Invex Therapeutics

Investor Presentation

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invex THERAPEUTICS

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Company Snapshot

Company	
Repurposed, Proven Drug	Presendin™ (Exenatide)
Clinical Stage	Entering Phase III
Orphan Disease Focus	Idiopathic Intracranial Hypertension (IIH)
Orphan Designation Granted	USA + EU
Total Addressable Market	$1.6 billion annually (US/EU)
Valuation Drivers	Clinical, regulatory, patent

Capital	
Shares on Issue	75.2 million
Unlisted Options	3.9 million
Cash (31 Dec-20)	$33.6 million
Market Capitalisation (17 Feb-20) [1]	$70.3 million
Enterprise Value (17 Feb-20)	$36.7 million

Major Shareholders	
Directors / Management	16.8%
Tattarang	11.8%
Tisia Nominees Pty Ltd	5.3%
JK Nominees Pty Ltd	4.0%
University of Birmingham	2.7%
Top 20 Shareholders	**58.0%**

Board of Directors	
Dr Jason Loveridge	Chairman
Professor Alexandra Sinclair	Executive Director & Chief Scientific Officer
Mr David McAuliffe	Non-Executive Director
Dr Megan Baldwin*	Non-Executive Director
Dr Tom Duthy	Executive Director

* Appointed 17 February 2021

[1] Based on closing price of $0.835

Invex Therapeutics - Executive Summary

Clinical stage drug development Company targeting the orphan disease Idiopathic Intracranial Hypertension (IIH)

Attractive Market Dynamics

- IIH Total Addressable Market (TAM) in the US and Europe of **A$1.6 billion** per annum and growing at **3.4% per annum**
- Unencumbered drug therapy market – no approved treatments, no new treatments in clinical trials
- Urgent market need, chronic administration required

Supportive Clinical Data

- Strong Phase II clinical data - clear statistical and clinical evidence of efficacy in primary and secondary endpoints demonstrating a strong and sustained drug effect in the IIH population
- No significant safety concerns over 12 weeks of treatment
- Plan to file with national health authorities in Europe & commence a Phase III registration trial in 2H CY2021

Significant Barriers to Competition

- Orphan drug designation in US (7 years exclusivity) and Europe (10 years exclusivity)
- Issued and pending patents for use of Exenatide in IIH. Formulation patents filed Q1 2020

Q1 2021 Highlights to Date

Dr Megan Baldwin Appointed to the Board of Directors

- Dr Baldwin is CEO and Managing Director of Opthea Limited (ASX:OPT; NASDAQ:OPT)
- Experienced biotechnology executive, having over 20 years' experience working on therapeutic drug development programs for cancer and ophthalmic indications
- Opthea has rapidly advanced its ophthalmology program through Phase I and Phase II clinical development
- Opthea included into the S&P/ASX 300 in June 2020
- Opthea raised $180 million and listed on NASDAQ Exchange in October 2020

Continued Preparations for Phase III Trial in IIH

- Selection of preferred formulation of Presendin™ for clinical development - **pending**
- Advanced discussions with lead contract manufacturer for supply of clinical-grade Presendin ™ for Phase III study – **pending**
- Significant expert input into planned study protocol and execution - **ongoing**
- Submission to US FDA for Pre-IND / Type B Meeting in Q1 CY2021 – **on-track**

What is Idiopathic Intracranial Hypertension (IIH)?

The Disease[1]

- >90% of cases are overweight women of childbearing age, with no known cause (idiopathic): approx. 4.7 per 100,000
- >90% suffer headaches that are progressively more severe and frequent: major cause of morbidity
- Up to 25% suffer permanent vision loss due to elevated intracranial pressure (ICP) effect on optic nerve function

The Impact[2]

- Invasive surgical and/or device interventions to temporarily lower ICP and preserve vision (significant side effects)
- 40% of patients have repeat hospital admissions, with average stays of 2.7 days
- Significant impact on quality of life and rapidly rising healthcare costs e.g. £462M in UK by 2030 (5x increase on 2017)

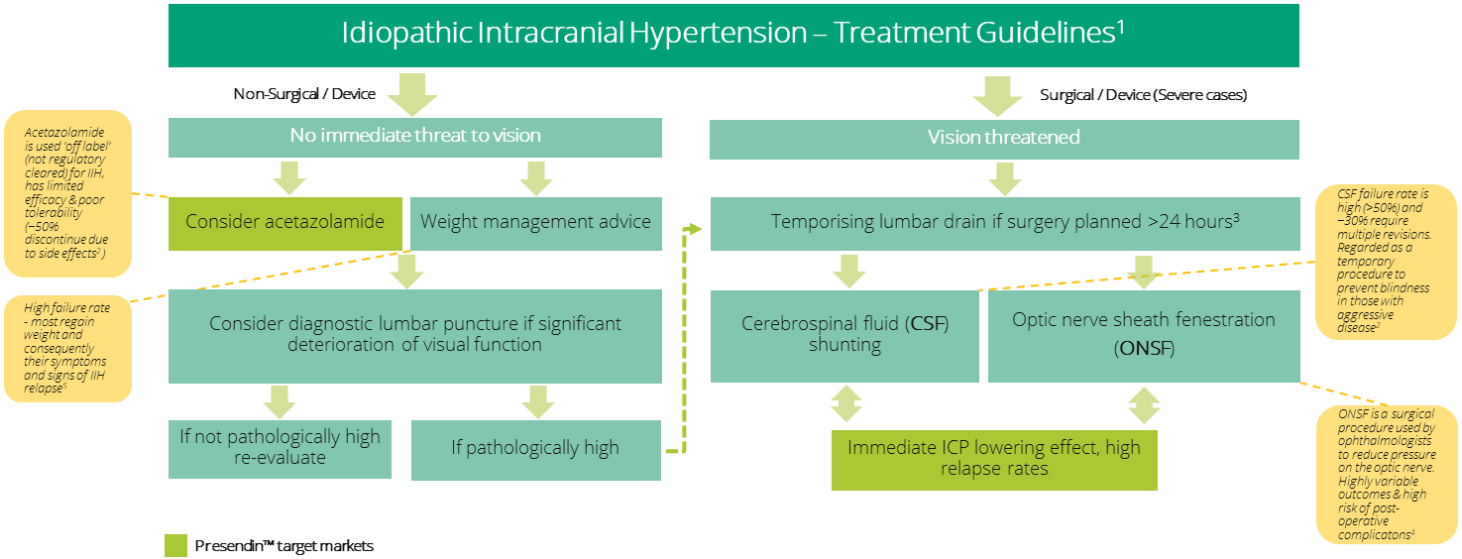
The Solution

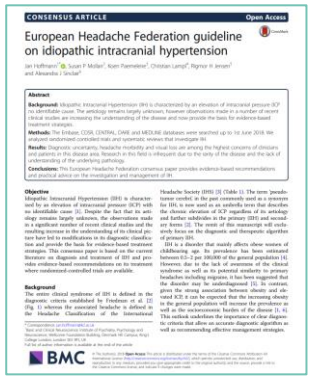
- Prof. Alex Sinclair (Invex CSO & Exec. Director) first to demonstrate glucagon like peptide 1 (GLP-1) receptor agonists commonly used in diabetes treatment (Exenatide formulated as Byetta® or Bydureon®) act on the choroid plexus in the brain to lower cerebral spinal fluid secretion and as a consequence, ICP
- Exenatide - strong scientific basis for benefit, well defined mechanism of action, patents secured - re-purposing opportunity to improve safety & efficacy → Presendin™
- Invex Phase II study in IIH - first clear demonstration of safety & efficacy in IIH

1. Corbett JJ, et al. Arch Neurol. Visual loss in pseudotumor cerebri. Follow-up of 57 patients from five to 41 years and a profile of 14 patients with permanent severe visual loss; Markey et al., Understanding idiopathic intracranial hypertension: mechanisms, management, and future directions (2016).
2. Mollan et al., EYE. The expanding burden of idiopathic intracranial hypertension (2019)

Current treatments for IIH are limited

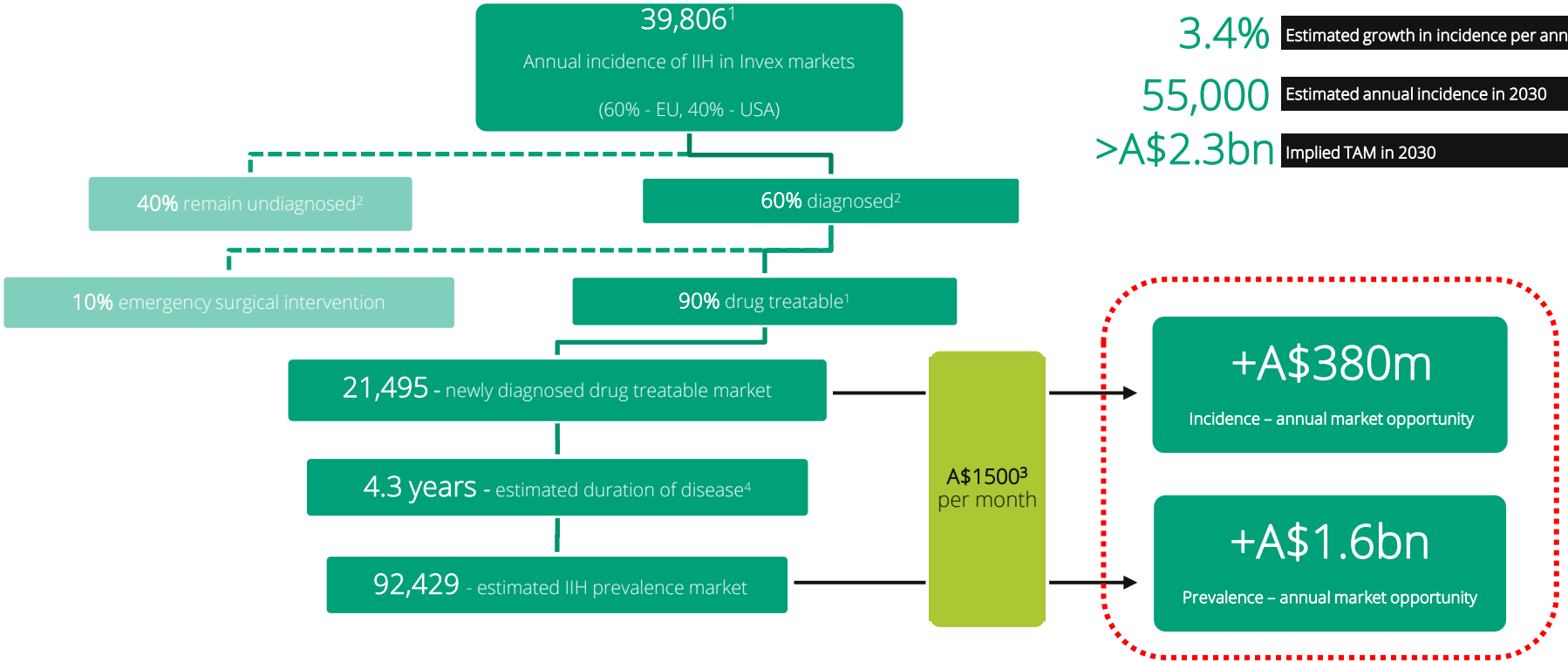
- Diagnostic criteria (2013) and treatment guidelines (2017/8) now well defined
- Recent IIH consensus guidelines written by Prof. Alex Sinclair & colleagues
- Treatment guidelines highlight the lack of a standard drug therapy in IIH and opportunity for rapid incorporation into treatment guidelines post regulatory clearance
  - Drives clinical use, important for payer coverage





1. Mollan SP, et al. Idiopathic intracranial hypertension: consensus guidelines on management (2018); 2. Ball et al., A randomised controlled trial of treatment for IIH (2011), Wall et al, The IIH treatment trial: clinical profile as baseline (2014); 3. Thurtell et al., IIH recognition, treatment and ongoing management (2013); 4. Sergott et al., Optic nerve sheath decompression: a clinical review..(1990); Banta and Farris, Pseudotumor cerebi and optic nerve sheath decompression (2000); 5. Li et al., Meta-analysis: pharmacologic treatment of obesity (2005), Ko et al., Weight gain and recurrence in idiopathic intracranial hypertension (2011)

IIH Total addressable market (TAM)



3.4% Estimated growth in incidence per annum[5]

55,000 Estimated annual incidence in 2030

>A$2.3bn Implied TAM in 2030

1. Mollan et al., EYE. The expanding burden of idiopathic intracranial hypertension (2019) incidence rate of 4.7/100,000 general population, n =23,182 . Targets markets are EU 27(& UK) + USA
2. Mollan SP, et al. Idiopathic intracranial hypertension: consensus guidelines on management (2018) ; Invex estimate re % presenting headache severity
3 Simoens et al., "what price do we pay for repurposing drugs for rare diseases"? (2016) – average 66x & Invex initial pricing analysis => pricing subject to change
4. D. Friesner et al., Idiopathic intracranial hypertension in the USA: the role of obesity in establishing prevalence and healthcare costs (2010)
5. Assumes average of obesity growth rates in UK (https://www.oecd.org/els/health-systems/Obesity-Update-2017.pdf) and historical incidence growth rate

Key clinician pathways in the management of IIH

No Immediate Threat to Vision

Optometrists

- Often patients with vision issues consult an optometrist, who in turn are primary referrers to ophthalmologists
- ~37,000 optometrists in the USA[1]

Ophthalmologists

- ~19,000 ophthalmologists in the USA[1]
- **~260** specialise in neuro-ophthalmology, specifically treating IIH patients[2]

Neurologists

- ~19,000 neurologists in the USA who see patients with significant headaches[1]
- **~1,500 to 2,000** sub-specialise as certified headache specialists[2]

Threat to Vision

- Hospitalisation and surgical / device intervention
- CSF shunting, ONSF to reduce pressure

1. Optometrist estimates: https://www.bls.gov/oes/2018/may/oes291041.htm; other specialist estimates: https://www.aamc.org/data-reports/workforce/interactive-data/active-physicians-largest-specialties-2017,
2. American Migraine Foundation and https://journals.lww.com/jneuro-ophthalmology/Fulltext/2018/03000/A_Profile_of_Neuro_Ophthalmic_Practice_Around_the.11.aspx

Invex Phase II trial – design & outcomes

Study Purpose

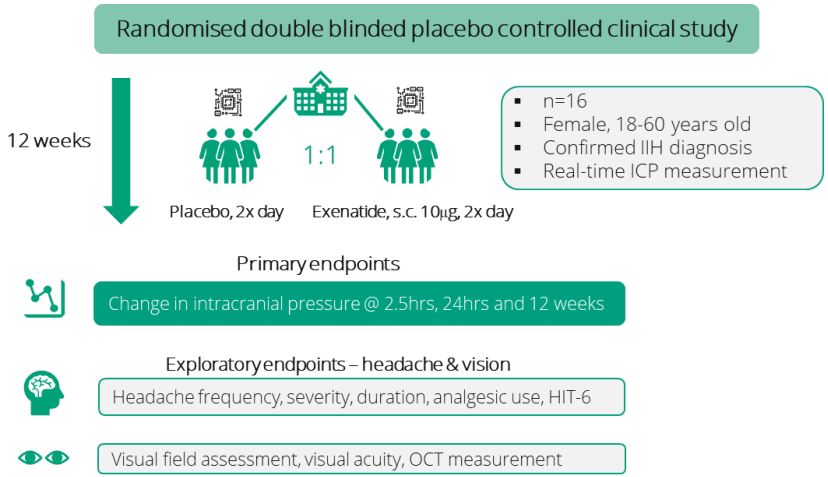
- Obtain first clinical proof of concept for Exenatide in IIH and provide a basis to move into pivotal Phase III trial by leveraging orphan drug status in Europe and the United States

Efficacy Outcomes

- Primary Endpoint (reduction in ICP) Met – 18-21% reduction across three time points; statistically significant and clinically meaningful
- Secondary Endpoint (Headache) Met – statistically significant & clinically meaningful reduction in headache days (7.7 days / 37% versus placebo)
- Secondary Endpoint (Vision) Met – statistically significant & clinically meaningful improvement in visual acuity (0.1 logMAR improvement at 12 weeks, equivalent to one line of visual acuity)

Safety Results

- No serious adverse events (SAEs) were observed related to the use of Exenatide
- Overall, adverse events were relatively low, with nausea the most common seen in >85% of patients treated with Exenatide
- Nausea is a known and the most frequent AE of sub-cutaneous administration of this formulation of Exenatide (Byetta®)



Conclusion

- Strength of the outcomes for both primary & key secondary clinical endpoints from the Phase II study implies a clear & strong drug effect in the IIH population & supports progression to a Phase III clinical trial for registration in the USA and Europe.

Lead-In Activities Ahead of Planned Phase III Trial

Reformulation

- Successfully completed a series of animal pharmacokinetic (PK) studies in CY2020 with proprietary formulations
- COVID-19 impacted access to laboratory personnel and testing facilities in Q4 CY2020
- Final formulation candidate for planned clinical studies pending
- Formulations are subject of additional patent filings made by Invex in Q1 CY2020

Tolerability*

- All Presendin™ formulation excipient(s) have been used in already approved drugs and have a well-established safety profile - hence Invex only required to undertake one additional safety study to assess local tolerability at the injection site (in animals)
- Study expected to commence in 1H CY2021

Manufacturing

- Require a Contract Manufacturing Organisation (CMO) to manufacture and supply clinical-grade Presendin™ for human clinical trials & perform other activities required by government regulators
- Discussions with globally-recognised manufacturers capable of production and supply are well-advanced
- Final sign off for supply of Good Manufacturing Practice (GMP) Presendin™ pending

Human PK Study*

- As a reformulation of an existing approved drug, a Phase I human pharmacokinetic (PK) study required
- Single and repeated sub-cutaneous doses in healthy (obese) volunteers
- Total amount of bioavailable drug must not exceed that approved for reference Exenatide drug product Byetta®
- Study expected to commence in 1H CY2021

* Subject to availability of GMP grade Presendin™

Regulatory update

Strength of the outcomes for both primary & key secondary clinical endpoints from the Phase II study implies a clear & strong drug effect in the IIH population & supports progression to a Phase III clinical trial for registration in the USA and EU

European Medicines Agency (EMA)

July 2020: First Response to Protocol Assistance

- One well controlled study providing compelling evidence of safety and efficacy required for marketing authorisation application (MAA) in EU
- CHMP[1] recommended ICP as primary endpoint versus placebo
- Noted headache would also be a clinically meaningful endpoint
- Broad acceptability of Invex's pre-clinical package and human PK study plans

December 2020: Second Protocol Assistance Feedback

- Follow up submission for advice lodged in October 2020
- Successfully concluded proceed with EMA in December 2020
- Following feedback in late Q4 CY2020, Invex intends to submit a Clinical Trial Application (CTA) within select European countries in 1H CY2021
- Single pivotal clinical trial for registration of Presendin™ in EU expected to commence thereafter (2H CY2021)

US Food and Drug Administration (FDA)

July 2020: First Response to Protocol Assistance

- Initial submission asked for advice on either headache or vision as the preferred primary endpoint – reviewed by Division of Ophthalmology
- Requested a complete protocol and statistical analysis plan prior to detailed scientific advice
- Reduction in headache days of moderate to severe headaches a clinically meaningful endpoint
- Broad acceptability of Invex's pre-clinical package

Q1 2021: Submit for Type B / Pre-IND Meeting

- Detailed protocol assistance to be sought following response from EMA and preparation of a full study protocol and statistical analysis plan – preferred review by Division of Neurology at FDA
- Pre-IND meeting request Q1 CY2021, results Q3 CY2021
- Over-arching strategy is to align study protocol acceptable to the FDA for a single registration trial that meets requirements of EMA & FDA leveraging orphan drug designations in both jurisdictions

CHMP[1] – Committee for Medicinal Products for Human Use

Summary & Outlook

- Large, growing market for IIH with no approved medical interventions
- Orphan Drug Designation in the USA and EU provides expedited, cost-effective clinical trial recruitment, reporting and approval/registration as well as commercial exclusivity for up to 10 years
- Strong Phase II clinical data established
- Financial:
  - $33.6M in cash at 31 December 2020 – expected to fully fund completion of a Phase III clinical trial in IIH for registration
  - Very attractive ~$37M Enterprise Value (EV) considering stage of development and market attributes
  - Large EV discount to ASX-listed orphan (ASX:CUV, ASX:NEU, ASX:RAC), ophthalmic (ASX:OPT) and re-purposing (ASX:PAR) companies
- 2021 Month Milestones:
  - Final Formulation Selection – Near Term
  - Appointment of contract manufacturer – Near Term
  - Pre-IND Submission / Type B Meeting request with FDA – Q1 CY2021
  - Type B Meeting Response from FDA – Q3 CY2021
  - Subject to availability of GMP Presendin™
    - Human PK study to commence 1H CY2021
    - Animal tolerability study to commence 1H CY2021
    - Filing of a CTA in Europe for Phase III clinical trial 1H CY2021
    - Commencement of Phase III clinical trial in Europe in 2H CY2021

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Thank you

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