Invex Therapeutics – Phase II Trial Readout Ahead

Invex Therapeutics (IXC: $0.92) is nearing an important milestone, which is the release of the results of its 16 patient, randomised, double-blind, placebo controlled Phase II trial of the re-purposed drug exenatide for the treatment of Idiopathic Intracranial Hypertension (IIH).

Exenatide (brand name Byetta, AstraZeneca) is approved in the USA as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes.

Exenatide is approved in Europe for the treatment of type 2 diabetes in combination with a range of other drugs.

Exenatide is delivered by subcutaneous injection from pre-filled pens of either of 5mcg or 10mcg.

A once-a-week 2mg version, Bydureon Bcise, has also been approved. This formulation obtains its extended release properties from the excipient Poly-lactic-co-glycolic acid (PLGA) which has been widely used for that purpose.

Mechanism

Exenatide is a glucagon-like peptide-1 (GLP-1) receptor agonist. Exenatide increases glucose-dependent insulin secretion from pancreatic beta cells and suppresses glucagon secretion. Glucagon is a hormone that promotes the amount of glucose in circulation. In the context of diabetes, the gut is the site of activity.

Exenatide has been shown to reduce cranial pressure by reducing CSF secretion through the choroid plexus tissue in animal studies. GLP1 receptors are abundant in human choroid plexus tissue.

Phase II Trial - Idiopathic Intracranial Hypertension

Idiopathic Intracranial Hypertension is a condition in which patients experience severe headaches which limit daily functioning. The condition can lead to vision loss because of compression of the optic nerve.

The results of the 16 patient Phase II trial are expected to be released in this quarter (Q2 CY2020). The last patient completed the 12 weeks of dosing in January.

Subjects in the trial were randomised to receive a placebo twice a day, or 10mcg of exenatide twice day.

The primary endpoint of the trial is the change in intracranial pressure, measured in real time using an implanted monitor, but at three different time points from baseline – every 2.5 hours (after drug administration), every 24 hours, and at the end of trial. This is an objective endpoint.

Secondary endpoints will reflect changes in headache frequency, severity and duration, as well as the use of analgesics, visual field assessment and quality-of-life measures.

The trial is evaluating the approved formulation of exenatide (Byetta) in the trial, which is however a dose form not regarded as suitable for treating IIH because of its short half-life.

Improved Dose Form for Phase III Trial

Invex has named its reformulated dosage form of exenatide as Presendin. The company has been testing different formulations of Presendin ahead of choosing a lead formulation to take forward – assuming positive Phase II results are achieved – into Phase III studies.

Byetta is effective for between one and three hours. However, IIH patients would arguably receive a better therapy with a drug that was effective across a 24 hour time span.

Invex has hired the team of formulation scientists which developed Byetta. The company has shown in animal models that a new formulation can be effective for 24 hours.

Invex intends to complete a pharmacokinetic (PK) study in approximately 20 healthy volunteers in order to confirm the results observed in animal studies and demonstrate that the new formulation is consistent with Byetta's safety profile. The safety confirmation would stand as a significant milestone for the company, because Presendin's preferred regulatory pathway and development economics is linked to the safety data (both positive and negative) established for Byetta.

Investment Thesis

Invex Therapeutics presents as an attractive investment proposition because it is developing a therapy for an Orphan Drug (rare disease) indication for which there is no satisfactory drug therapy, with high relapse rates for patients that receive surgery. The drug Diamox has been used to treat patients with IIH, but about half the patients are unable to tolerate the drug.

Idiopathic Intracranial Hypertension is a debilitating condition which more often affects obese females and can lead to blindness, an even worse outcome for sufferers which also results in even higher healthcare costs. IIH is growing in prevalence driven by growth trends in obesity.

A drug that could prevent blindness caused by IIH could arguably command a significant price premium based on potential healthcare system cost savings.

Orphan Drug development strategies have a proven track record in Australian biotech, with Clinuvel Pharmaceutical's Scenesse for patients with sunlight intolerance serving as an example of both clinical and commercial success. The advantages of Orphan Drug development include the ability of small biotechs to gain direct access to patients and the physicians who treat them, gain access to key opinion leaders, along with the potential to directly manage all aspects of drug development, clinical development and registration processes.

Some of CSL's commercial success has been built on the development of therapies to treat Orphan Drug diseases especially in hemophilia disorders. An example is Idelvion, a long-acting hemophilia B drug which is designed to replace a clotting factor missing in hemophilia B patients.

Continued over

Bioshares Model Portfolio (9 April 2020)

Company	Code	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
Opthea	OPT	$2.330	$0.160	Spec Hold A	$627	November 2014
Telix Pharmaceuticals	TLX	$1.195	$0.910	Spec Hold A	$303	May 2019
Volpara Health Technologies	VHT	$1.400	$0.375	Spec Hold A	$305	June 2017
Cyclopharm	CYC	$1.300	$1.35	Spec Buy A	$102	September 2019
Somnomed	SOM	$1.020	$0.94	Spec Hold B	$64	January 2011
Cogstate	CGS	$0.345	$0.24	Spec Hold A	$57	April 2019
Immutep	IMM	$0.135	$0.320	Spec Hold A	$52	March 2019
Pharmaxis	PXS	$0.100	$0.260	Spec Hold A	$39	December 2016
Micro-X	MX1	$0.160	$0.38	Spec Buy A	$40	May 2017
Dimerix	DXB	$0.150	$0.09	Spec Hold A	$24	December 2018
Acrux	ACR	$0.145	$0.31	Spec Hold A	$24	July 2017
Rhinomed	RNO	$0.081	$0.24	Spec Hold B	$14	Jun-19

Portfolio Changes – 13 April, 2020

IN:
No changes

OUT:
No changes

Stocks Removed from Bioshares Portfolio in TTM

Date removed	Stock
September 2019	1AD, ALC, BCT
June 2019	CUV

– Invex cont'd

Another feature worth noting is that Invex's new formulation would present a very strong barrier to competitors. The existing approved formulations of exenatide 10mcg twice daily and 2mg weekly, are unlikely to be prescribed because the 10mcg twice daily is not optimised to the address the 24-hour characteristic of IIH and the 2mg weekly dose is more likely to have safety limitations. (The FDA label for the 2mg weekly dose formulation (Bydureon) includes a Black Box warning.)

In addition, the delivery of exenatide (Presendin) through an injector pen device secures an additional barrier to entry, although adding cost and complexity from a development and manufacturing perspective.

Risks

The forthcoming Phase II trial results could show that exenatide does not reduce cranial pressure. That is the immediate risk with the stock. The trial is powered to deliver a statistically significant outcome for the primary endpoint.

Invex Therapeutics is capitalised at $51 million and retained cash of $10.4 million at March 31, 2020, which it believes will be sufficient to meet the company's requirements up until a Phase III study, planned for 2021.

Bioshares recommendation: **Speculative Hold Class B**

Bioshares

Invex – Key Milestones

Q2 2020 - Release Phase II results

Q2 2020 - Complete PK/safety study of new formulation in animals

Q3 2020 - Phase II trial design to be confirmed

Q4 2020 - Release PK/safety study of new formulation in humans

H1 2021 - Commence a Phase II trial in a second indication (currently not specified but could be one of the following indications: acute stroke, hydrocephalus, venous sinus thrombosis, brain tumours, meningitis, secondary pseudo tumour cerebri or traumatic brain injury)

H1 2021 - Commence Phase III trial

– Top Six Stock Picks Update cont'd

Bioshares recommendations:
Cyclopharm – **Speculative Buy Class A**
Micro-X – **Speculative Buy Class A**
Acrux – **Speculative Hold Class A**
Opthea – **Speculative Hold Class A**
Cogstate – **Speculative Hold Class A**
Pharmaxis – **Speculative Hold Class A**

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