



Invex Therapeutics

Phase II Clinical Results & Capital Raise
Investor Presentation

May 2020

ASX Code: IXC

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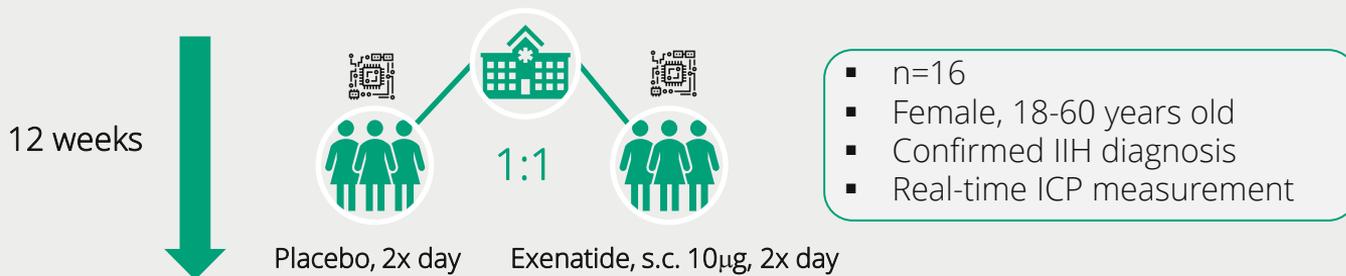
Invex Therapeutics - Executive Summary

- Clinical stage drug development company targeting the orphan disease Idiopathic Intracranial Hypertension (IIH)
 - Repurposed Exenatide (Presendin™) formulation
 - Large, growing market for IIH, Total Addressable Market of up to **~A\$1.6 billion** annually in the USA and Europe
 - No approved (regulatory cleared) or efficacious treatments currently available for IIH patients
 - **Orphan Drug Designation in the USA and EU** provides expedited, cost-effective drug development pathway, approval/registration as well as commercial exclusivity for up to 10 years
 - Invex expects top-line Phase III data in 2H 2023 and regulatory approval for Presendin™ in 2024
- Phase II data **strongly** supports moving Presendin™ into Phase III clinical development in **1H 2021**
 - **Met all Primary Endpoints** for a >10% reduction of Intracranial Pressure¹ (ICP) at 2.5 hours ($p < 0.048$), 24 hours ($p < 0.03$) and 12 weeks ($p < 0.058$)
 - **Statistically significant improvement in Key Clinical Endpoints²**
 - 7.7 day reduction in Monthly Headache Days
 - Visual acuity improvements equivalent to 1 full line on chart
- Transaction for entire Company preferred as value creation event for shareholders, versus licensing or partnering

Clear Statistical and clinical evidence of efficacy in primary and secondary endpoints demonstrates a strong and sustained drug effect in the IIH population

Phase II Trial Design

Randomised double blinded placebo controlled clinical study¹



Primary endpoints



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

80% statistically powered to see a 10% reduction in ICP

Exploratory endpoints – headache & vision



Headache frequency, severity, duration, analgesic use, HIT-6



Visual field assessment, visual acuity, OCT measurement

Not powered for significance



Phase II Trial - Design Considerations

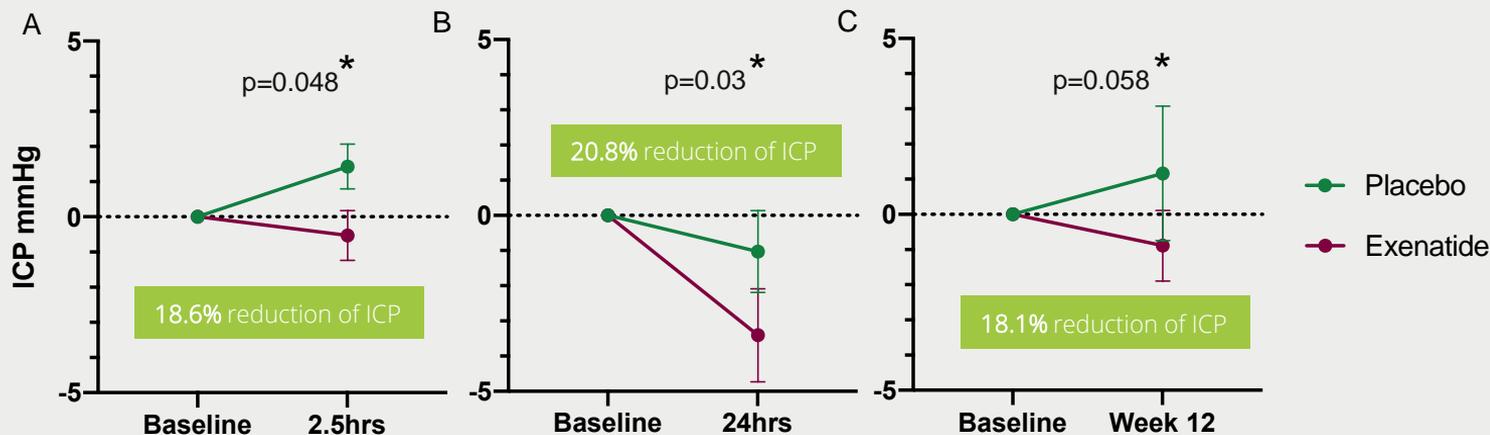
- Measuring ICP by lumbar puncture is inaccurate and highly variable
- **Reliable & stable baseline data established through substantial lead-in data collection**
 - Participants completed a daily headache diary in the month before visits 1 and 2
- IIH patients enrolled into the study underwent an invasive neurosurgery procedure to implant a **telemetric intracranial pressure monitor** into the right frontal lobe
 - Significantly increases the reliability (accuracy and number) of ICP measurement
 - Continuous ICP measurements @5Hz over 30 mins at each time point
 - ICP value per patient is the mean of ~9,000 individual pressure measurements
 - Each patient provides >36,000 individual data points to investigators over the study period
 - **Highly accurate, low variation = fewer patients required to achieve statistical power**
 - Approach limits the number of participants as requires invasive surgery not likely to result in patient benefit – i.e. ethical considerations
- ICP reduction in IIH patients of **16.5%** has been shown in a clinical study of weight loss in IIH patients to be clinically meaningful¹



Primary Endpoints – Exenatide Reduces ICP in IIH Patients



- The primary endpoints of the study assessed differences in intracranial pressure (ICP) between the Exenatide treatment arm and placebo at (A) 2.5 hours, (B) 24 hours and at (C) 12 weeks
- Exenatide reduced ICP at all three time points in a statistically significant manner (* $p < 0.10$, hierarchical regression¹)
- Confirmation Exenatide mechanism of action & clinical proof of concept



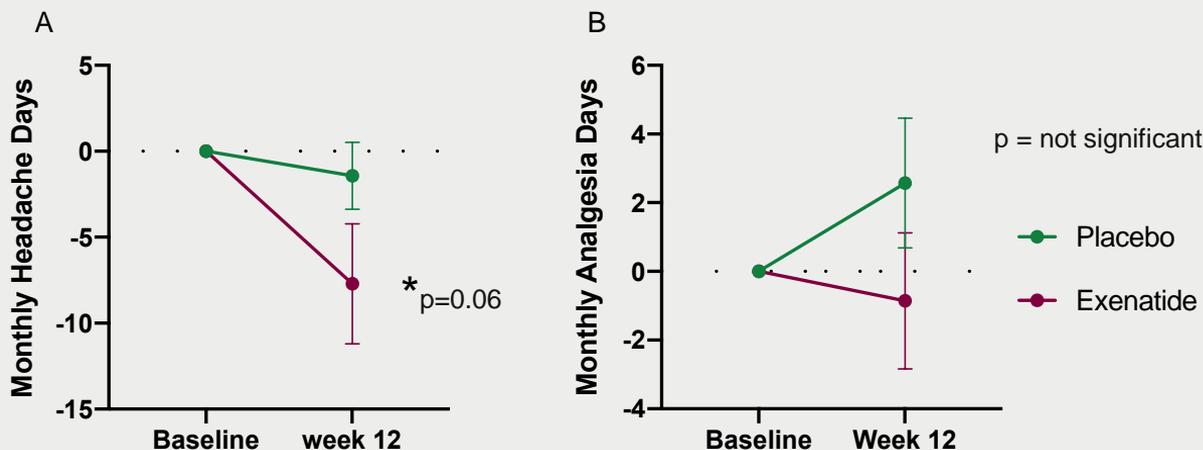
- Exenatide achieved a reduction in ICP of between 18.1%-20.8% in IIH patients versus placebo over the study duration
- The observed reduction in ICP was double the pre-study hurdle of 10%
- Significantly exceeds what is considered clinically meaningful (16.5%) in IIH



Secondary Endpoint – Exenatide Reduces Headache Frequency



- Headache frequency data shown in the figure below (A) highlights a statistically significant beneficial reduction in Monthly Headache Days in Exenatide treated patients
- Analgesic use (B) also shows a reduction in the use of pain medication by IHH patients taking Exenatide, though not statistically significant



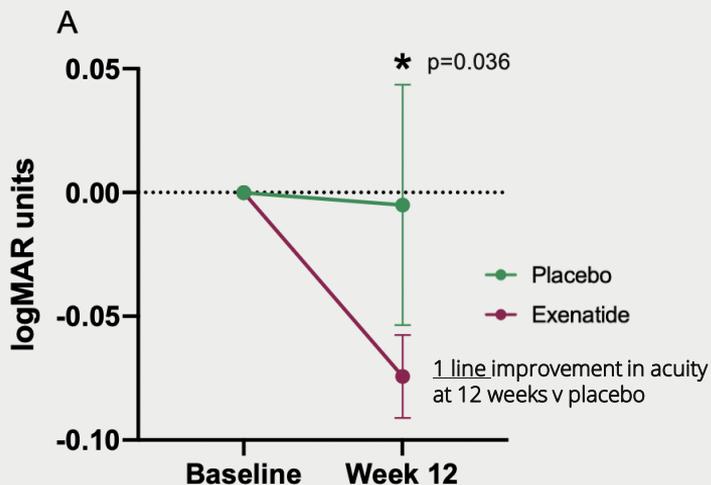
- A reduction of 7.7 days would be clinically meaningful in migraine
- IHH headaches share many features with migraine where the accepted minimal clinically important reduction is 1.5-2 headache days per month¹
- A reduction in Monthly Headache Days is a well recognised and validated endpoint by regulators in headache studies
 - appropriate primary endpoint in a Phase III registration study



Secondary Endpoint – Exenatide Improves Visual Acuity



- Visual acuity was assessed using a Logarithm of the Minimum Angle of Resolution Chart – LogMAR assessment
- Despite not being powered, the improvement in VA in the Exenatide arm was large enough to show a statistically significant and clinically meaningful improvement in visual acuity, an important clinical consideration for IIH patients¹



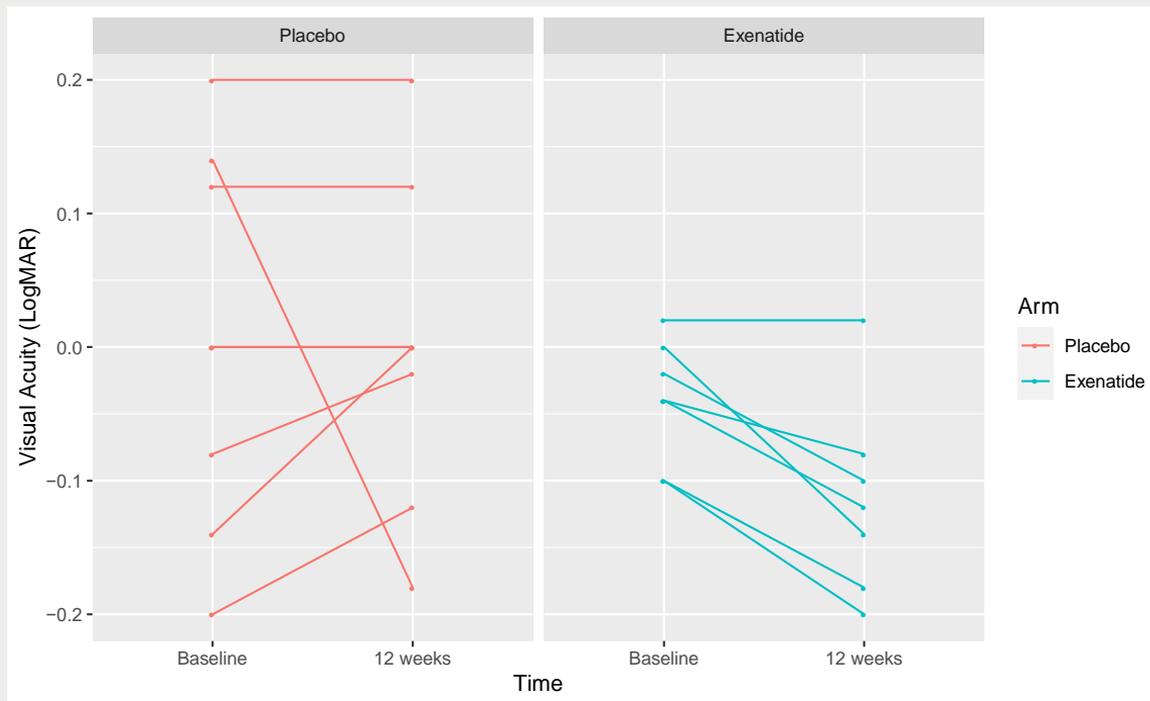
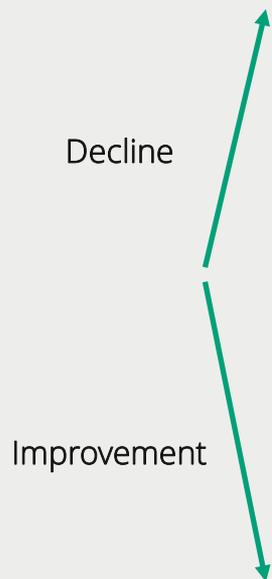
- No determination of a minimal clinically important improvement in LogMAR in IIH
- An improvement equivalent to a whole line (-0.1) on the acuity chart is a significant change for an IIH patient and would be considered a “clinically relevant recovery” by KOLs
- For patients, such an improvement could mean the difference between being able to drive or not (for example)



Exenatide Improved Visual Acuity in Majority of IIH Patients

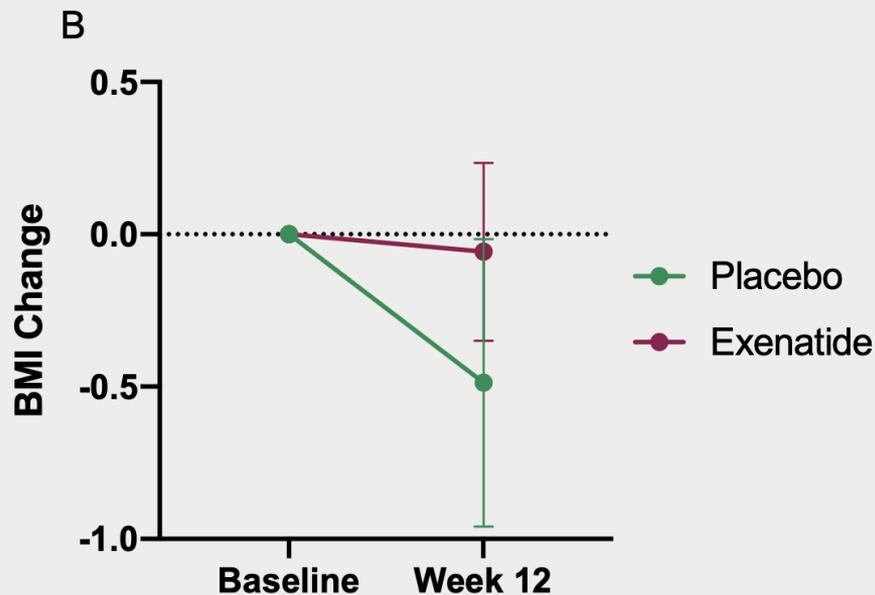


- LogMAR improved in all but one of the Exenatide treated patients, and in only a single patient on placebo, further supporting the breadth and certainty of this observed improvement in vision with Exenatide



Exenatide Benefit Not Due to Weight Loss

- IIH patients on Exenatide did not lose weight during the course of the study
- Patients on Placebo lost a small amount of weight equivalent to 0.5 BMI units
- The benefit of Exenatide use could not be explained by these patients losing weight



Safety & Adverse Events



- No serious adverse events (AE) 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®)¹

Event	Number & Arm*	Description
Serious Adverse Events (SAE)	1, P	Thyrotoxicosis (unrelated, participant continued in study)
Adverse Events (AE)	3, E	Nausea – required treatment
	4, E	Nausea - mild
	1, E 2, P	Minor wound infection (unrelated, participant continued in study)
	1, P	Post-operative swelling

* P = Placebo group, E = Exenatide Group



Patient Baseline Characteristics

	Exenatide		Placebo		Differences	
	Median (range)	Mean (SD)	Median (range)	Mean (SD)	Wilcoxon rank sum p	chi-squared p
Number	7		8			
Age	25 (18, 57)	28 (13)	26 (23, 38)	28 (6)	0.560	
Gender (% female)	100		100			
BMI (kg/m ²)	35.5 (31.3, 54.4)	37.6 (7.9)	39.9 (29.4, 44.2)	38.6 (4.7)	0.281	
ICP (mmHg)	21.9 (17.4, 28.5)	22.3 (3.6)	24.2 (19.3, 30.2)	24.6 (4.1)	0.281	
Monthly Headache Days	21 (13, 28)	22 (5)	12 (0, 21)	10 (9)	0.015*	
Monthly analgesic frequency	7 (3, 16)	7.9 (4.5)	3 (0, 8)	3.4 (2.8)	0.054	
Headache severity (VRS 0-10)						
Category 1						0.157
Mild, n (%)	0 (0%)		3 (38%)			
Moderate	6 (86%)		5 (62%)			
Severe	1 (14%)		0 (0%)			
LogMar visual acuity	0.0 (-0.1, 0.0)	0.0 (0.1)	0.0 (-0.2, 0.2)	0.0 (0.1)	0.522	
Perimetric mean deviation worst eye dB (HVF 24-2 Sita standard)	-0.4 (-2.5, 0.3)	-0.6 (1.0)	-2.5 (-5.1, 0.5)	-2.7 (1.9)	0.072	
Optical Coherence Tomography RNFL worst eye (um)	128 (91, 236)	153 (59)	161 (85, 337)	183 (100)	0.852	
Headache disability (HIT-6)						0.218
Little-to-no impact, n (%)	0 (0%)		2 (25%)			
Moderate	0 (0%)		1 (13%)			
Severe	5 (71%)		2 (25%)			
Substantial	2 (29%)		3 (38%)			
Quality of Life (SF-36)						
PCS summary	53.5 (10.2, 71.9)	50 (20)	59.1 (26.7, 80.2)	58 (17)	0.418	
MCS summary	46.1 (7.5, 67.0)	43 (23)	49.7 (26.0, 75.5)	47 (17)	0.852	
Creatinine (µmol/L)	69 (51, 77)	68 (9)	69 (48, 72,)	66 (8)	0.601	
ALT (IU/L)	22 (15, 45)	27 (14)	16 (12, 46)	21 (12)	0.363	
HDL (mmol/L)	1.15 (0.73, 1.82)	1.26 (0.36)	1.49 (1.18, 1.82)	1.48 (0.24)	0.117	
Cholesterol (mmol/L)	4.5 (3.7, 5.9)	4.53 (0.79)	4.2 (3.7, 6.2)	4.76 (1.0)	0.727	
Triglycerides (mmol/L)	1.0 (0.6, 2.2)	1.26 (0.65)	1.2 (0.9, 1.4)	1.14 (0.18)	0.907	
HbA1c (mmol/mol)	37 (32, 38)	35.4 (2.7)	37 (29, 38)	35.0 (3.9)	1.000	

Despite the relatively small number of participants, the study was well balanced at baseline

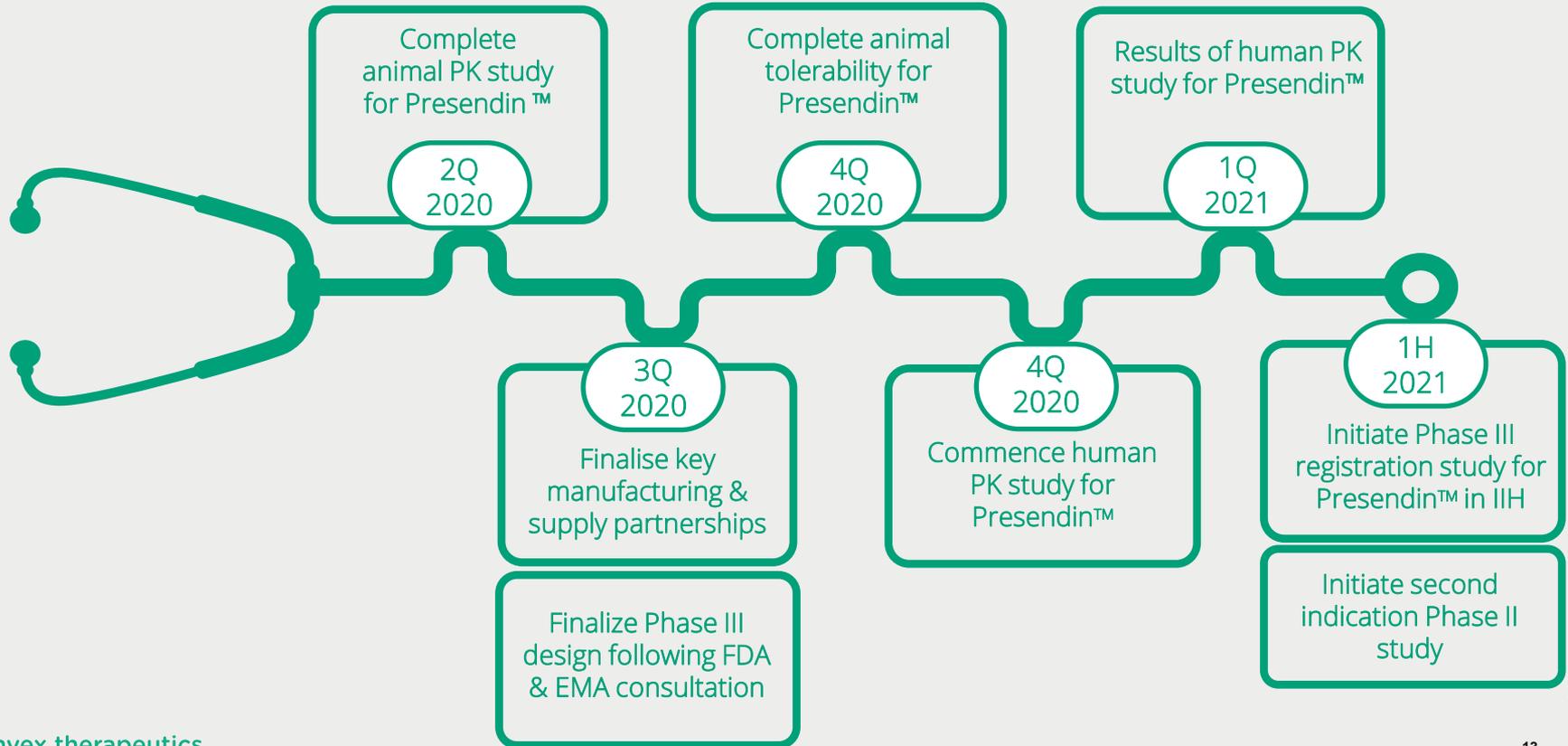
No significant difference in BMI or ICP between the arms at baseline

The only significant difference between the groups (at baseline) being in Monthly Headache Days (MHD), where the difference was skewed by 2 patients in the Placebo Group with very low MHD at baseline

No significant difference in visual acuity between the arms at baseline



Timeline – Key Milestones to Market Entry



Summary - Exenatide in IIH Clinical Study

- Phase II data **strongly** supports moving Presendin™ into Phase III clinical development in **1H 2021**
 - Met all Primary Endpoints** for a >10% reduction of Intracranial Pressure¹ (ICP) at 2.5 hours ($p<0.048$), 24 hours ($p<0.03$) and 12 weeks ($p<0.058$)
 - Statistically significant improvement in Key Clinical Endpoints²**
 - 7.7 day reduction in Monthly Headache Days
 - Visual acuity improvements equivalent to 1 full line on chart

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

Capital Raising

- \$26.2 million Share Placement to Sophisticated and Professional Investors at \$1.30 per share
- The offer price represents:
 - 13% discount to last closing price of \$1.495
 - 4% discount to the 15 day VWAP of \$1.35
- Bell Potter Securities Limited appointed Sole Lead Manager
- Forrest Capital & CPS Securities appointed Co-Managers

Pro-Forma Capital Structure - \$26.2 million placement	
Current Shares on Issue	55 million
Placement shares issued (Tranche 1)	12.5 million
Placement shares issued (Tranche 2)	7.65 million
Pro-forma Shares on Issue	75.15 million
Pro-forma Cash ¹	\$36.6 million
Pro-forma Enterprise Value (EV) ²	\$75.7 million

1. Cash as at 31 March 2020 - \$10.4 million; 2. Assumes share price of \$1.495



Use of Funds

- Seeking to raise \$26.2 million in a two tranche share placement

\$26.2 million	
Completion of Presendin™ pre-Phase III development	\$1.3 million
Presendin™ Phase III registration study in IIH	\$16.0 million
Drug manufacture and supply for Phase III & commercialisation	\$3.5 million
Clinical development second indication	\$3.9 million
Offer Costs / Other	\$1.5 million
TOTAL	\$26.2 million



Timetable*

Event	Date
Trading Halt	Monday 18 May 2020
ASX Announcement – Clinical Trial results	Wednesday 20 May 2020
Placement Bookbuild Commences	Wednesday 20 May 2020
Allocations and Signed Acceptances	Thursday 21 May 2020
ASX Announcement – Placement, Investor Presentation, Trading Halt Lifted	Friday 22 May 2020
Settlement of Tranche 1 Placement Shares	Wednesday 27 May 2020
Allotment of Tranche 1 Placement Shares on ASX	Thursday 28 May 2020
Extraordinary General Meeting (EGM) to Approve Tranche 2 Placement	On or around 29 June 2020
Settlement of Tranche 2 Placement Shares	On or around 2 July 2020
Allotment of Tranche 2 Placement Shares on ASX	On or around 3 July 2020



Reformulation & Regulatory Update

- ✓ Patent applications on the new formulation of Exenatide (Presendin™) filed in March 2020
- ✓ Pharmacokinetic (PK) evidence obtained in mouse models has shown that Invex's novel proprietary formulation (Presendin™) provides the targeted PK – i.e. immediate onset with a Cmax below that of Byetta combined with delayed release over 24 hours
 - Confirmatory second animal (rat) pharmacokinetic (PK) study results of Exenatide re-formulations expected by end 2Q CY2020
 - Complete animal (rat) tolerability study for Presendin™ in 4Q 2020
 - PK study in up to 30 healthy (but overweight) volunteers, utilising 1x daily sub cutaneous (s.c.) injection of Presendin™ and 48 hour monitoring under negotiation with qualified CROs - study commencing in 4Q CY2020 (data reported 1Q 2021)
 - Contract manufacturers for supply of Exenatide and formulation of Presendin™ for the human PK study, Phase III trial and commercial supply expected to be in place during 3Q CY2020
 - Phase III design submitted to US FDA and EMA for feedback on overall design, endpoints, statistical plan, etc
 - Based on Phase II data, Invex has the option to use either Monthly Headache Days or a Visual Acuity
 - Final design lock 3Q 2020
 - Company on track to commence the study in the 1H CY2021



Likely Second Orphan Indication: IIH-WOP

- Idiopathic Intracranial Hypertension (IIH) – Without Papilloedema (WOP)
- Rare sub-population of IIH patients, representing **5.7%** of IIH patients¹
- **1,225** patients in the EU/USA, representing a TAM of **A\$95 million** per annum
- Invex to initiate Phase II clinical trial in 1H 2021 using Presendin™
- Optimum development pathway under investigation
- This second orphan indication offers additional value creation from a portfolio of clinical assets for prospective third-party acquirers



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
- Strong Phase II clinical data
- Capital raise to fully fund Phase III clinical trial for Presendin™ through to top-line results in **2H 2023**
- Plan to initiate Phase II clinical trial in IIH-WOP with Presendin™ in **1H 2021**
- Transaction for entire Company preferred as value creation event for shareholders, versus licensing or partnering



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Company Overview



Company snapshot



Company	
Repurposed Proven Drug	Presendin™ (Exenatide)
Clinical Stage	Phase II
Orphan Disease Focus	IIH ^A + 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 (Pre Placement)	
Shares on Issue	55.0 million
Unlisted Options	3.51 million
Cash (31 Mar-20)	\$10.4 million
Market Cap (as at 15 May-20)	\$82.2 million

Major Shareholders



Directors / Management	20%
Minderoo Group	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.



Current treatments for IIH are limited

Idiopathic Intracranial Hypertension – Treatment Guidelines¹

Non-Surgical / Device

Surgical / Device (Severe cases)

No immediate threat to vision

Vision threatened

Consider acetazolamide

Weight management advice

Temporising lumbar drain if surgery planned >24 hours³

Consider diagnostic lumbar puncture if significant deterioration of visual function

Cerebrospinal fluid (CSF) shunting

Optic nerve sheath fenestration (ONSF)

If not pathologically high re-evaluate

If pathologically high

Immediate ICP lowering effect, high relapse rates

Acetazolamide is used 'off label' (not regulatory cleared) for IIH, has limited efficacy & poor tolerability (~50% discontinue due to side effects²)

High failure rate - most regain weight and consequently their symptoms and signs of IIH relapse²

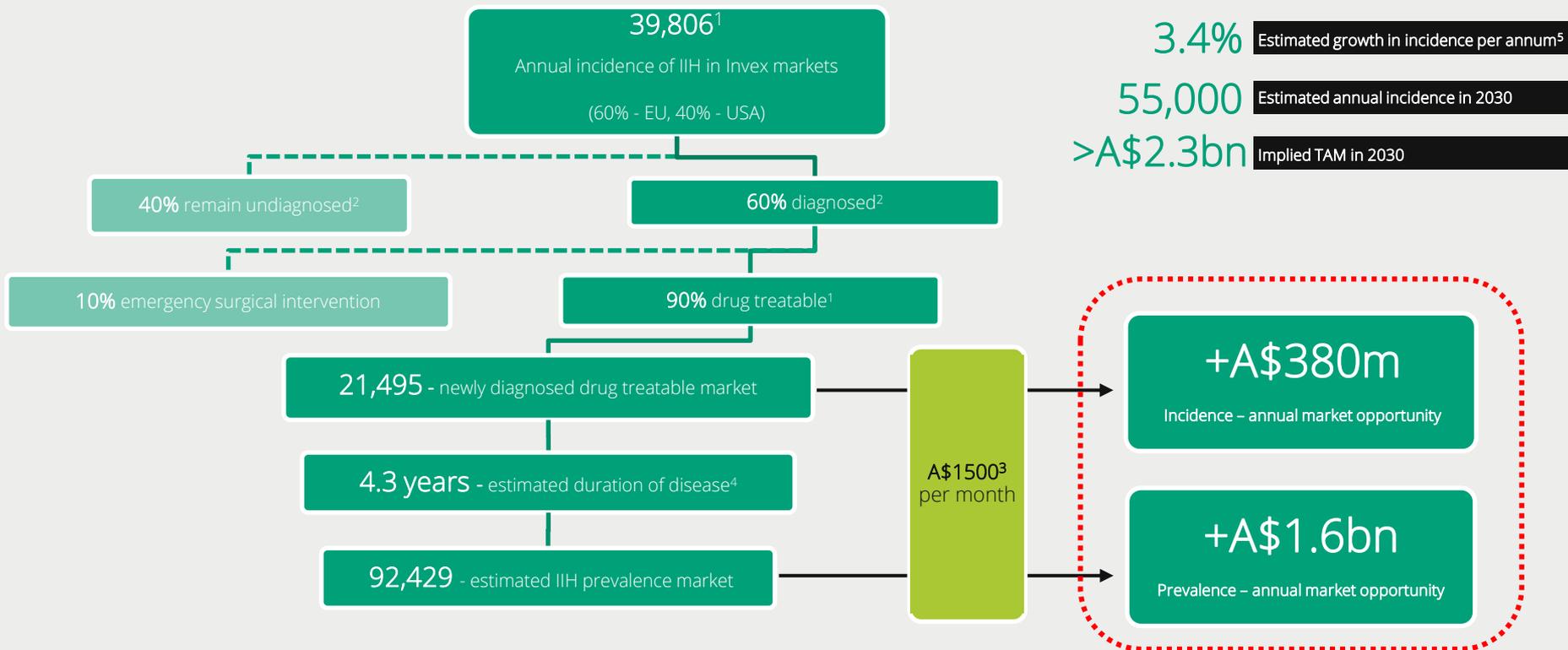
CSF failure rate is high (>50%) and ~30% require multiple revisions. Regarded as a temporary procedure to prevent blindness in those with aggressive disease²

ONSF is a surgical procedure used by ophthalmologists to reduce pressure on the optic nerve. Highly variable outcomes & high risk of post-operative complications⁴

Presendin™ target markets



Total addressable market (TAM) – expected to grow



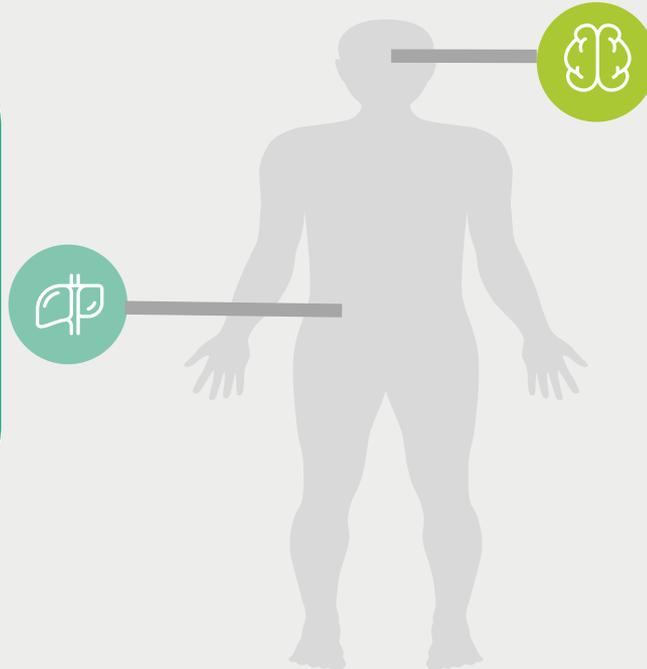
1. Mollan et al., The expanding burden of idiopathic intracranial hypertension (2019) Incidence rate of 4.7/100,000 general population, n =23,182. Targets markets are EU 27(& UK) + USA
 2. Mollan SP, et al. Idiopathic intracranial hypertension: consensus guidelines on management (2018); Invetx estimate re % presenting headache severity
 3 Simoens et al., "what price do we pay for repurposing drugs for rare diseases?" (2016) – avge 66x & Invetx initial pricing analysis => pricing subject to change
 4. D. Frieser 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



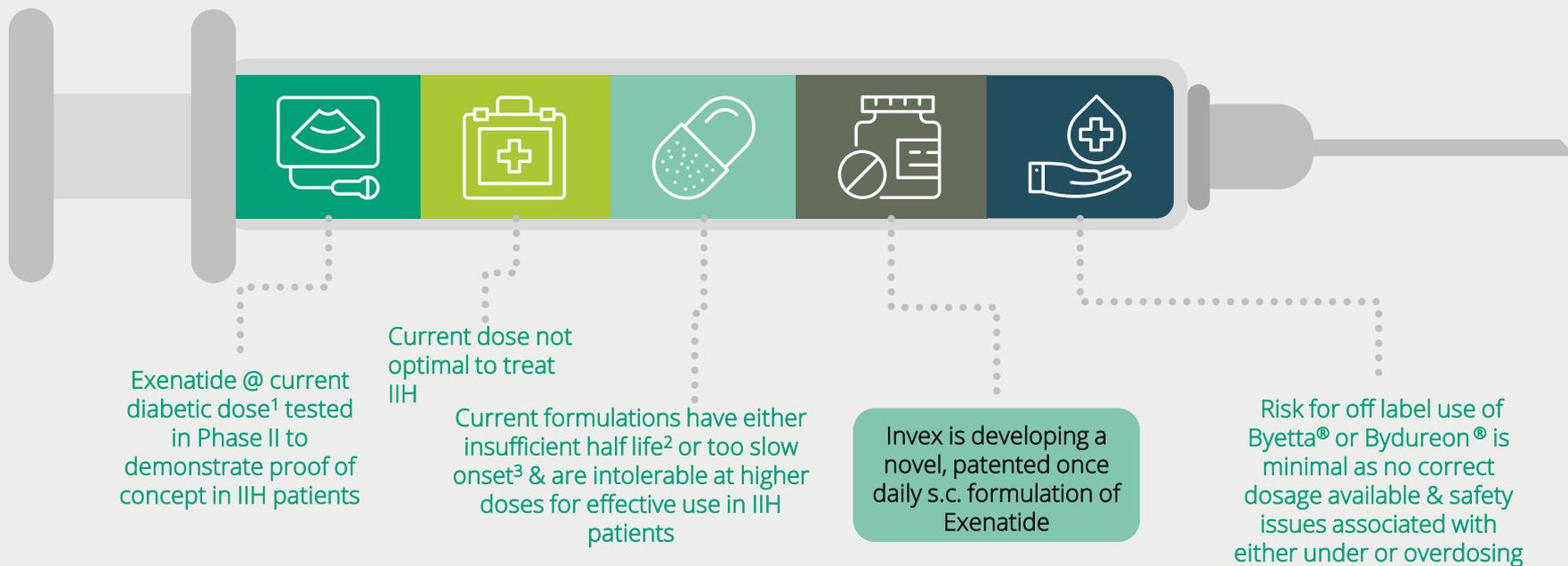
Exenatide - IIH

- 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

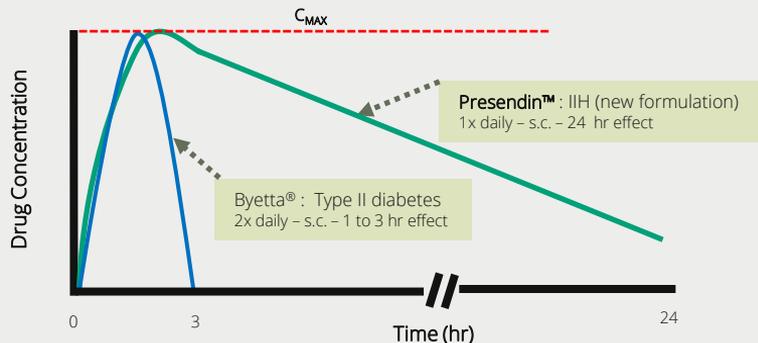


Exenatide reformulation strategy



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 below¹) 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%



How the Phase II Achieves Sufficient Statistical Power to Observe an Effect on ICP

Surgically implanted
Telemetric Intracranial
Pressure Monitor

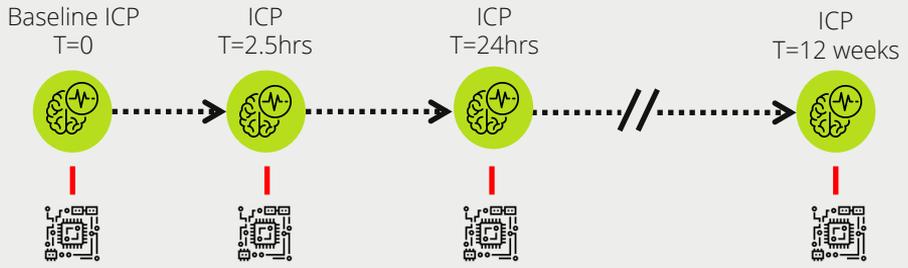


IIH Patient

ICP VARIABILITY CONTROLLED

- ICP varies throughout the day in tandem with posture and other variables
- ICP has not been studied in an IIH population before: utilisation of continuous ICP monitoring allows this for the **first time**
- Normal variation in ICP in study population analysed by monitoring ICP over a continuous period whilst patients undertook normal daily activities
- Additional short monitoring programme following changes in posture over 24 hours both before the baseline of the study and during the study period

- IIH patients enrolled with $>25\text{cm H}_2\text{O}$ ($>19\text{mm Hg}$) ICP [as per IIH diagnostic criteria]
- Normal range: $7.5\text{--}20\text{cm H}_2\text{O}$ ($5\text{--}15\text{ mm Hg}$) in supine position
- Statistically significant reduction in ICP will be achieved with $>10\%$ change from baseline ICP



- Continuous ICP measurements @5Hz over 30 mins at each time point
- ICP value per patient is the mean of **9,000** individual pressure measurements
- Each patient provides **>36,000** individual data points to investigators over study period
- Highly accurate, low variation = **fewer patients required to achieve statistical power**



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 EU¹



Single pivotal Phase III registration study required for approval

High patient need will facilitate rapid recruitment



7 years (USA) & 10 years (EU) marketing exclusivity¹

Exclusivity in IHH 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) disease² – Invex initial pricing estimate conservatively presented

Unmet need often drives closer alignment between KOLs and patient groups; reducing payer influence³



Tax incentives, filing fee waivers & greater regulator access¹

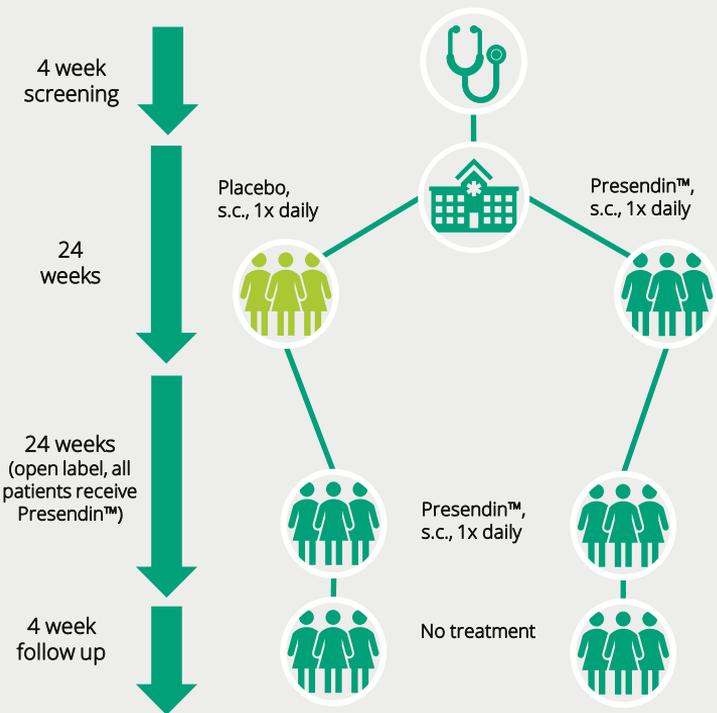
Tax credits of up to 50% of clinical development costs

Waive the ~US \$2.9 million Prescription Drug User Fee Act (PDUFA) application fee paid prior to regulatory review



Indicative Phase III design¹

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
- ~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

Probable Primary endpoints

90% statistical power to detect an effect



Headache²: Monthly headache days

OR

Probable Secondary endpoints

80% statistical power to detect an effect



Change in Perimetric Mean Deviation (PMD)³ at week 24



Visual Acuity, Optic Nerve Head magnitude, VFQ-25



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

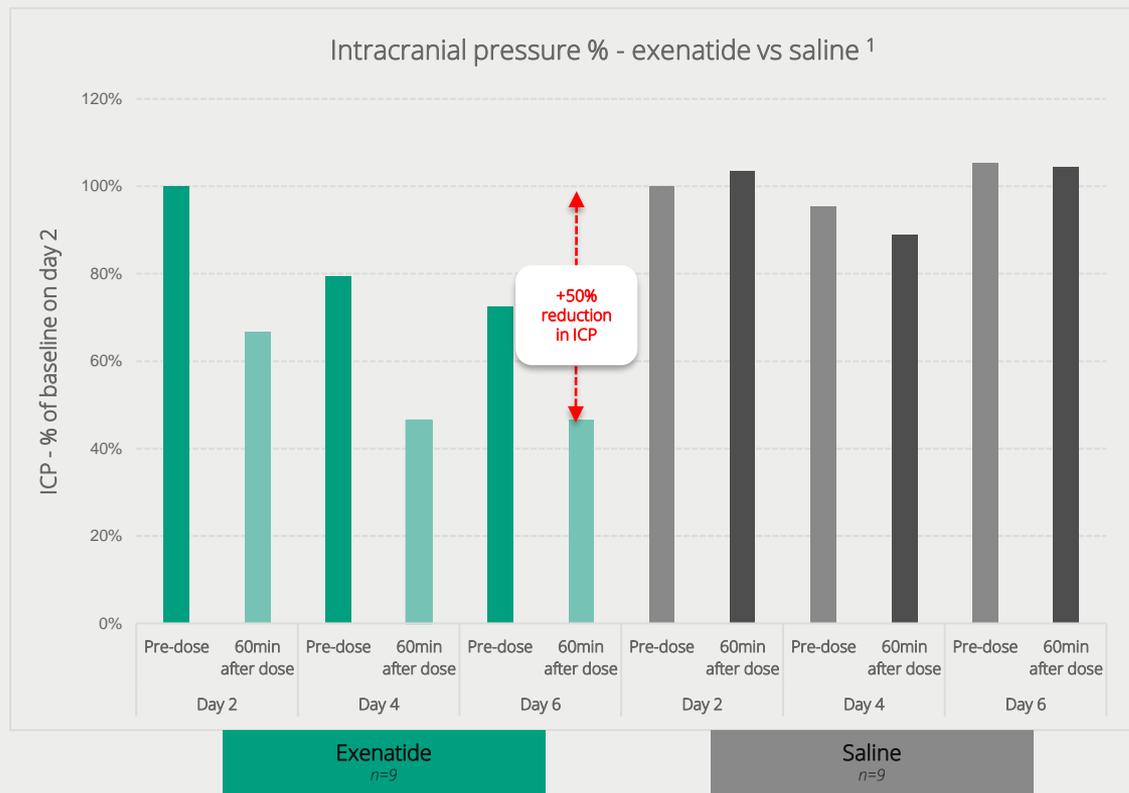
¹. Subject to final design considerations and regulatory clearance to commence a study

². Headache causes major morbidity in almost all patients with IIH

³. 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 Presdin™ clinical trial, the inclusion criteria requires patients with confirmed PMD of -7.0 to -2.0 decibels (dB)



Invex scientific data validates approach for IHH



- 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 exenatide-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

