Invex Therapeutics

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Invex overview

- Listed on ASX in July 2019
- Specialise in neurological conditions characterised by raised intracranial pressure
- Initial focus on treating idiopathic intracranial hypertension (IIH)

- IIH is a rapidly growing orphan indication
- Orphan Drug Designation granted in the US and Europe
- No regulatory cleared (approved) disease modifying therapies in use
- ~A$1.6 billion per annum total addressable market

- Repurposing existing diabetic drug Exenatide (Presendin™)
- Discovery of ability to also reduce production of cerebral spinal fluid
- Well understood safety profile & manufacturing of drug substance
- Orphan designation + repurposing = accelerated development

- Phase II read out expected mid to late May 2020
- Lead in pharmacokinetic (PK) study (est. n=20) 2H 2020
- Single registration-directed Phase III study 1H 2021
- IP assigned from University of Birmingham, UK
- World class Medical Advisory Board engaged for planned Phase III

Company snapshot

Company	
Repurposed Proven Drug	Presendin™ (Exenatide)
Clinical Stage	Phase II
Orphan Disease Focus	IIH^ + Other
Orphan Designation Granted	USA + EU
Development Path	Single Phase III for regulatory clearance
Total Addressable Market	~$1.6 billion annually
Valuation Drivers	Clinical, regulatory, patent

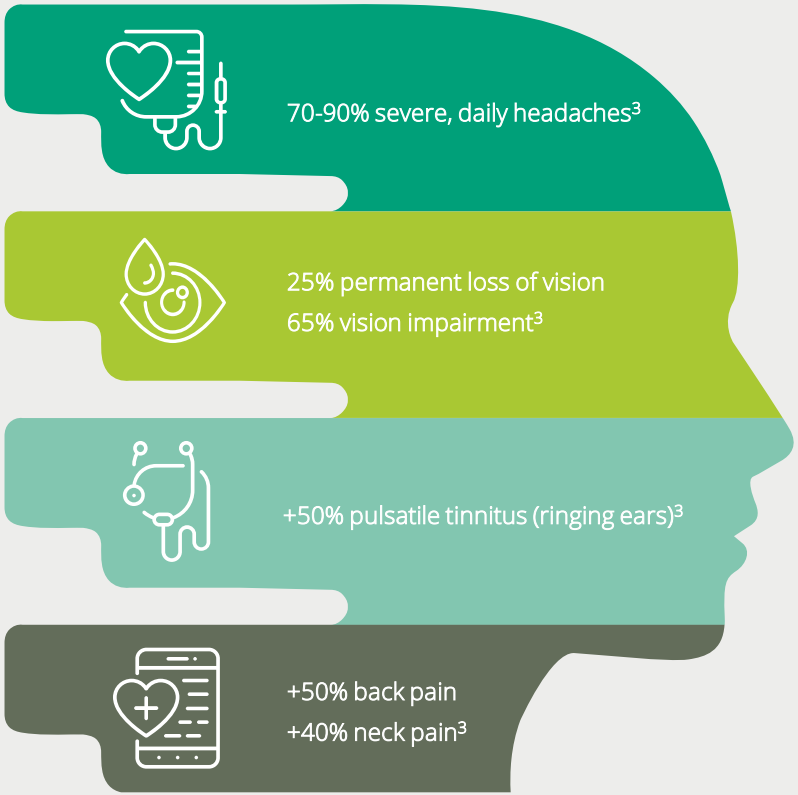
Capital Structure	
Shares on Issue	55 million
Unlisted Options	3.45 million
Cash (31 Mar-20)	$10.4 million
Market Cap (as at 27 Apr-20)	$57.8 million

Major Shareholders	
Directors / Management	20%
Minderoo Pty Ltd	9.1%
JK Nominees Pty Ltd	7.3%
Tisia Nominees Pty Ltd	7.2%
Oaktone Nominees	6.3%
University of Birmingham	3.6%
Top 20 Shareholders	**73%**

Board of Directors	
Dr Jason Loveridge	Chairman
Professor Alexandra Sinclair	Executive Director & Chief Scientific Officer
Mr David McAuliffe	Non-Executive Director
Ms Narelle Warren	Non-Executive Director, CFO & Co. Sec.

^IIH – Idiopathic Intracranial Hypertension

What is Idiopathic Intracranial Hypertension (IIH)?



Patient typically presents at A&E or to an optometrist with a combination of debilitating chronic daily headaches and on occasions severe vision impairment

Definitive diagnostic signal is raised intracranial hypertension / pressure (ICP) with no identifiable cause (idiopathic). All other causes of raised ICP are related to a secondary factor, e.g. a tumour, brain haemorrhage, meningitis, or trauma and brain tissue swelling. In diagnosing of IIH, these are excluded as the cause[1]

~90% of patients are obese women of childbearing age; can last for many years despite existing treatments and significantly reduces quality of life[2]

As the incidence has grown significantly in recent years, clinician awareness and diagnosis has improved, international guidelines published and more patients are seeking effective interventions (device/therapeutic)

1. Sinclair et al., Idiopathic intracranial hypertension : recent concepts and developments (2010)
2. Mulla et al., Headache determines quality of life in idiopathic intracranial hypertension (2015)
3. Markey et al., Understanding idiopathic intracranial hypertension: mechanisms, management, and future directions (2016)

Diagnosing Idiopathic Intracranial Hypertension[1]

Patient

~90% female
~10% male

1 – Papilloedema examination

To identify swollen/damage to the optic nerve typically using an ophthalmoscope

2 – Brain imaging within 24 hours

To rule out lesions or tumours-via MRI/CT

3 – Lumbar puncture

Needle is inserted into the spinal column to measure pressure and collect cerebrospinal fluid

4 – Cerebrospinal Fluid (CSF) testing

Normal fluid content and **elevated** opening pressure (≥ 25cm H_2O)

Gold Standard for definitive diagnosis

=

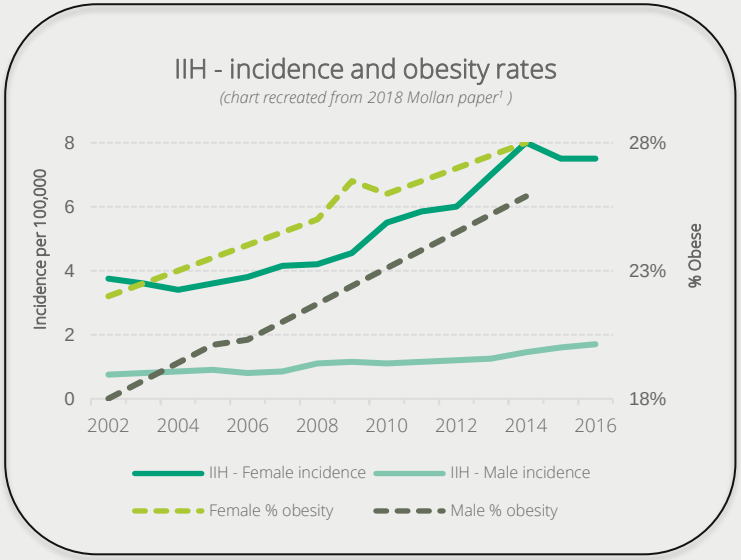
Idiopathic Intracranial Hypertension

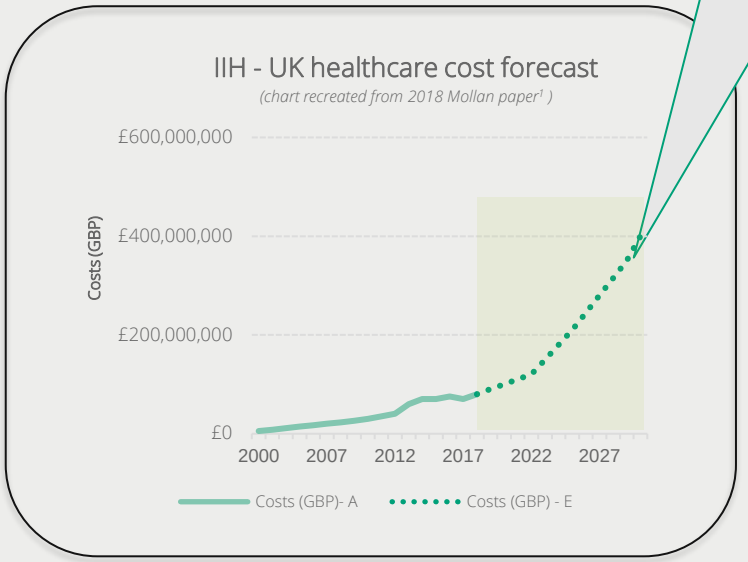
1. Mollan SP, et al. Idiopathic intracranial hypertension: consensus guidelines on management (2018)

Growing incidence of IIH

- IIH is a rapidly growing orphan indication driven by changing demographics, incidence CAGR of **5.2%** 2002-2016[1]
- **90%** of IIH patients are obese women of childbearing age[1]
- By 2030 IIH is projected to cost hospitals in England alone +**£400m** p.a[1], similar trend in USA[2]
- Key cost driver - ~**40%** of IIH patients have repeat hospital admissions, average length of stay being 2.7 days[1]

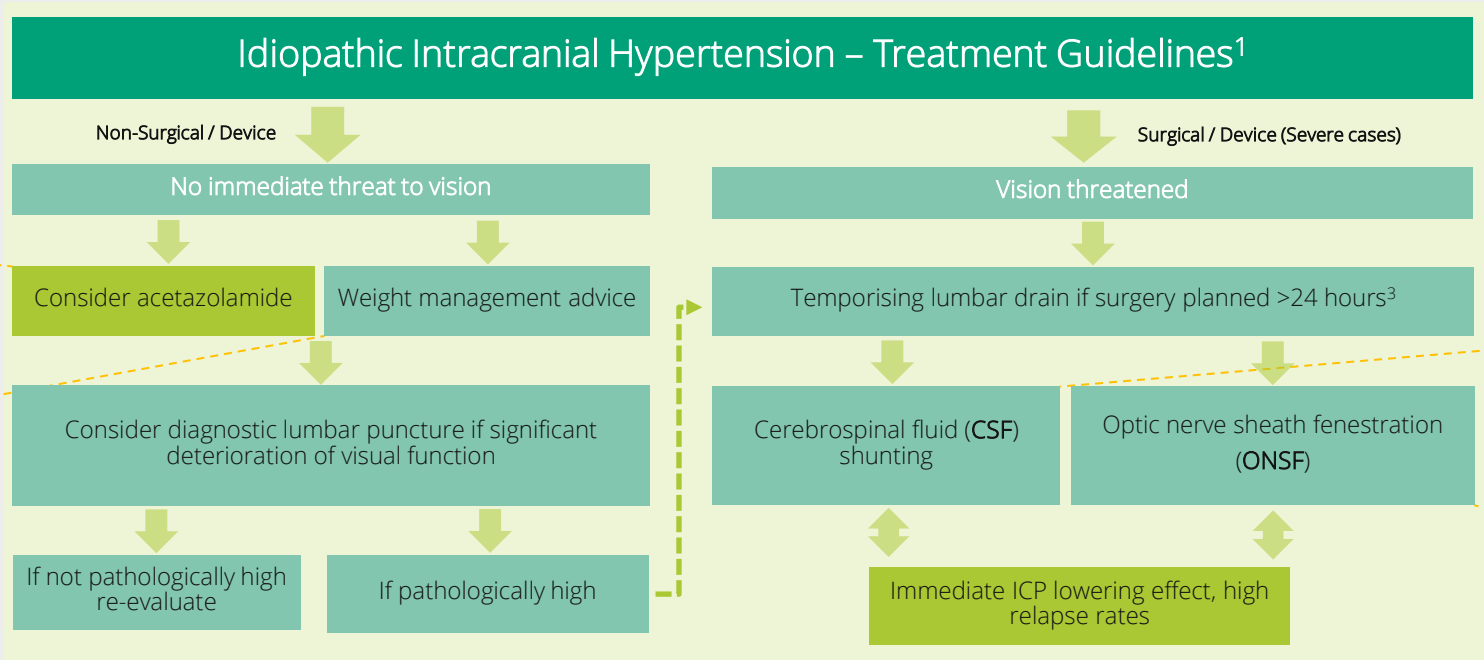
As the costs of managing a disease rise, the cost-effectiveness of an intervention such as Presendin™ improve; thereby lowering the threshold for payers to reimburse and accordingly more patients receive treatment





1. Mollan et al., The expanding burden of idiopathic intracranial hypertension (2018), 'Incidence and obesity rate' – Graphs recreated from Mollan et al. paper
2. Friesner et al., Idiopathic Intracranial hypertension in the USA: the role of obesity in establishing prevalence and healthcare costs (2010)

Current treatments for IIH are limited



Presendin™ target markets

Key IIH Treating Clinicians: Optometrists, Ophthalmologists and Neurologists

- Often patients with vision issues consult an optometrist, who in turn are primary referrers to ophthalmologists (**~37,000** optometrists in the USA)
- ~19,000 ophthalmologists in the USA; **~260** specialise in neuro-ophthalmology, specifically treating IIH patients
- ~19,000 neurologists in the USA who see patients with significant headaches; **~1,500 to 2,000** sub-specialise as certified headache specialists

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)

Total addressable market (TAM) – expected to grow

3.4% Estimated growth in incidence per annum[5]

55,000 Estimated annual incidence in 2030

>A$2.3bn Implied TAM in 2030

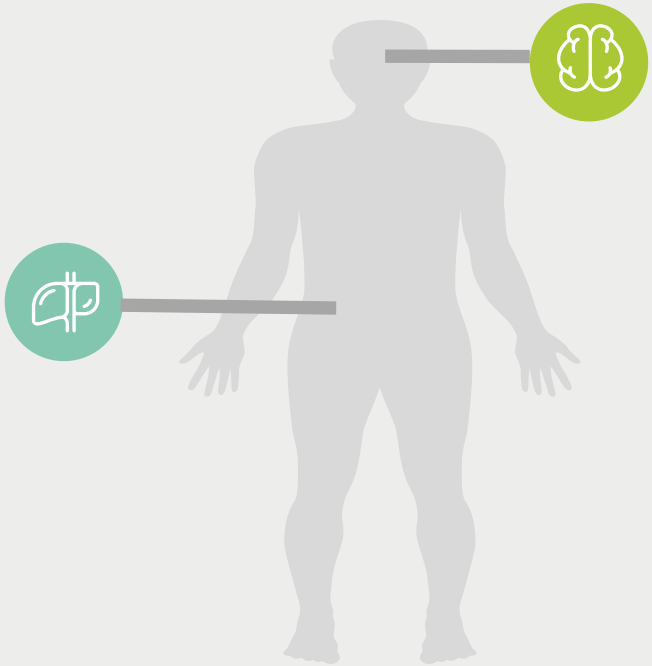
1. Mollan et al., The expanding burden of idiopathic intracranial hypertension (2019) incidence rate of 4.7/100,000 general population, n =23,182 . Targets markets are EU 27(& UK) + USA
2. Mollan SP, et al. Idiopathic intracranial hypertension: consensus guidelines on management (2018) ; Invex estimate re % presenting headache severity
3 Simoens et al., "what price do we pay for repurposing drugs for rare diseases"? (2016) – avge 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

Repurposing Exenatide for IIH

- Exenatide was approved in 2005 in the US & 2006 in the EU for the treatment of Type II diabetes]
- Currently marketed by AstraZeneca in two dosage formulations
- In its Byetta® form Exenatide is administered as a twice-daily, sub-cutaneous injection or as Bydureon®, as a once weekly injection
- Exenatide is well tolerated and considered a standard of care in Type II diabetic patients
- Invex has a robust, proprietary, patented position covering the use of Exenatide for IIH

Exenatide - Diabetes

- Small peptide that binds to the GLP-1 receptor
- GLP-1 receptor agonists, like Exenatide, decrease fluid secretion in the kidney and are used extensively to treat diabetes
- Byetta® CY19 sales of **US$110m,** Bydureon® CY19 sales of **US$549m**[1]
- Current formulations provide an exposure that is either too short or too long to effectively treat IIH



Exenatide - IIH

- Invex has demonstrated GLP-1 receptors are expressed in the choroid plexus region of the brain and that in animal models:
  - Exenatide can bind to these receptors
  - Provides fast onset of action (within 60 mins)
  - 50% reduction in ICP over 6 days in animal models
  - Reduce cerebrospinal fluid secretion (CFS)
- Current Phase II examining efficacy in IIH patients

Reduced CFS secretion reduces ICP and has the potential to alleviate severe headache and visual impairment caused by raised ICP in IIH patients

1. https://www.astrazeneca.com/content/dam/az/PDF/2019/full-year/Full-year_and_Q4_2019_results_announcement.pdf

Exenatide reformulation strategy

Exenatide @ current diabetic dose[1] tested in Phase II to demonstrate proof of concept in IIH patients

Current dose not optimal to treat IIH

Current formulations have either insufficient half life[2] or too slow onset[3] & are intolerable at higher doses for effective use in IIH patients

Invex is developing a novel, patented once daily s.c. formulation of Exenatide

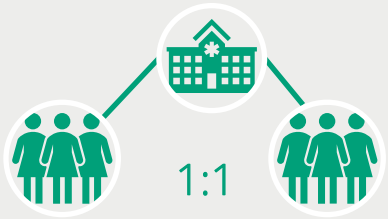
Risk for off label use of Byetta® or Bydureon® is minimal as no correct dosage available & safety issues associated with either under or overdosing

[1] 10mg pre-filled injection pens, [2] Byetta [3] Bydureon

Phase II trial design – results due mid to late May 2020

Randomised double blinded placebo controlled clinical study[1]

12 weeks



Placebo, 2x day

Exenatide, s.c. 10μg, 2x day

- n=16
- Female, 18-60 years old
- Confirmed IIH diagnosis
- Real-time ICP measurement

Primary endpoints[2]

Change in intracranial pressure @ 2.5hrs, 24hrs and 12 weeks

Exploratory endpoints – headache & vision

Headache frequency, severity, duration, analgesic use, HIT-6[3]

Visual field assessment, visual acuity, OCT measurement

Outcome Synopsis

- Confirmation that GLP-1 activity in brain drives ICP reduction and confirm MoA, providing clinical proof of concept
- Demonstration of a **clinical benefit** required for regulatory clearance in major markets
- Demonstrate that Byetta® is not suitable for treatment of IIH

- Confirmation that ICP reduction results in **clinical benefit** for patients
- All endpoints are acceptable measures of **clinical benefit** and could be utilised in a registration study

1. http://www.isrctn.com/ISRCTN12678718
2. Study powered only for the primary endpoint (p=0.1)
3. Headache Impact Test – 6 (Hit-6) is s a brief tool for assessing the impact of headache in both clinical research and practice and is a validated for use across headache disorders

Benefits of orphan drug designation

Orphan Drug Designation granted in 2017 by EMA (EU) & FDA (USA)	Designation granted for treating rare diseases: <200k patients in USA, < 5/10,000 in the EU[1]
Single pivotal Phase III registration study required for approval	High patient need will facilitate rapid recruitment
7 years (USA) & 10 years (EU) marketing exclusivity[1]	Exclusivity in IIH for Exenatide represents a significant barrier to entry for off-label use of Byetta® and Bydureon®
Price premium for orphan drugs, greater market access (reimbursement)	Pricing on average increases 66x repurposing drugs from common disease to treating a rare (orphan) disease[2] – Invex initial pricing estimate conservatively presented Unmet need often drives closer alignment between KOLs and patient groups; reducing payer influence[3]
Tax incentives, filing fee waivers & greater regulator access[1]	Tax credits of up to 50% of clinical development costs Waive the ~US $2.9 million Prescription Drug User Fee Act (PDUFA) application fee paid prior to regulatory review

1. https://rarediseases.info.nih.gov/files/fda%20orphan%20drugs.pdf ; https://www.ema.europa.eu/en/human-regulatory/research-development/orphan-designation/orphan-incentives / overview
2. Simoens et al., "what price do we pay for repurposing drugs for rare diseases"? (2016)
3. Ware et al, US Market Access: How Does It Differ for Orphan and Rare Disease States? (2015)

Key personnel for Presendin™ development

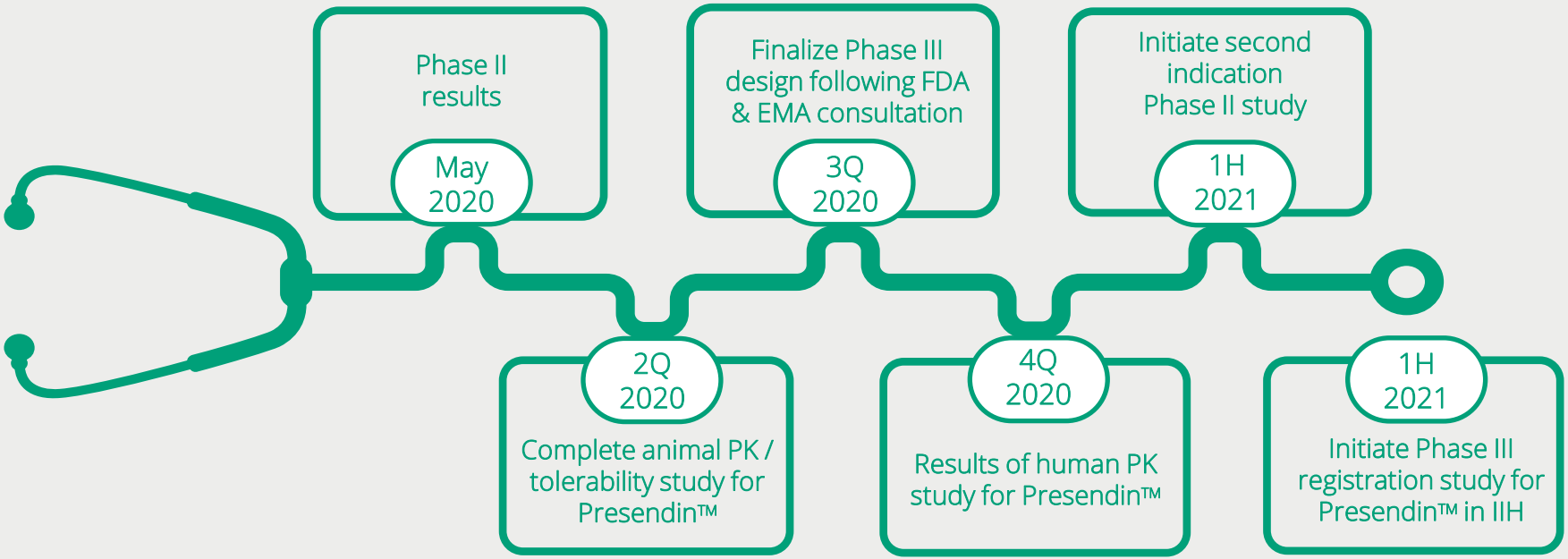
Prof. Alexandra Sinclair
Executive Director and Chief Scientific Officer

- Neurology consultant and clinician scientist
- Global leader in the pathophysiology of idiopathic intracranial hypertension and headaches, with over 10 years research in this field
- Sits on Board of the International Headache Society (IHS); Research committee member North American Neuro-Ophthalmology Society
- Leading role in developing International 2018 IIH Treatment Guidelines
- Lead Investigator on Exenatide Phase II Study

Dr. Jason Loveridge, Non-Exec Chairman

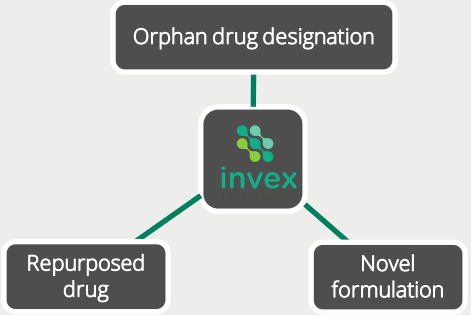
- Experienced life science investor and CEO
- Current CEO of 4SC AG (ETR:VSC), a listed German oncology drug developer
- Strong transaction background in biotech - successful sale of multiple drug assets; including most recently Genable Technologies Ltd. to Spark Therapeutics (NASDAQ: ONCE). Anaconda Pharma to Aviragen (NASDAQ: AVIR)
- Founder of numerous life science companies and experienced board director

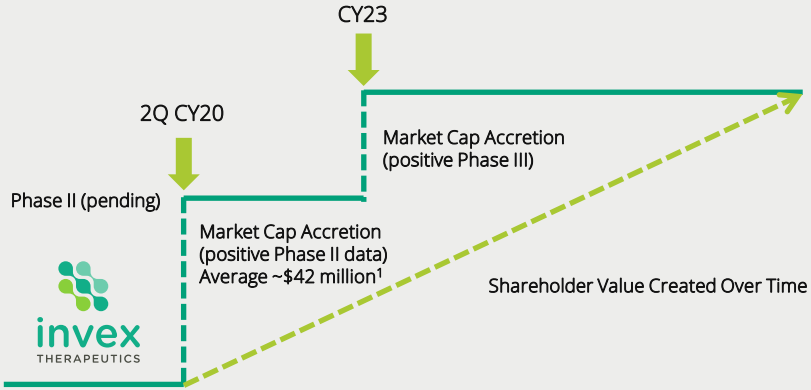
Timeline – key milestones



Repurposed, orphan drug comparable company with Phase II data

- **Invex is unique amongst ASX listed peers**, with a repurposed, proprietary drug with orphan designation in the USA and EU
- **Proven mechanism of action and safety** with clinical trial endpoints well recognised by regulatory agencies for registration
- **Lower clinical risk profile** - no approved standard of care treatment means registration study versus placebo only
- **Imminent Phase II data to be reported**; with peer ASX listed companies showing an average of ~$42 million increase in market capitalisation following positive early Phase II clinical data over last 12 months[1]
  - **Repurposed** Drug Developer: Paradigm Biopharmaceuticals (ASX:PAR) – market capitalisation +$650 million[1] (Phase II)
  - **Orphan** Drug Developer: Clinuvel Pharmaceuticals (ASX:CUV) – market capitalisation $1.1 billion[1] (FDA approval 4Q 2019)





1. Invex Analysis. Companies included in analysis on a pre and post data analysis are: ASX:ANP, ASX: PAR, ASX:KZA. If the analysis included ASX:OPT Phase IIb study the average would be $128m

Summary

- Large, growing market for IIH with **no approved (regulatory cleared) or efficacious drug-based 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
- Major milestone imminent – **Phase II efficacy data in intended patient population due mid to late May 2020**
- New clinical indications under active investigation: likely second indication initiated in **1H 2021**
- Proprietary, repurposed orphan drug Presendin™ in a Phase III clinical trial for registration by **1H 2021**
- Modest Enterprise Value (EV) and sufficient cash to deliver re-rating subject to clinical and development milestones delivered
- Transaction for entire Company preferred as value creation event for shareholders, versus licensing or partnering

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