Invex Therapeutics

Bell Potter Healthcare Conference

Dr Tom Duthy, Executive Director

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invex THERAPEUTICS

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Company Snapshot

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

Capital	
Shares on Issue	75.2 million
Unlisted Options	4.6 million
Ave. Quarterly Cash Burn (12 mth trailing)	$0.49 million
Cash (30 Sep-21)	$32.0 million
Market Capitalisation (8 Nov-21) [1]	$49.6 million
Enterprise Value (8 Nov-21)	$17.6 million

[1]Based on a closing price of $0.66

Major Shareholders (as at 18 October 2021)	
Directors / Management	16.8%
Tattarang	11.8%
Tisia Nominees Pty Ltd	5.3%
Anthony Grist	4.0%
JK Nominees Pty Ltd	4.0%
University of Birmingham	2.7%
Top 20 Shareholders	59.4%

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

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 EU/UK of **A$1.6 billion** per annum (**~A$1 billion** EU/UK, **~A$0.6 billion** US) 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
- Phase III clinical trial commencing Q4 CY2021, targeting registration in the EU, UK and Australia

Significant Barriers to Competition

- Orphan drug designation in US (7 years exclusivity) and Europe (10 years exclusivity)
- Issued patents for use of Exenatide in IIH in US, EU and Japan out to beyond 2035

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 Pressure Trial 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)

IIH Total addressable market (TAM)

Key Inputs[1-5]


~24,000 EU/UK patients


~16,000 US patients


60% Diagnosed


90% Drug Treatable


4.3 year disease duration


A$1,500 cost per month*

*Example only (ref. drug pricing) – final market price for Presendin™ TBD

Market Size (Annual)


~A$1.0 Billion


~A$0.6 Billion


~A$1.6 Billion


3.4% growth

Market Drivers


Increasing obesity rates


Increasing awareness


10% ↑ in diagnosis rate =
↑ A$300 million in TAM


>A$2.3 Billion market by 2030

invex THERAPEUTICS | INITIAL TARGET MARKETS – EU, UK, AU

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]

~40
~50
~355

Focussed target market of prescribers following first regulatory approvals for Presendin™ in EU, UK, AU

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; RANZCO; EU estimates based on population comparison to US

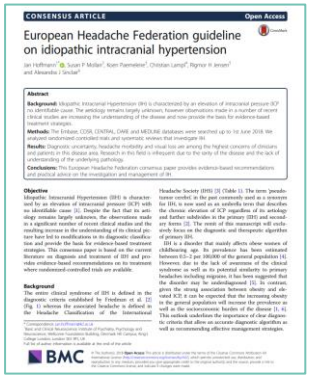
How IIH Treatment Could Change post Presendin™ Approval

General neurology

OPEN ACCESS

REVIEW

Idiopathic intracranial hypertension: consensus guidelines on management



CONSENSUS ARTICLE

Open Access

European Headache Federation guideline on idiopathic intracranial hypertension

Current

Idiopathic Intracranial Hypertension – Treatment Guidelines[1]

Non-Surgical / Device

No immediate threat to vision

Consider acetazolamide

Weight management advice

If deterioration, re-evaluate visual function (PMD,OCT)

Vision not threatened

Continue medical management

Rapid visual loss (~7%)

Surgical / Device (Severe cases)

Vision threatened

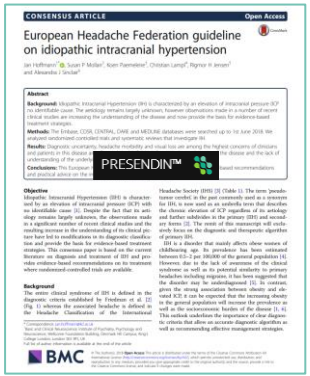
Temporising lumbar drain if surgery planned >24 hours[3]

Cerebrospinal fluid (CSF) shunting

Optic nerve sheath fenestration (ONSF)

Immediate ICP lowering effect, high relapse & complication rates

How IIH Treatment Could Change post Presendin™ Approval



Future

Idiopathic Intracranial Hypertension – Treatment Guidelines[1]

Non-Surgical / Device

No immediate threat to vision

PRESENDIN™

Weight management advice

If deterioration, re-evaluate visual function (PMD,OCT)

Vision not threatened

Continue medical management

Rapid visual loss (~7%)

Surgical / Device (Severe cases)

Vision threatened

Temporising lumbar drain if surgery planned >24 hours[3]

Cerebrospinal fluid (CSF) shunting

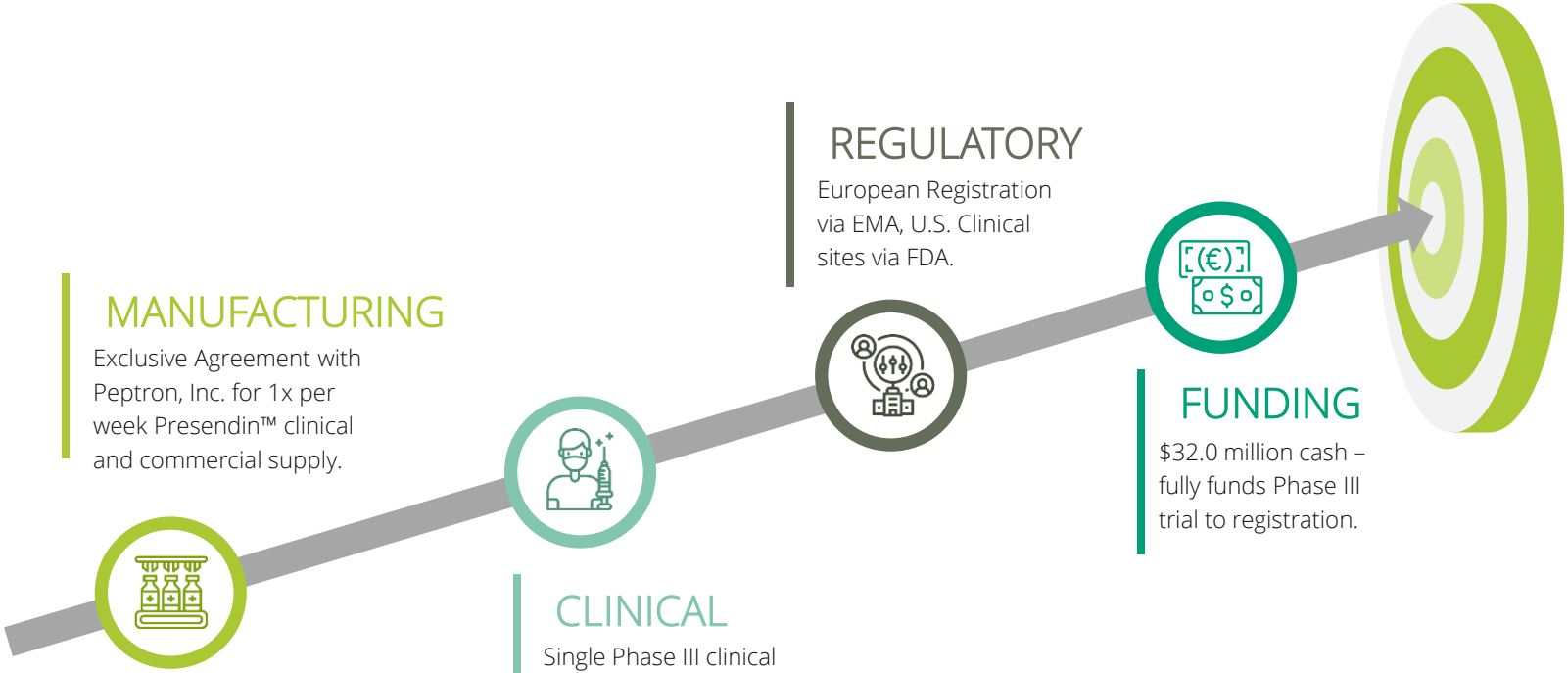
Optic nerve sheath fenestration (ONSF)

Immediate ICP lowering effect, high relapse & complication rates

Maintenance

PRESENDIN™

Critical Components for Invex's Success



MANUFACTURING

Exclusive Agreement with Peptron, Inc. for 1x per week Presendin™ clinical and commercial supply.

CLINICAL

Single Phase III clinical trial designed with expert input.

REGULATORY

European Registration via EMA, U.S. Clinical sites via FDA.

FUNDING

$32.0 million cash – fully funds Phase III trial to registration.

Manufacturing

Presendin™ Manufacturing Partnership

Exclusive Collaboration & Manufacturing Agreement with Peptron Inc. (South Korea)

- Executed 27 September 2021
- Worldwide collaboration, manufacturing and supply agreement for Presendin™ in Idiopathic Intracranial Hypertension (IIH)
- A 1x per week, sustained-release (SR) Exenatide microsphere formulation, originally developed by Peptron
- Exclusive manufacturing and supply to Invex for IIH in all major markets
- Peptron gains exclusive commercial rights for Presendin™ in South Korea for IIH
- Contract expires at the later of either the expiry of the last relevant Peptron patent or ten years following first commercial sale

Key Financial Terms

- Fixed price per dose for supply of Presendin™ and placebo for all Invex's clinical studies in IIH
- Fixed price per dose for supply of Presendin™ for commercial sale by Invex
- No royalties payable
- No upfront or milestone payments

Benefits of Partnering for Manufacturing

STRATEGIC PARTNER

Establishes a long term strategic partner for Invex

TIME & RISK REDUCTION

Significant clinical and non-clinical data package provided by Peptron

12 months of lead-in activities no longer required to be performed by Invex

Significantly de-risking Invex's development of Presendin™ in IIH

PEPTRON EXPERTISE

Invex receives the benefit of Peptron's expertise and ongoing product development activities

FINANCIAL

~$3M in Invex cost savings

Strong economics

- no royalties
- no milestone payments

MANUFACTURING

Financially robust

Commercial-scale capacity

PATIENTS

Once weekly dosing

Clinical

Clinical

IIH EVOLVE - a Phase III clinical trial evaluating the safety and efficacy of Presendin™ in IIH .
Designed based on substantial data analysis from previous IIH trials, extensive expert clinical and regulatory input, patient outreach, as well as scientific / protocol advice received from the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA)

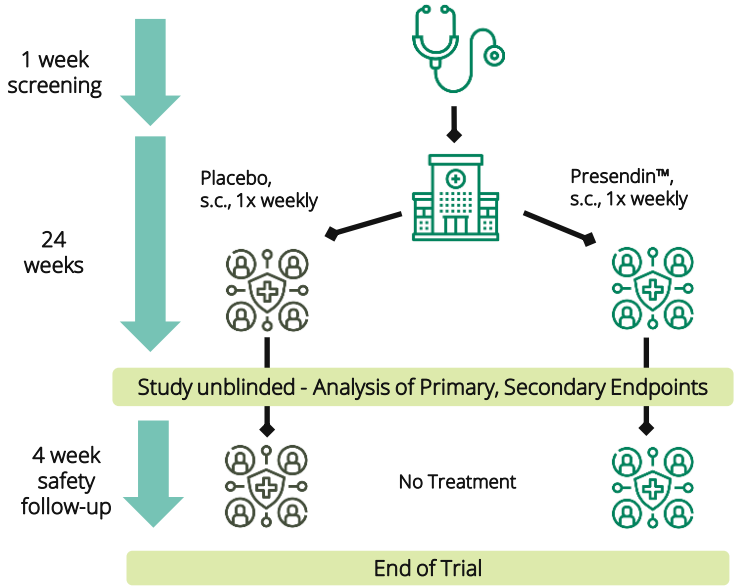
- Randomised double-blinded, placebo controlled, multi-centre clinical trial to determine efficacy and safety of Presendin™ in IIH
  - ~37 centres planned to participate across Europe, the UK, the US and Australia
    - Investigational New Drug Application (IND) to be filed in the US
  - 240 patients with IIH to be randomised 1:1 versus placebo
  - Patients self-medicate with either a once weekly PLGA formulation of Exenatide (Presendin™) or placebo
  - Appointment of Key Trial Committees and Overall International Lead Investigator to be announced shortly
  - Recruitment anticipated to take up to 24 months
- Designed to meet the regulatory requirements for market approval of Presendin™ in the EU, UK and Australia
- Based on the Company's analysis of proprietary clinical data in IIH, the endpoints in IIH EVOLVE trial have sufficient statistical power to meet the primary outcome of Intracranial Pressure (ICP) along with the secondary endpoints of Perimetric Mean Deviation (PMD), papilloedema and Monthly Headache Days (MHD)
- Fully funded from Invex's existing cash on hand

IIH EVOLVE

Randomised double-blinded, placebo controlled multi-centre clinical trial to determine safety and efficacy of Presendin™ in IIH

Primary Endpoint	Change in Intracranial Pressure (ICP) from baseline at 24 weeks
Secondary Endpoint	Change in Perimetric Mean Deviation (PMD) from baseline over 24 weeks
Secondary Endpoint	Papilloedema (optic nerve swelling) by change in OCT[1] measures over 24 weeks
Secondary Endpoint	Change in Monthly Headache Days (MHD) from baseline over 24 weeks
Safety	Adverse events rate, anti-drug antibodies, PK and general lab measures
Quality of Life	Patient reported outcomes (SF-36, ED-5D-5L, VFQ-25), monthly patient diary

Phase III Schematic



1. OCT – Optical Coherence Tomography is an imaging tool accepted by professional bodies for monitoring papilloedema in IIH by measuring different aspects of the optic nerve. The optic nerve head size and retinal nerve fibre layer (RNFL) are measurements that both reflect swelling of the optic nerve and hence the extent of papilledema. Optic nerve head measures on OCT correlate with visual field sensitivity loss.
2. s.c. – sub cutaneous

IIH EVOLVE Endpoint Assessment

Why ICP is Important

- A reduction in ICP is a requirement for approval by EMA
- Pure physical measurement
- Direct measurement of the mechanism of action of Presendin™
- Key diagnostic criteria of IIH

Why MHD is important

- >90% of IIH patients suffer from chronic headaches
- MHDs accepted clinically relevant endpoint by all regulators
- Headache has a detrimental effect on patient quality of life
- Headache management is an unmet need in IIH

Why PMD is Important

- Clinically meaningful measure used in prior IIH interventional trials as a primary endpoint
- Accepted clinically relevant endpoint by all regulators
  - PMD MCIC in IIH established by the Neuro-Ophthalmology Research Disease Investigator Consortium and the IIH Treatment Trial (IIHTT)
- Vision loss is the primary concern of all IIH clinicians

Why Papilloedema is important

- Measuring papilloedema is a vital measure clinically
- Key diagnostic criteria of IIH
- Change in papilloedema has been used by all randomised control trials in IIH to date to determine clinical improvement
- Measurement by OCT accepted in clinical practice and routinely used to monitor IIH patients all over the world – fast, objective

Regulatory

Regulatory

The Invex Phase III IIH EVOLVE clinical trial for Presendin™ is intended to support a European Medicines Agency (EMA), Medicines & Healthcare products Regulatory Agency (MHRA) and Therapeutic Goods Administration (TGA) approval for the treatment of IIH

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Medicines & Healthcare products Regulatory Agency

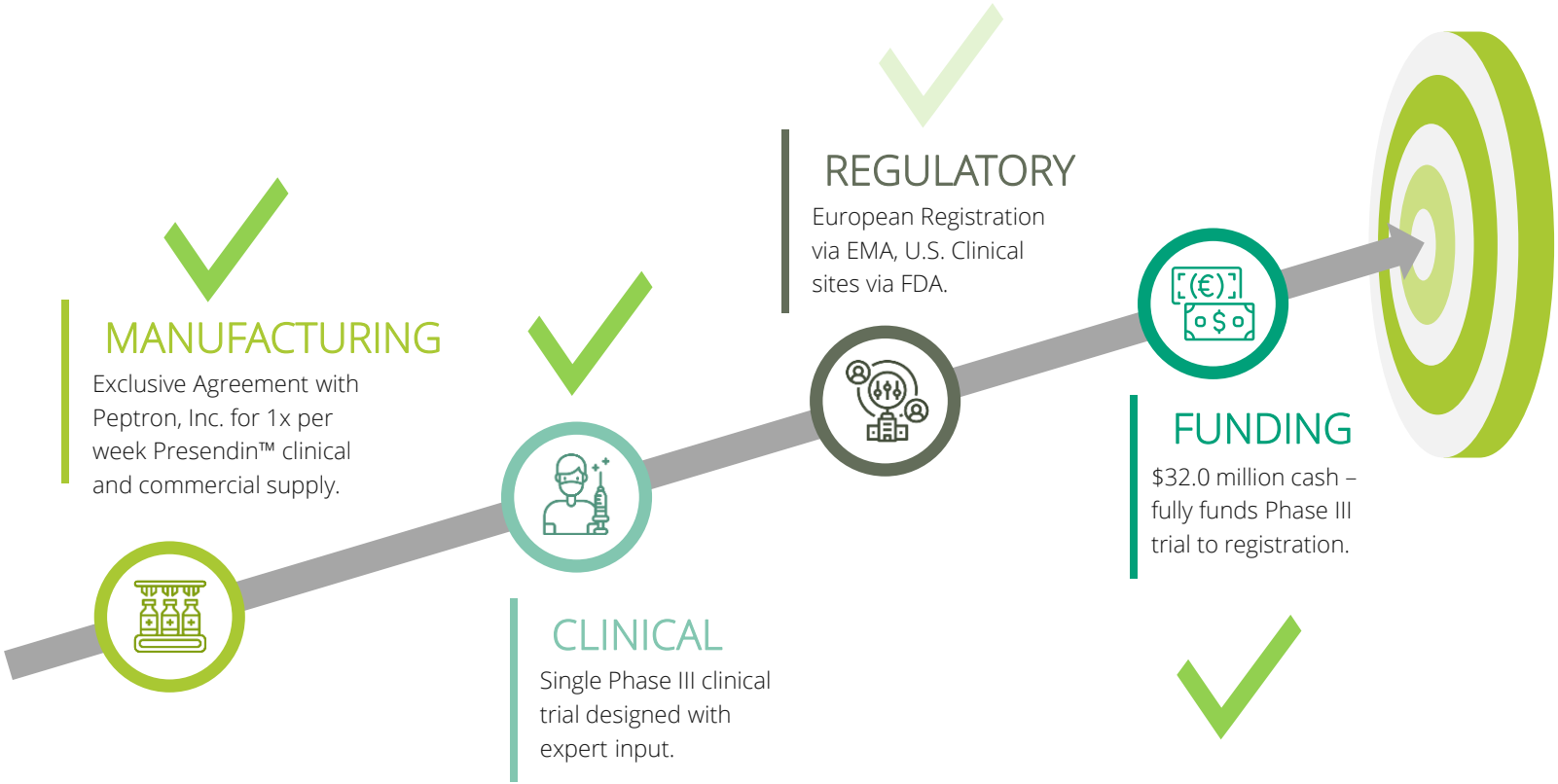
Australian Government
Department of Health
Therapeutic Goods Administration

- Strategy of seeking EU, UK and Australian market approvals ahead of the US based on a detailed risked based assessment following scientific advice and protocol assistance from both EMA and FDA
  - Informed by a detailed review of both published and proprietary IIH clinical data
- Selected approach is the lowest risk pathway
  - Global Phase III trial design difficult to achieve due to challenges in getting equivalence between the different regulatory agencies on endpoints and the definition of minimal clinical important change (MCIC)

- Outcomes from IIH EVOLVE will facilitate future discussions with the US FDA regarding registration of Presendin™ in the United States

FDA

Critical Pathways for Success



Funding

Funding

- $26 million capital raise completed in May 2020
- Cash as at 30 September 2021: $32 million
- Corporate overheads remain low: 9 months YTD total cash outflows of $1.6 million with average quarterly cash burn of $0.5 million
- Phase III trial fully costed and to be funded from existing cash reserves
- Cash runway sufficient to complete Phase III & market approvals (subject to clinical success)
- Cash burn to increase in coming periods as Phase III commences and contracts executed
- No additional capital required to achieve these milestones

Summary & Outlook

- First clinical batches of Presendin™ from Peptron for IIH EVOLVE Phase III trial anticipated in Q4 CY2021
- Invex anticipates announcing the overall Lead International Investigator for the study and executing agreements with key service providers before the end of CY2021
- Single Phase III trial designed to support Presendin™ market approvals in the EU, UK and Australia
- First CTA for IIH EVOLVE to be submitted in Q4 CY2021
- Data generated from trial and inclusion of US sites will inform continued dialogue with FDA for future regulatory filings
- Potential for rapid incorporation of Presendin™ into IIH treatment guidelines
- IIH EVOLVE includes an economic evaluation to facilitate the health technology assessment (HTA) process – advantages with an orphan designation
- IIH EVOLVE fully funded from existing cash on hand ($32 million as at 30 September 2021)
- Potentially first-ever regulatory approved drug for IIH in any jurisdiction world-wide
- A $1 billion p.a. opportunity in the UK/EU and growing in-line with the obesity epidemic

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Thank you

Q&A

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