



Invex Therapeutics

Repurposing An Approved Drug

Open Briefing
November 2019
ASX Code: IXC

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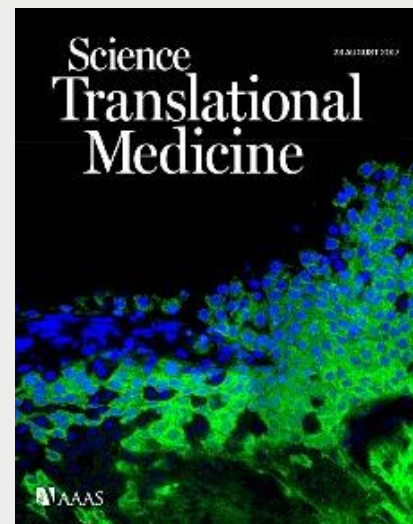
Invex Therapeutics - ASX:IXC

- Invex Therapeutics (Invex or the Company) was established March 2019
- Focused on repurposing Exenatide for neurological conditions involving raised intracranial pressure such as idiopathic intracranial hypertension (IIH)
- Assignment of intellectual property from University of Birmingham, United Kingdom
- Prof Alexandra Sinclair is a founder of Invex, CSO and Executive Director
 - clinician and global leader in the pathophysiology of idiopathic intracranial hypertension and headache, with over 10 years research in this field
- Successful Initial Public Offering (IPO) raised the maximum of \$A12 million to fund the proposed later stage research and development programme
- Directors and founding shareholders committed more than \$A2.5 million in seed capital and investment at IPO



Investment Highlights

- Completed proof-of-concept preclinical *in-vitro* and *in-vivo* studies
 - data published in world leading scientific journal
- Orphan Drug Designations granted for IIH in Europe (EMA) and in the US (FDA)
- Clinical study initiated in IIH
- Lower development risk
- Faster commercialisation strategy
 - an established lower cost business model
- World-class scientific and management team
- Key patent applications filed in 2014 (UK, US, EU, JP)
 - assigned to Invex from University of Birmingham, UK @ IPO
 - Japanese patent recently granted



Botfield et al., *Sci. Transl. Med.* 9 (2017)



Capital Structure & Major Shareholders

Capital Structure	
Shares on issue	55 mil
Unlisted Options	3 mil @60c
Cash	~\$A11.3 mil
Market Cap	\$A42 mil

Major Shareholders

Directors / Management	20%
Minderoo Pty Ltd	9.1%
Kim Hogan	7.3%
Tony Grist	7.3%
Tom Henderson	7.3%
Jason Peterson	4.5%
University of Birmingham	3.6%
Top 20 Shareholders	80%





Board and Management Team

- **Dr Jason Loveridge, Chairman**
 - Experienced life science investor & CEO
- **Prof Alexandra Sinclair, Executive Director and Chief Scientific Officer**
 - Global scientific & clinical leader in IHH
- **Mr David McAuliffe, Non Executive Director**
 - Founder of numerous life science companies
- **Ms Narelle Warren, Non Executive Director and Company Secretary**
 - Expertise in finance and compliance



Professor Sinclair MBChB, FRCP, PhD

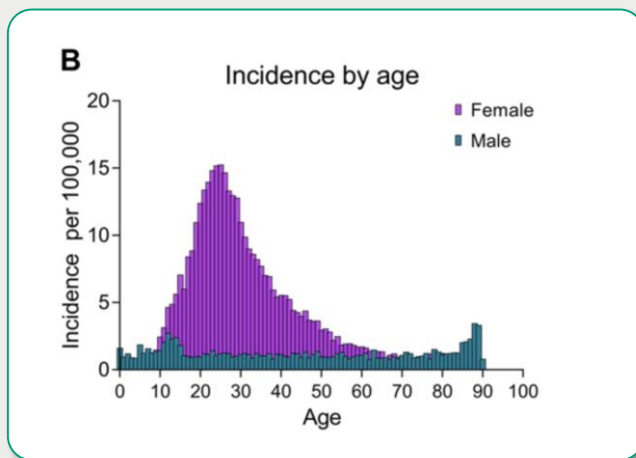


- Clinician Scientist & Neurology Consultant
- Leads a translational research program focused on defining the pathophysiological mechanisms of raised intracranial pressure and developing therapeutics strategies to take through to clinical trials
- Leads the multidisciplinary headache and ITH service at University Hospital NHS Foundation Trust, UK
- Council Member International Headache Society and European Headache Federation
- Council Member for the British Association for the Study of Headache
- Research Committee Member North American Neuro-Ophthalmology Society
- Research Committee Member and Deputy Chair of the Headache & Pain group of the Association for British Neurologists



Idiopathic Intracranial Hypertension (IIH)

- Disease characterised by raised intracranial pressure & papilloedema
- Symptoms
 - severe headaches
 - visual impairment, with ~25% of patients experiencing permanent loss of vision
- 90% of IIH patients are obese women of childbearing age

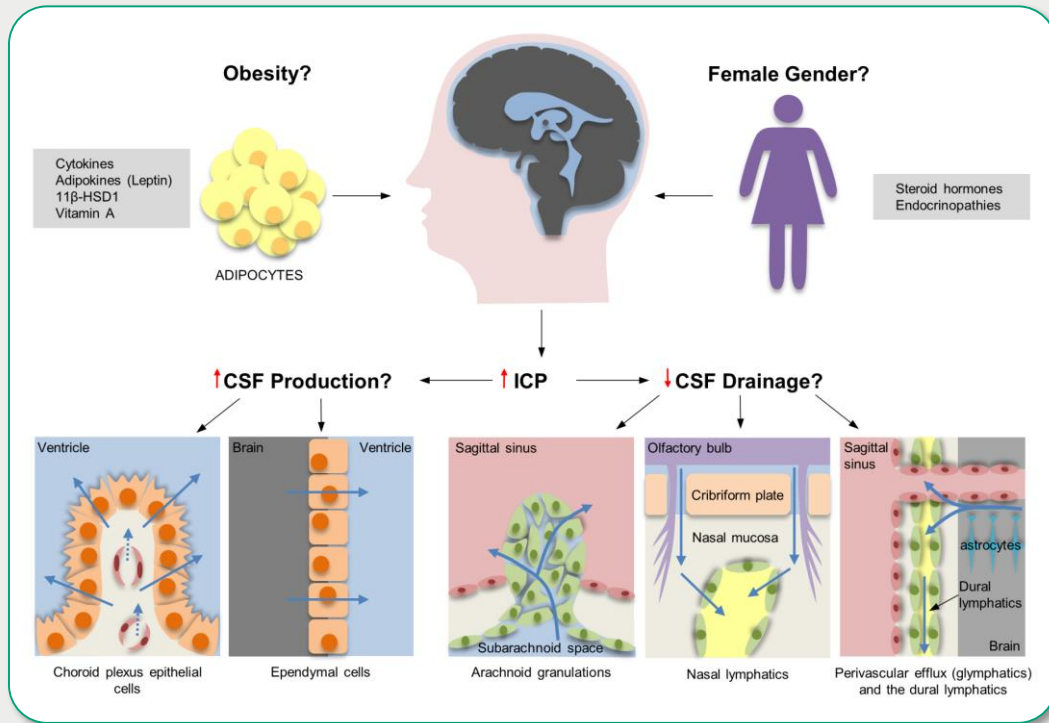


IIH peaks between years 20-30

The expanding burden of idiopathic intracranial hypertension, Susan P. Mollan, Magda Aguiar, Felicity Evison, Emma Frew & Alexandra J. Sinclair, Nature Eye volume 33, pages 478–485 (2019)



Cause of Raised Intracranial Pressure

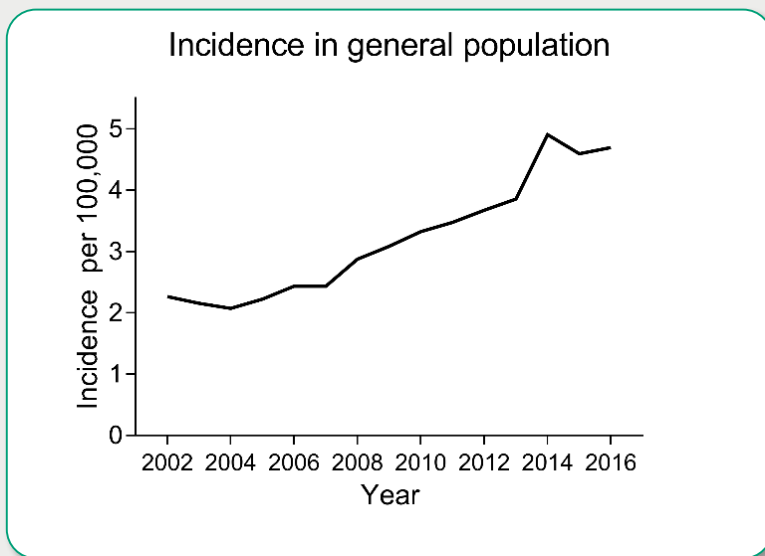


Mollan S & Sinclair A JNNP 2016



Rising IIH Incidence Linked to Obesity

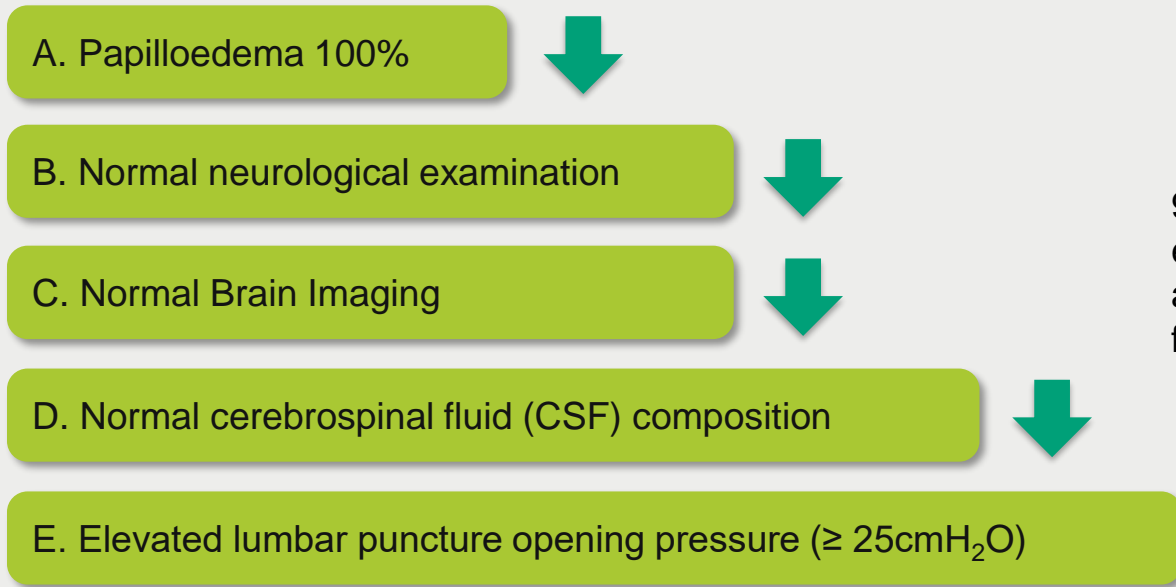
- IIH is a rapidly growing orphan indication
 - incidence of IIH has more than doubled in the last 10 years
 - incidence is strongly linked to obesity in women



The expanding burden of idiopathic intracranial hypertension, Susan P. Mollan, Magda Aguiar, Felicity Evison, Emma Frew & Alexandra J. Sinclair, Nature Eye volume 33, pages 478–485 (2019)



IIH Diagnosis: 5-steps, Standardised, Rapid



95% of IIH patients present at either A&E or opticians and are referred to a neurologist for diagnosis & treatment

Mollan SP, et al. J Neurol Neurosurg Psychiatry 2018;0:1-13

No approved drugs in IIH and a lack of an effective treatment is the real issue!!



IIH Treatment Guidelines

- Leading role played by Invex's founder Prof Alexandra Sinclair
- Currently no approved drugs for IIH

General neurology



REVIEW

Idiopathic intracranial hypertension: consensus guidelines on management

Susan P Mollan,^{1,2} Brendan Davies,³ Nick C Silver,⁴ Simon Shaw,⁵ Conor L Mallucci,^{6,7} Benjamin R Wakerley,^{8,9} Anita Krishnan,⁴ Swarupsinh V Chavda,¹⁰ Sathesh Ramalingam,¹⁰ Julie Edwards,^{11,12} Krystal Hemmings,¹³ Michelle Williamson,¹³ Michael A Burdon,² Ghaniah Hassan-Smith,^{1,12} Kathleen Digre,¹⁴ Grant T Liu,¹⁵ Rigmor Højland Jensen,¹⁶ Alexandra J Sinclair^{1,2,12,17}

Hoffmann et al. *The Journal of Headache and Pain* (2018) 19:93
<https://doi.org/10.1186/s10194-018-0919-2>

The Journal of Headache
and Pain

CONSENSUS ARTICLE

Open Access



European Headache Federation guideline on idiopathic intracranial hypertension

Jan Hoffmann^{1*}, Susan P Mollan², Koen Paemeleire³, Christian Lampl⁴, Rigmor H Jensen⁵ and Alexandra J Sinclair⁶

HOW TO DO IT



OPEN ACCESS

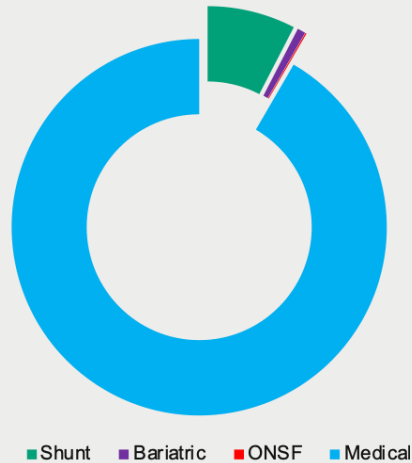
Evaluation and management of adult idiopathic intracranial hypertension

Susan P Mollan,^{1,2} Catherine Hornby,^{1,3} James Mitchell,^{1,3,4} Alexandra J Sinclair^{1,2,3,4}



Current Therapeutic Options are Ineffective

All current medicines for IIH are unapproved*, outdated, work poorly and cause debilitating side effects



* In IIH, ONSF: Optic Nerve Sheath Fenestration, ICP: Intracranial pressure, *The expanding burden of idiopathic intracranial hypertension*, Susan P. Mollan, Magda Aguiar, Felicity Evison, Emma Frew & Alexandra J. Sinclair, *Nature Eye* volume 33, pages 478–485 (2019)

invex therapeutics

Acetazolamide (1954)

Most commonly used drug in IIH

Cochrane review IIH in August 2015 concluded:

“Insufficient evidence to recommend or reject the efficacy of acetazolamide for treating IIH”



Topiramate (2012)

Prospective open label trial ACZ vs. TOP (Çelebisoy et al. 2007)

Reduction in ICP in both groups, equivalence between groups

Furosemide/Amiloride

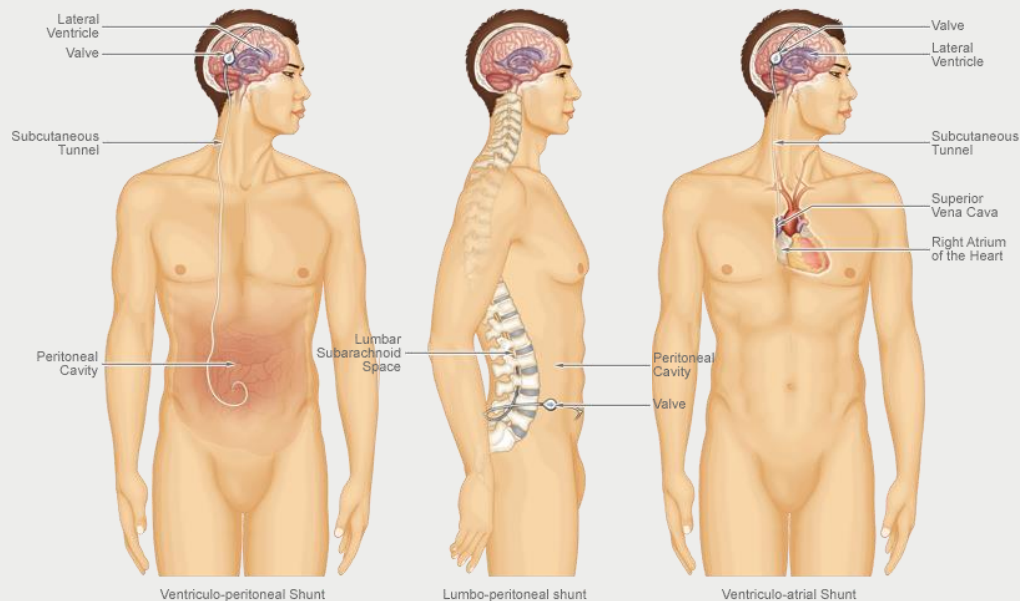
Animal studies only, showing reduction in CSF production (Vogh et al. 1982, Melby et al. 1982)

Octreotide

Small prospective open label study with no control showed significant reduction in headache, ICP, and papilloedema (Panagopolous et al. 2007)



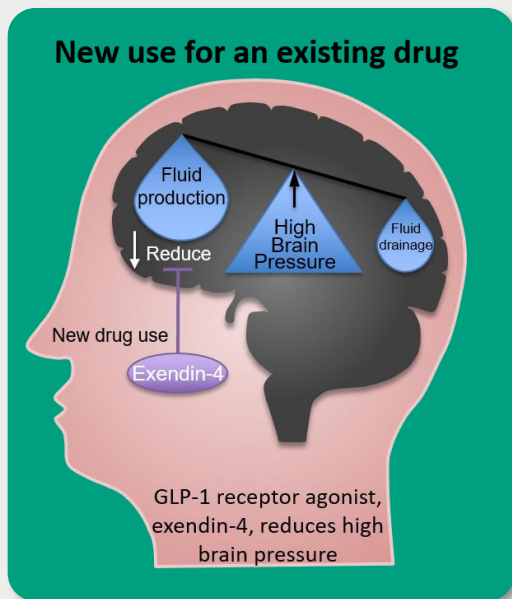
Neurosurgery Is Currently Needed



- CSF shunting (tube)
 - Drains fluid to reduce brain pressure
 - Can save vision, BUT
- Shunts have serious issues
 - Over 50% require shunt revision
 - 63% are revised within 1 year
 - Over-drainage in >20%
- AT BEST, a short-term fix!



Exenatide – Novel Approach to Raised ICP



- Exenatide is a small peptide that binds the GLP-1 receptor
- GLP-1 receptor agonists – like Exenatide – decrease fluid secretion in the kidney and are used extensively to treat diabetes
- Prof Alexandra Sinclair has shown that GLP-1 receptors are also expressed in the choroid plexus (in the brain), and that in animals
 - Exenatide can bind to these receptors
 - reduce cerebrospinal fluid secretion
 - provide fast onset of action making it suitable for treating patients with raised intracranial pressure

Exendin-4 = Exenatide

Botfield et al., *Sci. Transl. Med.* 9 (2017)



Exenatide – Where Does It Come From?



Exenatide is derived from a chemical found in the saliva of the Gila monster, a venomous lizard



Ongoing Clinical Trial in IIH

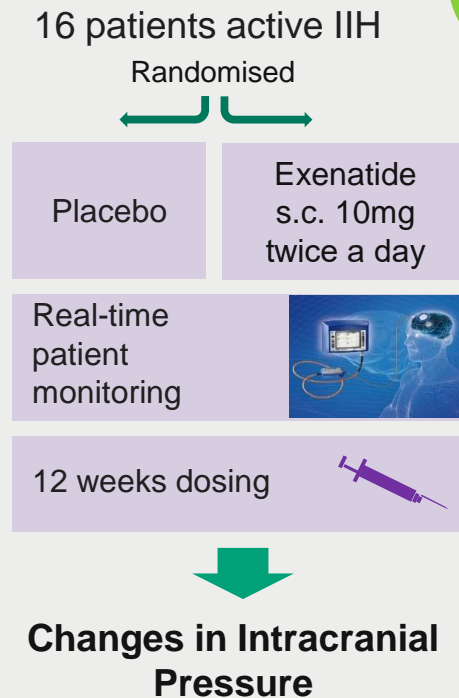
- Single centre study
- Randomised double blinded clinical study
 - 10 patients enrolled & completed to date
 - 6 additional patients now enrolled
 - top-line dataset available 1H, 2020

Secondary

- Headache measures (frequency, severity, duration, analgesic use, Hit-6)
- Visual assessments (visual field, papilloedema measured by OCT)
- Quality of Life measures

Exploratory

- Serum Exenatide levels
- Weight and fat distribution



Invex Proprietary Patented* ICP Blocker

- Exenatide - in its Byetta® form - was approved in 2005 for the treatment of type II diabetes in both the EU & US
 - administered as a twice-daily sub-cutaneous injection
 - commercialized by AstraZeneca
 - safe and well tolerated drug used in millions of diabetic patients**
- Current Exenatide dosing forms are not optimised for IIH
 - only available in 5 or 10mg pre-filled injection pens or long acting weekly injection
- Invex intends to utilise its unique insight into diseases characterised by raised ICP to develop proprietary, patented* dosage forms of Exenatide for IIH and other diseases characterised by raised ICP

*ICP: intracranial pressure, * Patent applications licensed for Birmingham University & additional IP filed in 2019 **
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2005/021773_byettatoc.cfm*



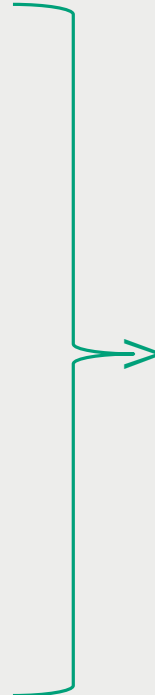
Invex's Repurposed Pressure Blocker

- Proprietary and patented
- Aim to be the first & only drug for IIH patients
 - approved for the disease (IIH) by EMA & FDA
 - safety and efficacy established by statistical significance in randomised, double blinded clinical trials
 - assigned unique National Drug Codes
- First mover advantage ensures competing drugs would need to be compared to and be better than Invex's IIH drug in order to gain approval
- Proprietary dosage supported by clinical safety and efficacy prevents substitution with Byetta®



Repurposing Approved Drugs - An Established, Successful Business Model

Drug	Original Disease
Azathioprine	Rheumatoid arthritis
Bleomycin	Various cancers
Colchicine	Gout
Cycloserine	Urinary tract infection
Cyclosporine	Rheumatoid arthritis
Eflornithine	Unwanted facial hair
Everolimus	Renal cancer
Histrelin	Prostate cancer
Infliximab	Ulcerative colitis
Interferon alpha	Hepatitis B & C
Rituximab	Rheumatoid arthritis



New Orphan Disease
Renal transplant
Pleural effusion
Mediterranean fever
Tuberculosis
Transplant rejection
Sleeping sickness
Renal transplant
Precocious puberty
Chronic disease
Cancer
Cancer



5 Key Goals to Drive Value in 2020

1. Complete reformulation of Exenatide
2. Establish manufacturing for clinical studies and commercial sales
3. Complete ongoing clinical trial and publish top-line data in IIH
4. Define and initiate with key regulatory agencies – FDA & EMA – a registration study for repurposed Exenatide in IIH
5. Initiate a phase II clinical study in a second indication



Exenatide – out of this world



- Raised intracranial pressure occurs after 3 months space flight
 - Papilloedema
 - Cognitive slowing
 - No treatment
- Mars expedition is 9 months away and NASA is looking for solutions
- Ongoing discussions to plan a trial on the International Space Station



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