Invex Therapeutics

Investor Presentation

June 2021

ASX Code: IXC

invex THERAPEUTICS

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Company Snapshot

Company	
Repurposed, Proven Drug	Presendin™ (Exenatide)
Clinical Stage	Entering Phase III
Orphan Disease Focus	Idiopathic Intracranial Hypertension (IIH)
Orphan Designation Granted	USA + EU
Total Addressable Market	$1.6 billion annually (US/EU)
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 (31 Mar-21)	$33.2 million
Market Capitalisation (17 Jun-20) [1]	$42.9 million
Enterprise Value (17 Jun-20)	$9.7 million

[1]Based on closing price of $0.57

Major Shareholders	
Directors / Management	16.8%
Tattarang	11.8%
Tisia Nominees Pty Ltd	5.3%
Anthony Grist	4.8%
JK Nominees Pty Ltd	4.0%
University of Birmingham	2.7%
Top 20 Shareholders	59.5%

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 Europe of **A$1.6 billion** per annum 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
- Plan to file with national health authorities in Europe & commence a Phase III registration trial

Significant Barriers to Competition

- Orphan drug designation in US (7 years exclusivity) and Europe (10 years exclusivity)
- Issued and pending patents for use of Exenatide in IIH; Formulation patents filed Q1 2020

Q1/Q2 2021 Highlights

Dr Megan Baldwin Appointed to the Board of Directors

- Dr Baldwin is CEO and Managing Director of Opthea Limited (ASX:OPT; NASDAQ:OPT)
- Opthea included into the S&P/ASX 300 in June 2020
- Opthea raised $180 million and listed on NASDAQ Exchange in October 2020

Continued Preparations for Phase III Trial in IIH

- Selection of preferred 1x per day sub cutaneous formulation of Presendin™ for clinical development - **achieved**
- Continued evaluation of several contract manufacturing organisations (CMO) capable of supplying of clinical-grade Presendin™ for Phase III study and thereafter commercial supply – **contract discussions well-advanced, but not yet complete**

Regulatory

- Written response received from FDA – Type C Meeting

FDA Response Type C Meeting – June 21

- Filing to Division of Neurology, based on finalised protocol assistance from European Medicines Agency (EMA) in December 2020 – aim to harmonise a single Phase III study across both EMA & FDA:
  - Intracranial Pressure (ICP): Primary Endpoint
  - Monthly Headache Days: Key Secondary Endpoint
- FDA consider a clinically meaningful effect on visual function, such as Perimetric Mean Deviation (PMD) as a recommended primary endpoint – FDA open to Invex providing proposals on this or other visual measures
- ICP a supported secondary endpoint. Very few comments on planned measure of monthly headache days and other key headache measures noted

Next Steps

- Invex to meet with key regulatory and scientific advisors in coming weeks, to further understand FDA thinking and clinical strategies
- Decision scenarios:
  - Effect of FDA advice on EMA Phase III design, if any
  - Ability to meet requirements of both regulators in 1x clinical trial, or not
  - Finalisation of clinical strategy for Europe and the US

Current Status of Phase III Clinical Trial

	FDA	EMA
Regulatory Agency		
Primary Endpoint Preference[1]	Vision	Intracranial Pressure (ICP)
Secondary Endpoints[3]	Intracranial Pressure (ICP); Headache Days	Headache Days[2]; Vision[4]
Protocol Assistance/Advice	Further Review	Complete

[1] Based on Protocol assistance received 20 July 2020 (FDA,EMA), 23 Dec 2020 (EMA) & 15 June 2021 (FDA)
[2] The EMA provided advice that both a reduction in ICP and a clinical outcome measure such as headache days for Presendin™ v placebo would be required to support a market clearance
[3] The FDA did not consider ICP as a primary endpoint for regulatory clearance, but a secondary endpoint. Invex considers headache days as an important clinical outcome measure.
[4] A preferred measure of visual function is to be determined prior to submitting a final study protocol to commence a Phase III trial; for EMA, ICP + a clinical outcome measure such as headache days or vision is required

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**)

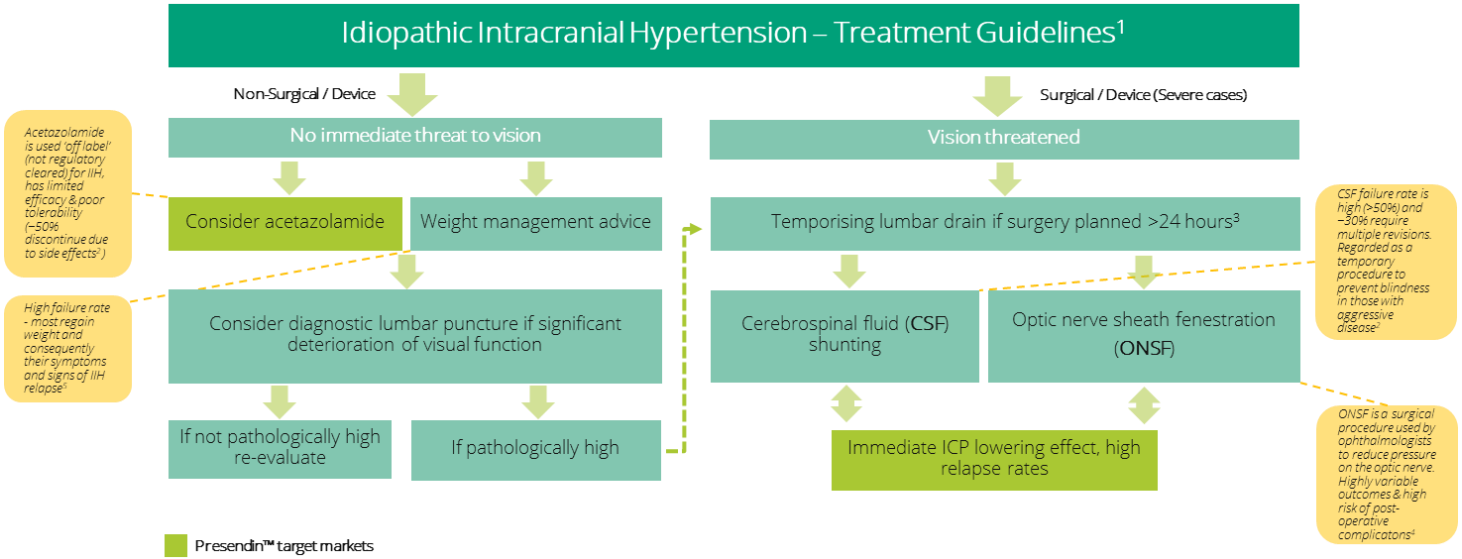
The Solution

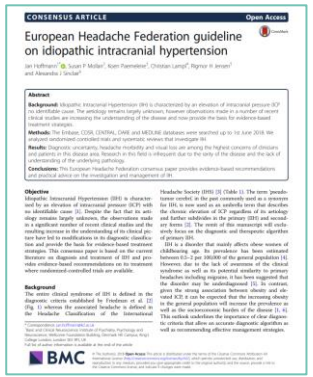
- Prof. Alex Sinclair (Invex CSO & Exec. Director) first to demonstrate glucagon like peptide 1 (GLP-1) receptor agonists commonly used in diabetes treatment (Exenatide formulated as Byetta® or Bydureon®) act on the choroid plexus in the brain to lower cerebral spinal fluid secretion and as a consequence, 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 study 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)

Current treatments for IIH are limited

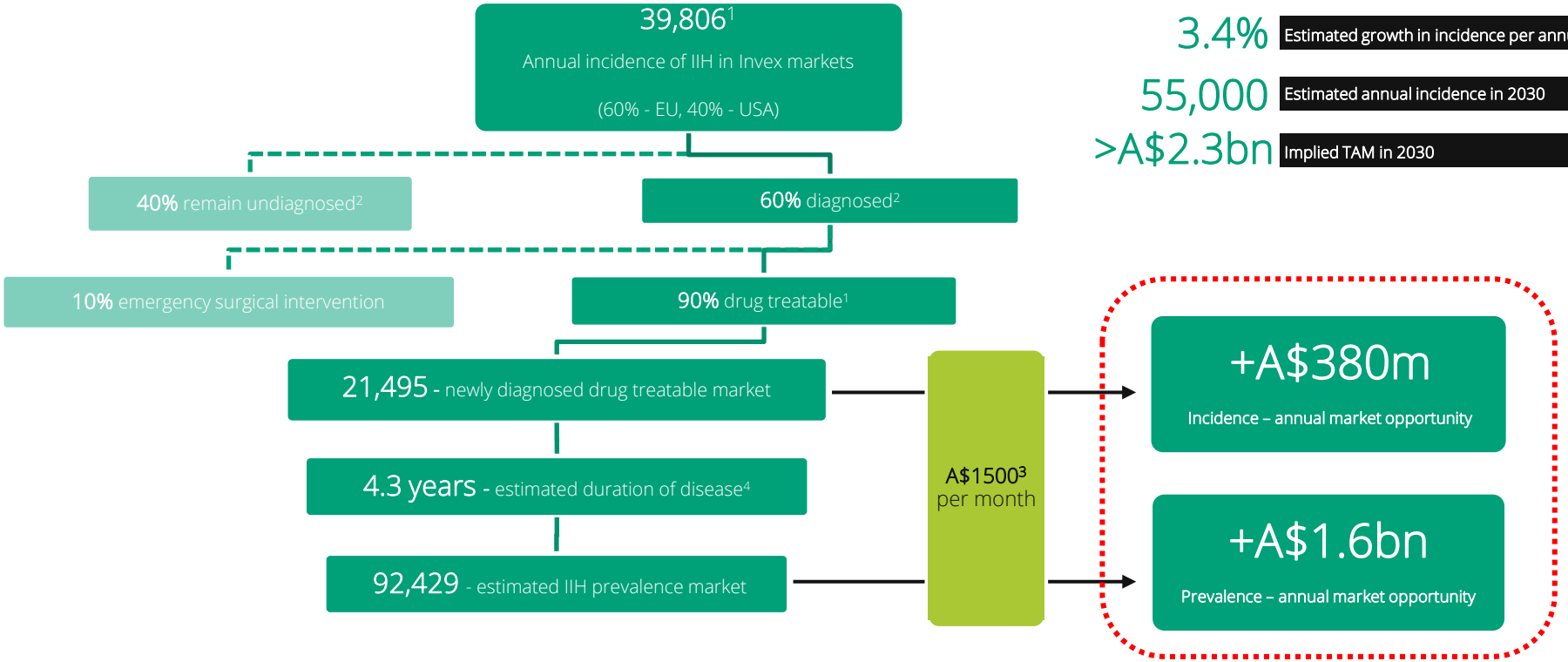
- Diagnostic criteria (2013) and treatment guidelines (2017/8) now well defined
- IIH consensus guidelines written by Prof. Alex Sinclair & colleagues
- Treatment guidelines highlight the lack of a standard drug therapy in IIH and opportunity for rapid incorporation into treatment guidelines post regulatory clearance
  - Drives clinical use, important for payer coverage





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)

IIH Total addressable market (TAM)



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., 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]

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

Invex Phase II trial – design & outcomes

Study Purpose

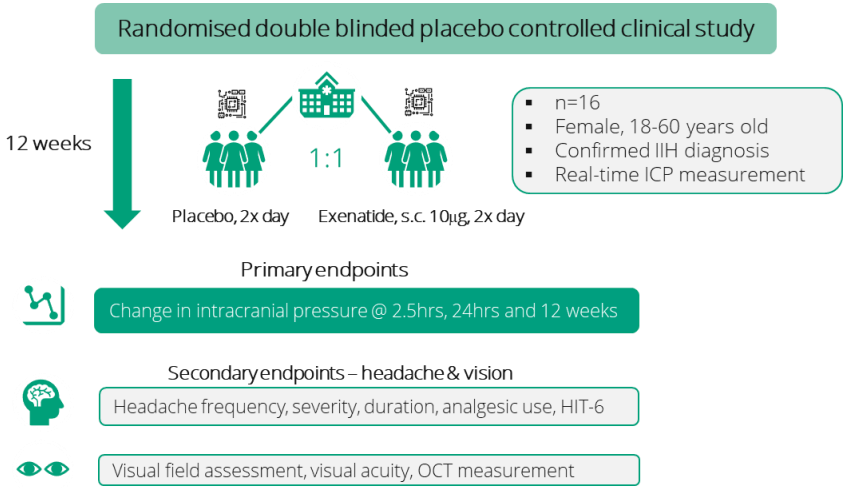
- Obtain first clinical proof of concept for Exenatide in IIH and provide a basis to move into pivotal Phase III trial by leveraging orphan drug status in Europe and the United States

Efficacy Outcomes

- Primary Endpoint (reduction in ICP) Met – 18-21% reduction across three time points; statistically significant and clinically meaningful
- Secondary Endpoint (Headache) Met – statistically significant & clinically meaningful reduction in headache days (7.7 days / 37% versus placebo)
- Secondary Endpoint (Vision) Met – statistically significant & clinically meaningful improvement in visual acuity (0.1 logMAR improvement at 12 weeks, equivalent to one line of visual acuity)

Safety Results

- No serious adverse events (SAEs) 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®)



Conclusion

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

Lead-In Activities Ahead of Planned Phase III Trial

Reformulation

- Successfully completed a series of animal pharmacokinetic (PK) studies in CY2020 with proprietary formulations
- COVID-19 impacted access to laboratory personnel and testing facilities in Q4 CY2020
- Final formulation candidate for planned clinical studies pending
- Formulations are subject of additional patent filings made by Invex in Q1 CY2020

Tolerability*

- All Presendin™ formulation excipient(s) have been used in already approved drugs and have a well-established safety profile
- Invex only required to undertake one additional safety study to assess local tolerability at the injection site (in animals)
- Straightforward and rapid process

Manufacturing

- Require a Contract Manufacturing Organisation (CMO) to manufacture and supply clinical-grade Presendin™ for human clinical trials & perform other activities required by government regulators
- Discussions with globally-recognised manufacturers capable of production and supply are well-advanced
- Final sign off for supply of Good Manufacturing Practice (GMP) Presendin™ pending

Human PK Study*

- As a reformulation of an existing approved drug, a Phase I human pharmacokinetic (PK) study required
- Single and repeated sub-cutaneous doses in healthy (obese) volunteers
- Total amount of bioavailable drug must not exceed that approved for reference Exenatide drug product Byetta®

* Subject to availability of GMP grade Presendin™

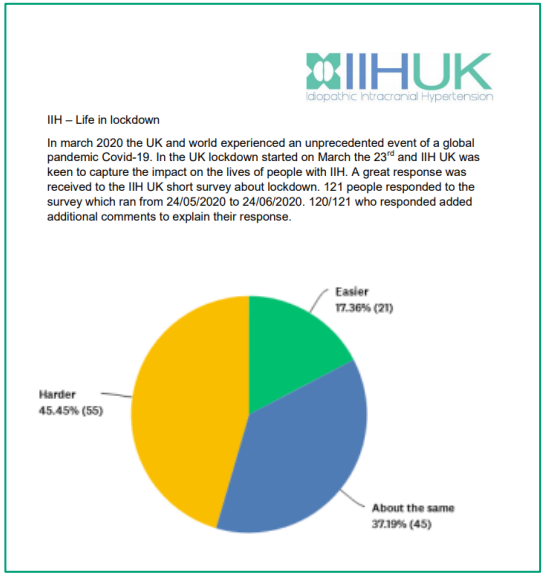
Negative Impact of COVID-19 Lockdown in the UK on IIH

Prospective Evaluation Study Showed 4.7 Fold Increase in Emergency Surgical Interventions to Avoid Permanent Vision Loss

- Study (n=139 over 10 weeks) showed increased risk of disease deterioration and CSF shunting in those with both existing and new IIH
- **367% increase** in surgical rate due to impaired access to emergency care, delayed routine waiting times and lifestyle changes under lockdown
- Increases in anxiety and depression noted, and weight gain

IIH UK Survey[2] Highlights Significant Quality of Life Impacts on IIH Patients

- **45%** felt living with IIH was **harder** under UK lockdown
- Challenges of access to medical care was a common theme with cancelled appointments, unable to get hold of medical teams and a lack of information
- Increase in stress, reduction in activity and increase in weight made IIH condition worse



Multi-City Lockdowns During COVID-19 Have Highlighted the Significant Market Need for New Effective (Non-Surgical) Therapies for IIH Patients Outside of Hospital Setting

1. Thaller M, Tsermoulas G, Sun R, *et al* Negative impact of COVID-19 lockdown on papilloedema and idiopathic intracranial hypertension *Journal of Neurology, Neurosurgery & Psychiatry* Published Online First: 24 December 2020. doi: 10.1136/jnnp-2020-325519
2. https://www.iih.org.uk/images/Life_in_lockdown_result_summary.pdf

Summary & Outlook

- Large, growing market for IIH with no approved medical 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 7 -10 years, jurisdiction dependent
- Strong Phase II clinical data established
- European regulatory pathway completed: ICP + clinical measure (headache or vision) acceptable for 1x Phase III trial & regulatory clearance (subject to safety and efficacy)
- Financial:
  - $33.2M in cash at 31 March 2021 – sufficient to fully fund completion of a Phase III clinical trial in IIH for registration
  - No requirement for additional capital
  - Low corporate overheads, very modest quarterly cash burn of ~$0.5M per Q over last 12 months
  - Very attractive ~$10M Enterprise Value (EV) considering stage of development and market attributes
  - Large EV discount to ASX-listed orphan (ASX:CUV, ASX:NEU, ASX:RAC), ophthalmic (ASX:OPT) and re-purposing (ASX:PAR, ASX:ILA) companies
- 2021 Milestones:
  - Appointment of contract manufacturer for clinical and commercial supply of Presendin™
  - Subject to availability of GMP Presendin™*
    - Human PK study and Animal tolerability study to commence as soon as practicable following receipt of clinical doses
    - Preparations for, and filing of, a CTA in Europe for a Phase III clinical trial 2H CY2021
    - Commencement of Phase III clinical trial in Europe in late 2H CY2021 - 1H CY2022

* Determined by the contract manufacturer based on available manufacturing slots following formal appointment and supply of clinical material.

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Thank you

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