results	Late 2018
Varlitinib GC interim results	H218
Varlitinib Chinese BTC results	Late 2018

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ASLAN004 to enter Phase I

On 3 July 2018, ASLAN announced that it had submitted an application for clinical trial authorisation to the Singapore Health Science Authority to initiate a Phase I study of ASLAN004 for the treatment of atopic dermatitis (AD). It also provided a brief outline of the study which will consist of a single ascending dose portion in healthy volunteers and a multiple ascending dose portion in AD patients. We expect the trial to be initiated shortly after the application is approved (in our forecasts at the beginning of 2019). The dosing information found in this study can serve as the basis for further clinical study in the US and other geographies. The compound was licensed from CSL in 2014 and had a patent runway to 2027 (extendable to 2032).

ASLAN004 is an antibody that binds the interleukin 13 receptor α 1 (IL13Rα1), which is a receptor present on the surface of macrophages. This protein regulates the balance between the pro-inflammatory (M1) and anti-inflammatory (M2) states of the cell. This mechanism of action has already been validated by the approval of Dupixent (dupilumab, Regeneron/Sanofi), which was approved for the treatment of atopic dermatitis in 2017. Dupixent binds to IL4Rα, which is part of the same receptor complex as IL13Rα1, and generated revenues of €219m in its launch year. The drug has also been submitted for approval for severe asthma. AstraZeneca and Dermira also have programmes targeting this axis (Exhibit 1).

Exhibit 1: Programmes targeting IL-4/IL-13

Drug	Company	Target	Development
Dupixent (dupilumab)	Regeneron/Sanofi	anti-IL4Rα	Approved
Tralokinumab	AstraZeneca	anti-IL-13	Phase III
Lebrikizumab	Dermira	anti-IL-13	Phase 2b
ASLAN004	ASLAN	anti-IL13Rα1	Phase I

Source: EvaluatePharma

AD is the most common type of eczema, affecting an estimated 18 million adults in the US.[1] Approximately 20% of these patients have moderate to severe disease necessitating medication, and approximately 4% develop a chronic form of the disease. If the condition is poorly controlled without medication, topical steroids are typically prescribed in the first line. However, about half of all patients with chronic disease become refractory to steroids, necessitating other pharmacological interventions, such as the PDE4 inhibitor Eucrisa (crisaborole, Pfizer) and calcineurin inhibitors such as Elidel (pimecrolimus, Valeant). We expect ASLAN004 to target a similar market of refractory moderate to severe patients.

Valuation

We have increased our valuation to $399m or $12.13 per ADS from $364m or $11.04 per ADS due to the inclusion of ASLAN004 in our models. We value the programme at $36m based on a relatively conservative 2% market share of chronic steroid refractory patients. We expect there to be substantial competition in the space among drugs targeting the IL-4/IL-13 axis as well as PDE4 inhibitors and others. Given the late entry of ASLAN004 to the market (launch in 2024), we remain conservative with our market share estimates. Despite this, we model a peak sales forecast of $587m. We expect pricing on par with Dupixent ($37,000 pa in 2017), adjusted for future price growth. The expected R&D programme is also based on Dupixent, with a total of 1,900 patients, although we expect a low cost of enrolment of $20,000 given the milder nature of the disease. Our probability of success for the programme is 15% because we have not seen any clinical data,

[1] National Eczema Association

although the mechanism of action has some validation through other programmes. Otherwise our valuation remains unchanged.

Exhibit 2: Valuation of ASLAN

Programme	Indication	Region	Clinical stage	Prob. of success	Launch year	Peak sales ($m)	Margin/royalties (%)	rNPV ($m)
Varlitinib	2nd line BTC	US + Europe	Phase II/III	30%	2020	277	59%	121.6
		East Asia	Phase II/III	30%	2019-2020	195	53-58%	73.9
		R&D						-7.2
	1st line GC	US + Europe	Phase II/III	20%	2021	182	57%	31.8
		East Asia	Phase II/III	20%	2021	302	54-60%	51.5
		R&D						-7.7
	Upfront and sales milestones payable							-9.5
ASLAN003	1st line AML	US + Europe	Phase II ready	10%	2022	308	59%	38.0
		R&D						-4.0
ASLAN002 Royalties	1st line BC + GC	US + Europe	Phase II	15%	2022	909	5%	16.9
ASLAN004	Refractory AD	US + Europe	Phase I	15%	2024	587	55%	42.1
		R&D						-6.4
Unallocated costs								-11.8
Total								**329.1**
Net cash and equivalents (Q118+ IPO + greenshoe) ($m)								70.2
Total firm value ($m)								**399.4**
Total basic ADSs (m)								32.9
Value per ADS ($)								**12.13**

Source: ASLAN reports, Edison Investment Research. Note: BTC=biliary tract cancer, GC=gastric cancer, AML=acute myeloid leukemia, AD=atopic dermatitis.

Financials

We have added the expected development costs of ASLAN004 to our financial projections, which has increased our financing requirements for the company. We expect the company to require $82m in additional capital before profitability in 2022, up from $60m previously. We expect this financing requirement to be met through the out-licensing of its products, including ASLAN004. However, in lieu of this agreement we record this as illustrative debt.

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Exhibit 3: Financial summary

	US$k	2016	2017	2018e	2019e
31-December		IFRS	IFRS	IFRS	IFRS
INCOME STATEMENT					
Revenue		11,547	0	0	743
Cost of Sales		(125)	0	0	(111)
Gross Profit		11,422	0	0	631
R&D		(13,165)	(30,001)	(30,526)	(34,813)
SG&A		(6,956)	(9,139)	(10,966)	(31,260)
EBITDA		(7,204)	(37,803)	(38,308)	(62,113)
Normalised operating profit		(7,280)	(38,013)	(38,533)	(62,337)
Amortisation of acquired intangibles		0	0	0	0
Exceptionals		0	0	0	3
Share-based payments		(1,420)	(1,127)	(2,959)	(3,107)
Reported operating profit		(8,700)	(39,140)	(41,492)	(65,441)
Net Interest		(477)	(54)	(198)	(124)
Joint ventures & associates (post tax)		0	0	0	0
Exceptionals		127	(699)	(197)	0
Profit Before Tax (norm)		(7,629)	(38,765)	(38,929)	(62,460)
Profit Before Tax (reported)		(9,049)	(39,892)	(41,888)	(65,565)
Reported tax		0	0	0	0
Profit After Tax (norm)		(7,629)	(38,765)	(38,929)	(62,460)
Profit After Tax (reported)		(9,049)	(39,892)	(41,888)	(65,565)
Minority interests		0	0	0	0
Discontinued operations		0	0	0	0
Net income (normalised)		(7,629)	(38,765)	(38,929)	(62,460)
Net income (reported)		(9,049)	(39,892)	(41,888)	(65,565)
Basic average number of shares outstanding (m)		105	124	157	175
EPS - basic normalised (US$)		(0.07)	(0.31)	(0.25)	(0.36)
EPS - diluted normalised (US$)		(0.07)	(0.31)	(0.25)	(0.36)
EPS - basic reported (US$)		(0.09)	(0.32)	(0.27)	(0.38)
Dividend (US$)		0.00	0.00	0.00	0.00
BALANCE SHEET					
Fixed Assets		593	689	21,615	19,561
Intangible Assets		84	84	21,053	18,999
Tangible Assets		384	444	405	405
Investments & other		125	161	158	158
Current Assets		53,121	50,645	41,128	33,719
Stocks		0	0	0	27
Debtors		1,294	0	0	122
Cash & cash equivalents		51,737	50,573	41,047	33,488
Other		90	72	82	82
Current Liabilities		(3,804)	(5,979)	(14,608)	(7,161)
Creditors		(3,804)	(5,979)	(14,608)	(7,161)
Tax and social security		0	0	0	0
Short term borrowings		0	0	0	0
Other		0	0	0	0
Long Term Liabilities		(8,336)	(9,841)	(10,524)	(70,966)
Long term borrowings		(8,336)	(9,679)	(10,099)	(70,541)
Other long term liabilities		0	(162)	(425)	(425)
Net Assets		41,575	35,513	37,611	(24,846)
Minority interests		0	0	0	0
Shareholders' equity		41,575	35,513	37,611	(24,846)
CASH FLOW					
Op Cash Flow before WC and tax		(7,204)	(37,803)	(38,308)	(62,113)
Working capital		1,524	3,274	(2,325)	4,204
Exceptional & other		(109)	(5)	1,320	1,933
Tax		0	0	0	0
Net operating cash flow		(5,789)	(34,534)	(39,313)	(55,975)
Capex		(374)	(291)	(195)	(224)
Acquisitions/disposals		(81)	(9)	(11,801)	(11,801)
Net interest		0	0	0	0
Equity financing		31,364	33,061	42,320	0
Dividends		0	0	0	0
Other		(68)	(36)	0	0
Net Cash Flow		25,052	(1,809)	(8,989)	(68,001)
Opening net debt/(cash)		0	(25,052)	(22,544)	(12,598)
FX		0	0	(979)	0
Other non-cash movements		0	(699)	22	0
Closing net debt/(cash)		(25,052)	(22,544)	(12,598)	55,403

Source: ASLAN reports, Edison Investment Research

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