Invex Therapeutics

Repurposing an approved drug

Business update

March 2020

ASX Code: IXC

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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 early 2Q 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

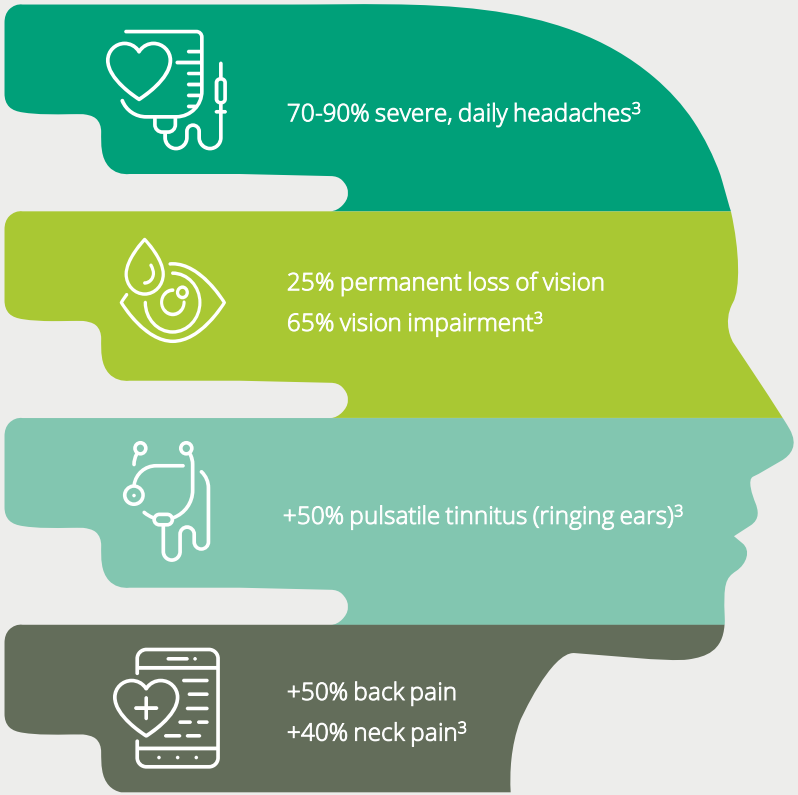
Capital Structure	
Shares on Issue	55 million
Unlisted Options	3.45 million
Cash (31 Dec 19)	$10.8 million
Market Cap (as at 4 Mar)	$59.4 million

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 daily headaches and 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

=

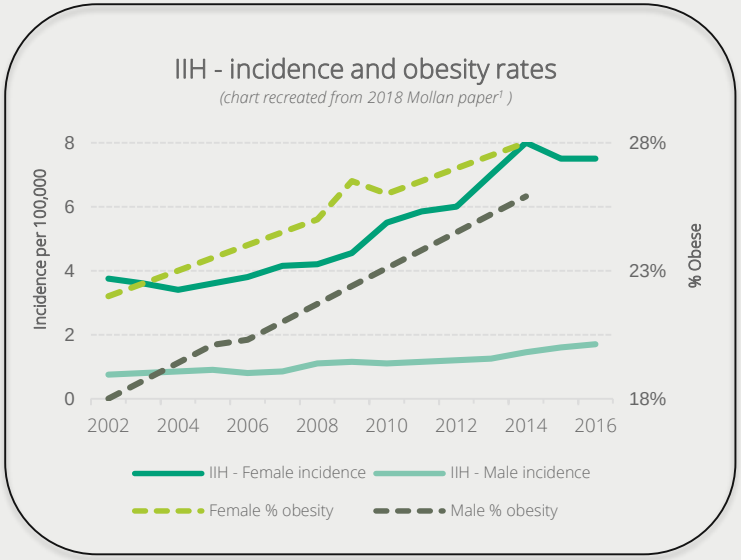
Idiopathic Intracranial Hypertension

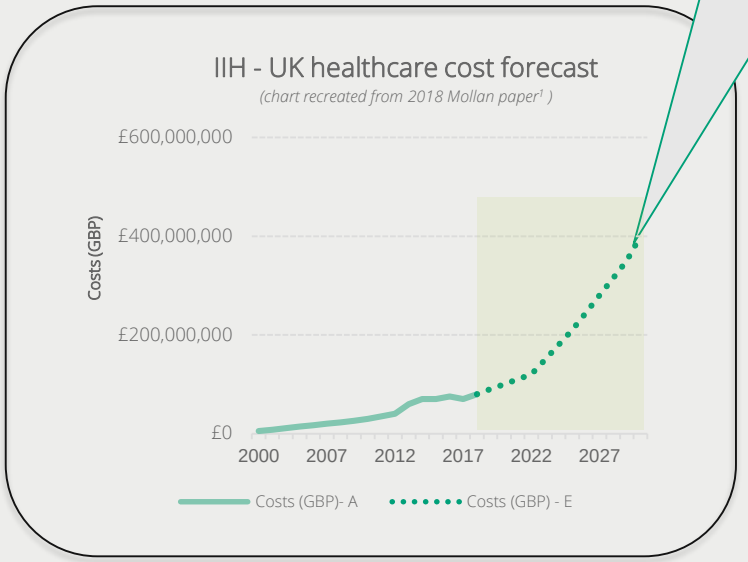
1. Mollan SP, et al. Idiopathic intracranial hypertension: consensus guidelines on management (2018)

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]
- A key cost driver is an estimated **40%** of IIH patients have repeat hospital admissions, average length of stay being 2.7 days[1]

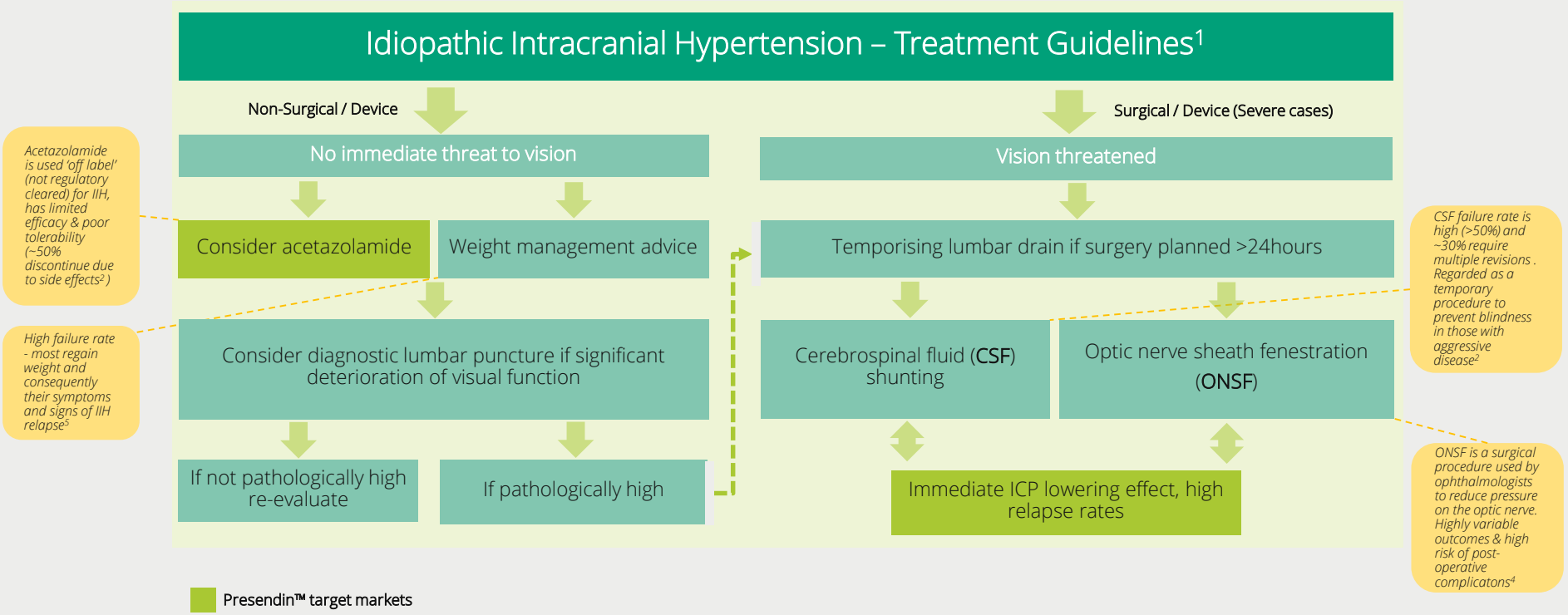
As the costs of managing a disease rise, the cost-effectiveness of an intervention such as Presendin™ improve; thereby lowering the threshold for payers to reimburse and accordingly more patients receive treatment





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



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)

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

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

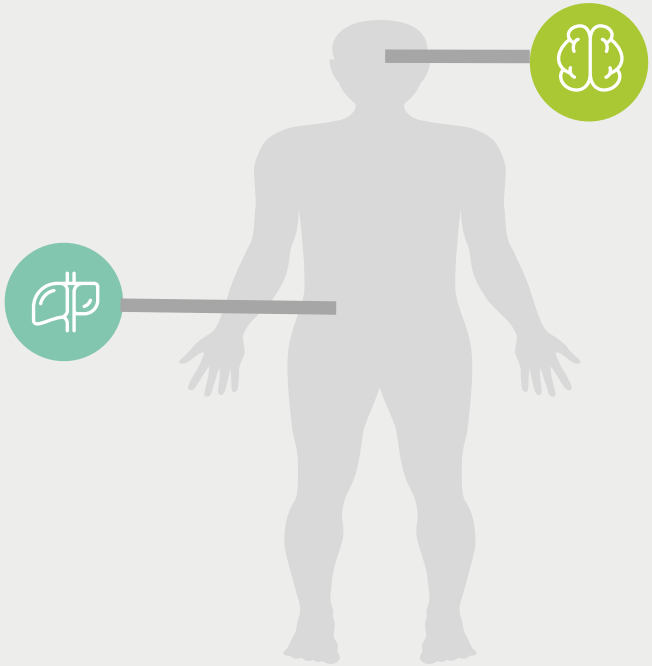
1. Mollan et al., The expanding burden of idiopathic intracranial hypertension (2019) incidence rate of 4.7/100,000 general population, n =23,182 . Targets markets are EU 27(& UK) + USA
2. Mollan SP, et al. Idiopathic intracranial hypertension: consensus guidelines on management (2018) ; Invex estimate 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

- Exenatide was approved in 2005 in the US & 2006 in the EU for the treatment of Type II diabetes
- In its Byetta® form Exenatide is administered as a twice-daily, sub-cutaneous injection or as Bydureon®, as a once weekly injection
- Exenatide is a well tolerated drug and considered a standard of care in Type II diabetic patients
- Currently marketed by AstraZeneca
- 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 also 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 elevated ICP, and therefore 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

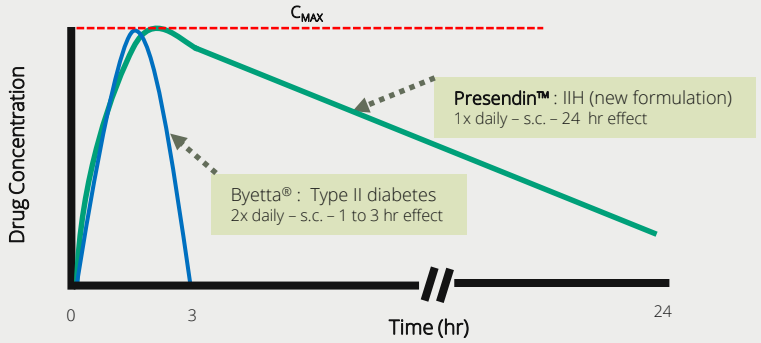
Invex is developing a novel, patented once daily s.c. formulation of Exenatide

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

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

Reformulation – Clinical and regulatory requirements

- Ex-AstraZeneca's Exenatide formulation team engaged to help work on Presendin™ repurposing
- Pharmacokinetic (PK) evidence obtained in mouse models has shown that Invex's novel 24 hour proprietary formulation of Exenatide (i.e. Presendin™) provides both immediate onset and delayed release (see chart below[1]) of Exenatide, consistent with Invex's re-formulation strategy for Exenatide
- A second animal (rat) PK & local tolerability study is required to confirm the local safety and PK of Presendin™
- A final PK study in ~20 healthy volunteers, utilising 1x daily sub cutaneous (s.c.) injection of Presendin™ and 48 hour monitoring to be performed
  - Confirm the PK profile of Presendin™ established in animal models
  - Demonstrate in man that the PK profile of Presendin™ is within the already established safety profile of Byetta®
- Patent applications for novel Presendin™ formulation are in process
- Formulation excipients are confidential, but are commonly used, safe and already known to and cleared by regulators in the USA and Europe
- Commercial manufacture of Exenatide is already well established
- Manufacture of final formulation (at commercial scale) likely to be straightforward
- Target gross margins estimated at ~90%



[1] *Illustrative, not actual data*

Benefits of orphan drug designation

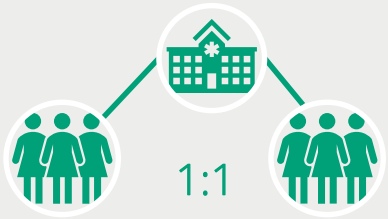
Orphan Drug Designation granted in 2017 by EMA (EU) & FDA (USA)	Designation granted for treating rare diseases: <200k patients in USA, < 5/10,000 in the EU[1]
Single pivotal Phase III registration study required for approval	Invex anticipates a Phase III study v placebo will meet regulatory requirements for regulatory clearance in major market. High patient need will facilitate rapid recruitment
7 years (USA) & 10 years (EU) marketing exclusivity[1]	Exclusivity in Idiopathic Intracranial Hypertension for Exenatide; representing 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

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)

Phase II trial design – results due early 2Q 2020

Randomised double blinded placebo controlled clinical study[1]

12 weeks



- n=16
- Female, 18-60 years old
- Confirmed Idiopathic Intracranial Hypertension diagnosis

Primary endpoint[2]

Change in intracranial pressure, real-time monitoring

Secondary endpoints

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

Visual field assessment, papilloedema measurement

Quality of life measures

Outcome Synopsis

Confirmation of GLP-1 activity in brain driving ICP reduction (confirms MoA, proof of concept). p<0.05 desirable. ICP is a **physical** measurement. Demonstration of a significant **clinical benefit** required for regulatory clearance in major markets.

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

Quality of life benefits are important for influencing reimbursement outcomes.

1. http://www.isrctn.com/ISRCTN12678718
2. Study powered only for the primary endpoint
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

Key personnel for Presendin™ development

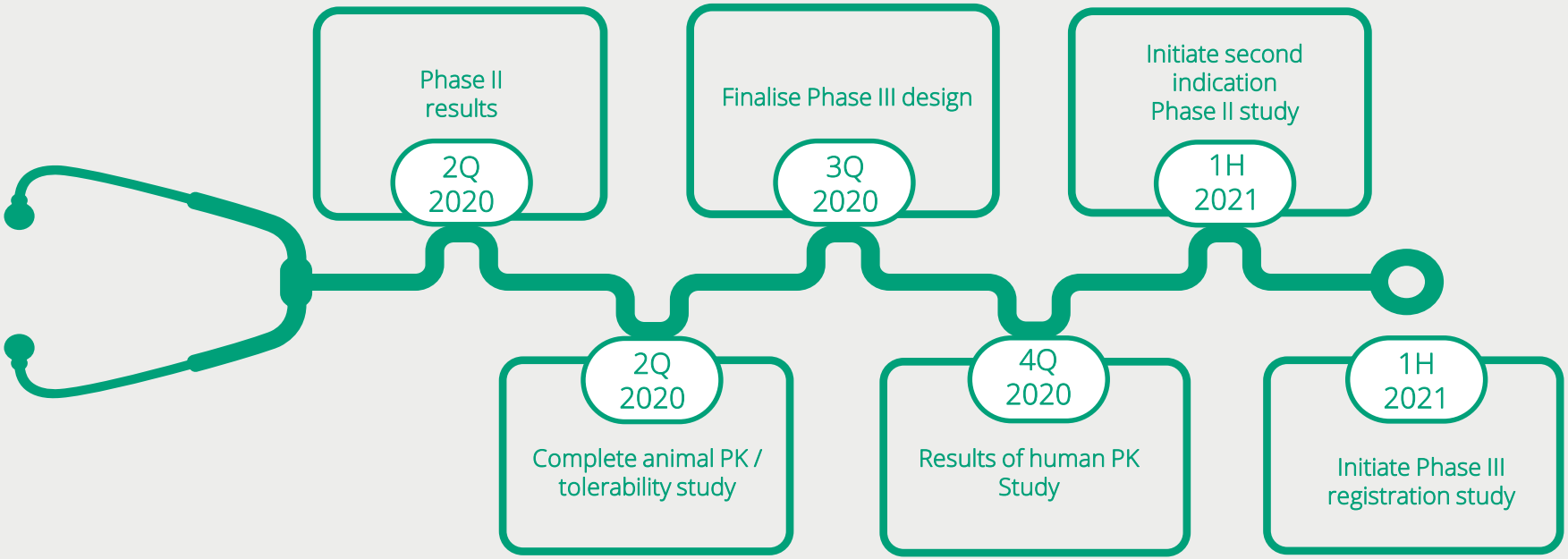
Prof Alexandra Sinclair
Executive Director and Chief Scientific Officer

- 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, proposed Lead investigator on Presendin™ Phase III study

Dr Jason Loveridge, Chairman

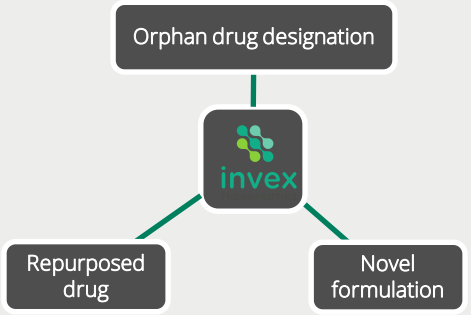
- Experienced life science investor and CEO
- Current CEO of 4SC AG (ETR:VSC), a listed German oncology drug developer
- Strong transaction background in biotech - successful sale of multiple drug assets; including most recently Genable Technologies Ltd. to Spark Therapeutics (NASDAQ: ONCE). Anaconda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

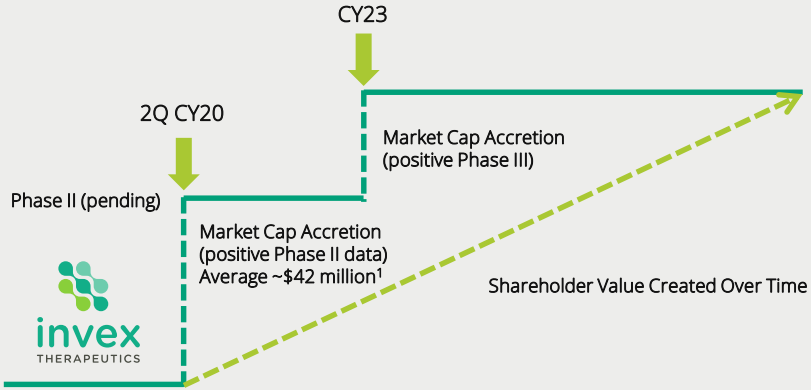
Timeline – key milestones



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)

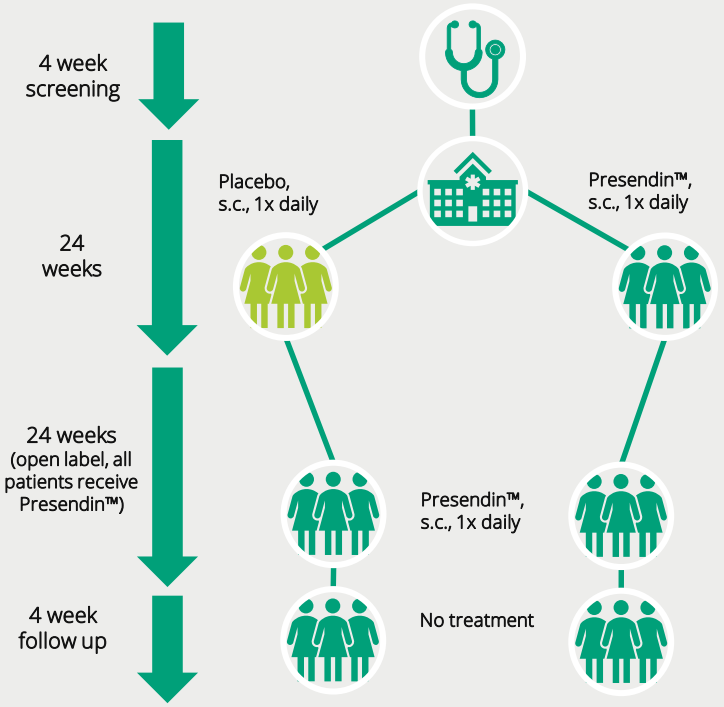




1. Invex Analysis. Companies included in analysis on a pre and post data analysis are: ASX:ANP, ASX: PAR, ASX:KZA. If the analysis included ASX:OPT Phase IIb study the average would be $128m

Indicative Phase III design[1]

Randomised double blinded placebo controlled multi-centre clinical study



Criteria

- >18 years old
- Sig. raised ICP & confirmed IIH diagnosis by Updated Modified Dandy criteria
- No previous surgery for IIH (ONSF, CSF shunts)
- 1:1 randomisation
- 200-250 patients
- Interim analysis at 6 month follow up once 50% patients treated (not assessing efficacy)

World class Medical Advisory Board established by Invex to provide input on trial design as well as regulatory and reimbursement requirements

Possible Primary endpoints

Change in Perimetric Mean Deviation (**PMD**)[2] at week 24

OR

Headache[3]: Monthly Mod-Severe headache days / severity or other

Possible Secondary endpoints (inc. one of the above)

Visual Acuity, Optic Nerve Head magnitude, VFQ-25

Adverse events, weight, Quality of Life measures, HIT-6

1. Subject to final design considerations and regulatory clearance to commence a study
2. PMD gives an overall value of the total amount of visual field loss, with normal values typically within 0 decibels dB to -2dB. The MD value becomes more negative as the overall field worsens. For the Presendin™ clinical trial, the inclusion criteria requires patients with confirmed PMD of -7.0 to -2.0 decibels (db)
3. Headache causes major morbidity in almost all patients with IIH

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 early 2Q 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

Contacts

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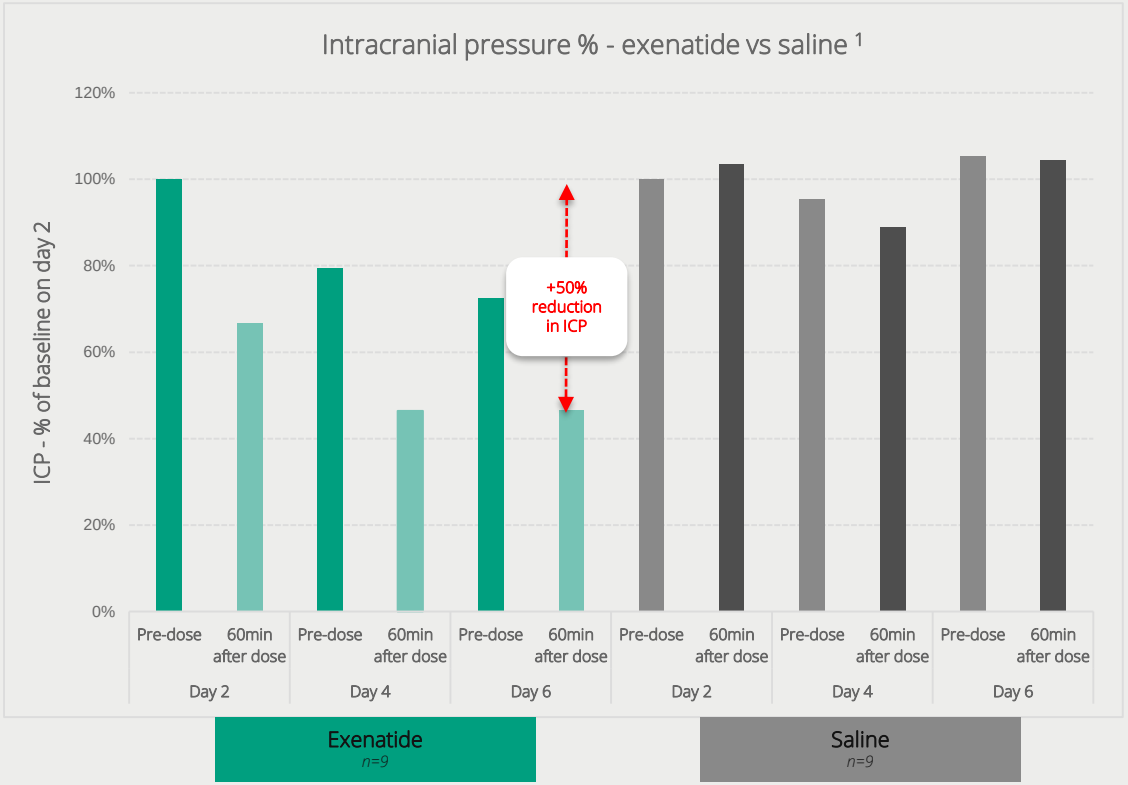
Appendix

Invex scientific data validates approach for IIH



- *Treatment was given daily for 5 days, and ICP was recorded on days 2, 4, and 6, before and after the rats received a subcutaneous (SC) injection of either saline (n = 9) or exendin-4 (20 µg/kg) (n = 9)*
- *Demonstrated +50% reduction in intracranial pressure compared to control*
- *Data published in leading journal - Botfield et al., Sci. Transl. Med. 9 (2017)*

Science Translational Medicine AAAS

1. Hannah F. Botfield et al., Sci Transl Med (2017)