

bioasis

The Blood-Brain Barrier Company

xB³™ Proprietary Platform Technology

June 2019

BTI.V (TSX), BIOAF (OTCQB)

Forward Looking Information

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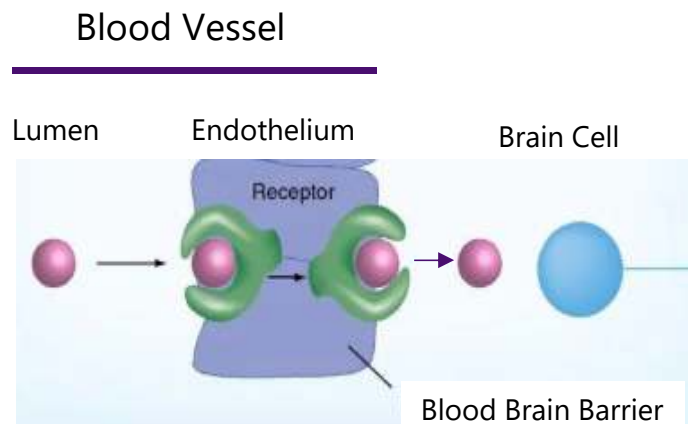
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Bioasis Highlights

<p><i>xB³™ Platform Technology: Novel, cutting-edge, best-in-class platform technology for BBB drug delivery</i></p>	<p>Focused on the Non-Invasive Delivery of Therapeutics Across the BBB with Proprietary xB³ Platform Technology</p> <ul style="list-style-type: none"> • Enables delivery of multiple therapeutics across the BBB, including small molecules, enzymes, siRNA, antibodies and potentially other biologics • Outperforms all other BBB technologies by delivering 4-6% of the injected dose into the brain, competitor technologies deliver 1-1.5% • 120+ patents relating to the xB³ delivery vector, xB³ fusions and conjugates with active agents and therapies for treating various diseases associated with the central nervous system; foundation patents through 2034; additional patent term extension up to five years and ongoing work anticipated to provide further long-term patent protection
<p><i>Developing risk-mitigated, wholly-owned programs with potential for fast track, early approval</i></p>	<p>Initial Focus on Orphan Indications & Rare Genetic Diseases with High Unmet Medical Need Where Proof-of-Concept Exists</p> <ul style="list-style-type: none"> • Lead program xB³-001 fuses xB³ peptide to Herceptin® (\$7.1B in sales in 2017) for the treatment of HER2+ breast cancer brain metastases; FDA pre-IND feedback anticipated in June 2019, first-in-human (FIH) 2020; potential for accelerated approval after Ph 1b/2a • Second program xB³-007 (xB³+Cerezyme®; \$8.3M in sales in 2017) for the treatment of Gaucher’s Type 2, an LSD; pre-clinical POC to generate biomarker data, translatable endpoints into humans in 2019; FDA pre-IND meeting anticipated date 4Q20, FIH 4Q21, potential for accelerated approval after Ph 1b/2a
<p><i>Strategic partnering ensures wide uptake of the technology with partner taking on technical risk and Bioasis sharing in the upside</i></p>	<p>Opportunities to Out-License Technology to Address Novel Targets with Multiple Treatment Modalities including Antibodies, enzymes, siRNA and gene therapy</p> <ul style="list-style-type: none"> • Licensing agreement with Prothena and a new research alliance with a major global pharma company • xB³ peptide can penetrate the lymphatic system, offering additional non-CNS opportunities

The Bioasis Platform Technology Works via the LRP1 Receptor

MOA Facilitates Rapid, Active Transport Across BBB and Confers Broad Utility



xB³ Peptide

Derived from an iron-binding human protein found at low concentrations in the blood

- xB³ has been optimized by Bioasis scientists to its key constituents (12 amino acids)
- xB³ has shown improved brain penetration over the full-length protein

Mechanism of Action (MOA)

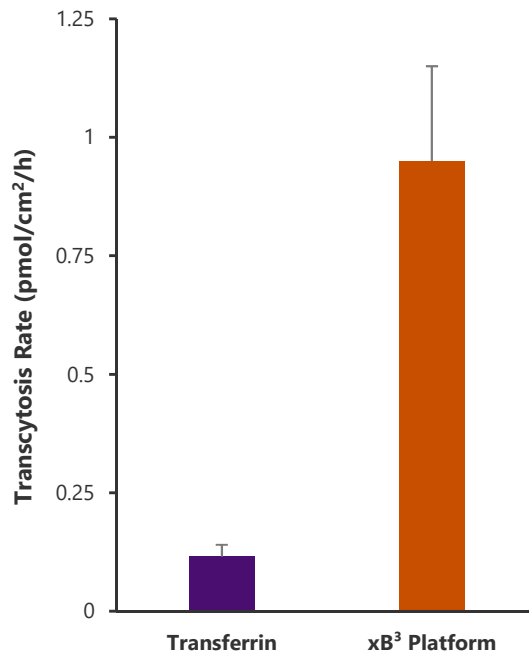
xB³ binds to the BBB endothelium via the Low Density Lipoprotein Receptor-related protein (LRP1) receptor

- High efficiency receptor with fast endocytosis and recycling
- LRP1 is highly expressed in critical brain regions and across multiple brain cell types
- LRP1 is overexpressed in multiple disease states including brain cancers, Alzheimer's disease and Parkinson's disease

The xB³ Platform Technology

Advantages Over Competing BBB Technologies

Transcytosis across *in vitro* BBB model (BBCEC)



Features	Bioasis xB ³ Platform	Denali	Genentech	Roche	Armagen	Angiochem
% injected dose in brain	4-6%	<1%	<1%	<1%	<1%	~1.5%
Mode of Action	LRP1	TfR	TfR	TfR	TfR and IR	LRP1
Payload Modalities						
Antibodies	✓	✓	✓	✓	✓	
Enzymes	✓				✓	
siRNA	✓					
Small molecules	✓					✓

Diversification and De-Risking of Internal and External Development

Internal Development

Approved, High Value Medicines

- Making non-brain penetrant medicines into the new standard of care for CNS disorders
- Faster, cost-efficient path to NDA/BLA filing
- Wholly-owned assets
- Lead programs utilize established products (Herceptin and Cerezyme), with proven efficacy and known safety profiles
- Focus on orphan indications, including brain cancers, and rare genetic diseases

Business Development

New Drug Candidates and Novel Targets

- Selective partnering ensures wide uptake of the technology with partner taking on technical risk and Bioasis sharing in the upside
- Opportunities to out-license technology to improve efficacy via enhanced blood-brain barrier penetration by small molecules, enzymes, siRNA, antibodies and other biologics
- Licensing agreement with Prothena, a new research alliance with a major global pharma company & in discussions with a second major global pharma company deal on xB³ platform announced in January 2019

Advantages include Early Proof-of-Concept

Target engagement milestone can be determined early in the clinical program, establishing brain penetration and verifying dose

Bioasis Pipeline: Robust and Designed to Mitigate Risk

Turning Non-Brain Penetrant Medicines into the New Standard of Care for CNS Disorders

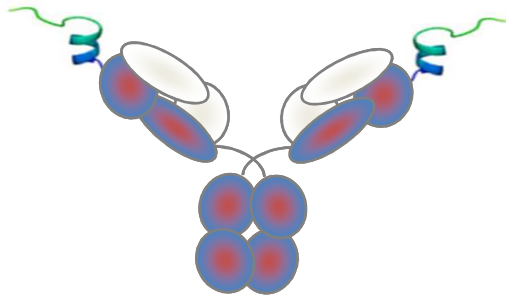
Lead Indication	Research	Pre-Clinical POC	IND-Enabling	Phase 1	Phase 2
			IND-Ready		
xB³-001 HER2+ Brain Metastases			2H20	Potential for accelerated BLA submission (2023)	
			Proof-of-Concept		
xB³-007 Type II Gaucher's Disease			2H21	~3 years from IND to BLA (2024)	
xB³-002 Glioblastoma					
xB³-008 MPS I, II & III					

- Orphan indications, including CNS cancers and rare genetic diseases
- Faster, cost-efficient path to BLA submission
- Lead programs utilize established products with proven efficacy and known safety profiles (e.g., xB³-001: Herceptin[®] (trastuzumab), xB³-002: Avastin[®] (bevacizumab), xB³-007: Cerezyme[®] (imiglucerase), xB³-008: undisclosed)

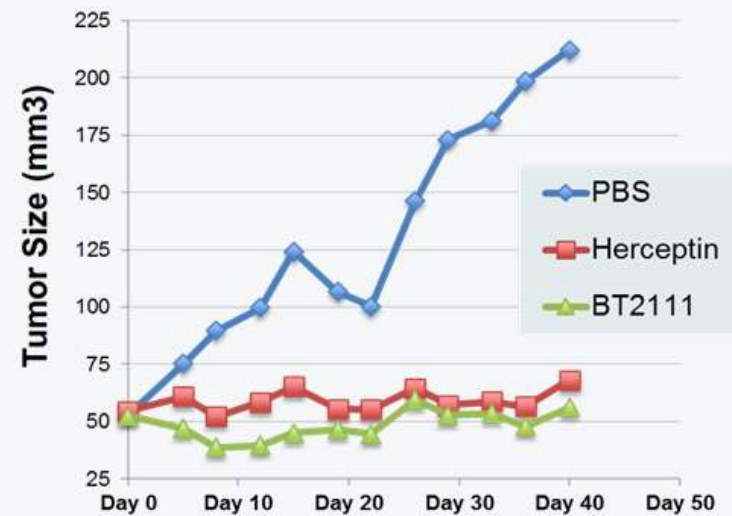
Herceptin[®] is a registered trademark of Genentech, Inc., Avastin[®] is a registered trademark of Genentech, Inc., Cerezyme[®] is a registered trademark of Genzyme Corporation.

xB³-Herceptin Retains Tumor Inhibition Efficacy in the BT474 Xenograft Model

xB³ can be added to a therapeutic through chemical conjugation or fusion



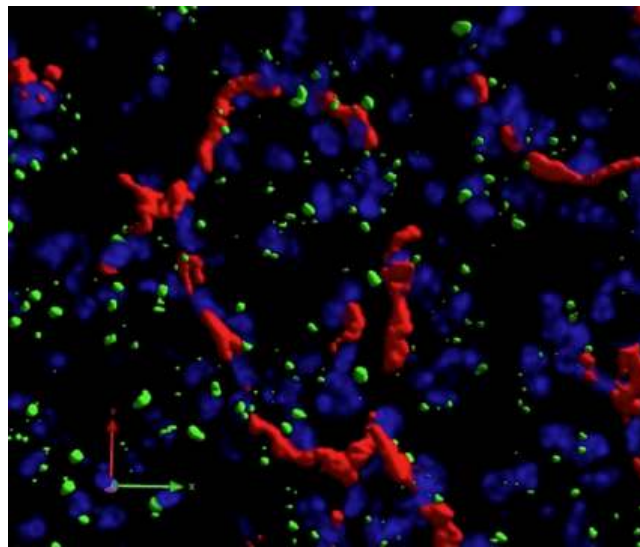
BT2111 & Herceptin® Halt Growth of BT474 HER-2/*neu* Over-Expressing Tumors



Ip injection 2x/wk for 5 weeks; 10mg/kg
xB³-TZM = BT2111

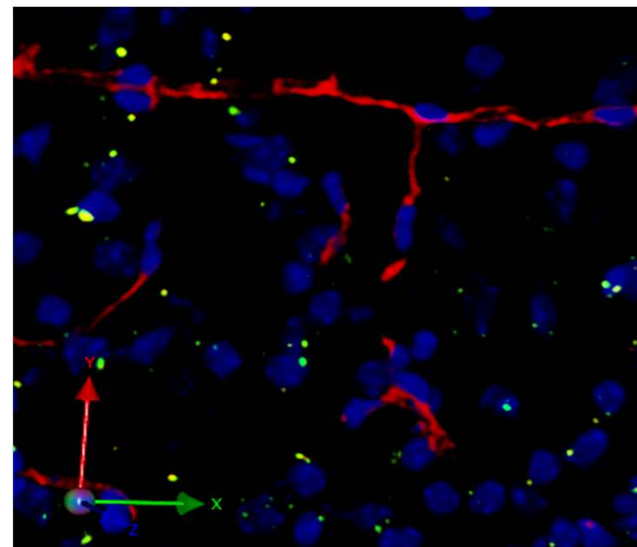
xB³-Herceptin[®] Significantly Increases Localization in Brain Parenchyma

Confocal Images Two Hours Post IV Administration (10mg/kg)



xB³-Herceptin

Red: Brain capillaries
Blue: Nuclei
Green: xB³-Herceptin



Herceptin alone

Red: Brain capillaries
Blue: Nuclei
Green: Herceptin alone

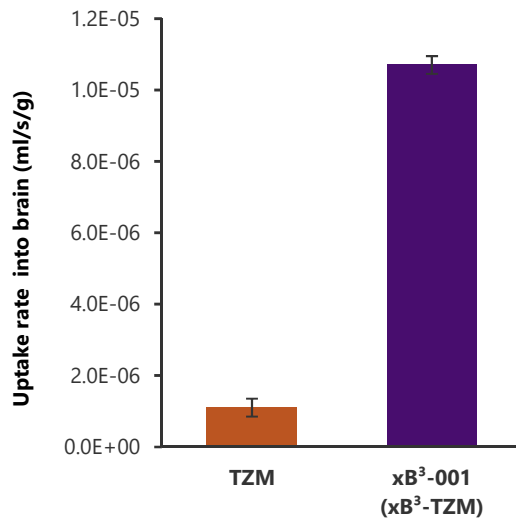
Work performed at National Research Council of Canada – Research Facility **bioasis**

xB³-001 for the treatment of Breast Cancer Brain Metastases

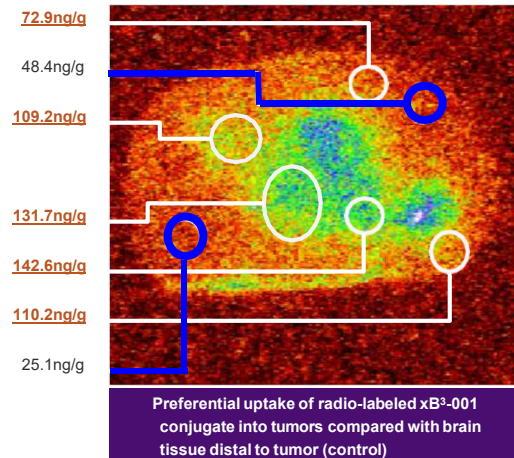
Human HER2+ Breast Cancer Brain Metastases in Murine Model

xB³-001 Achieves Successful Delivery of Trastuzumab (Herceptin, TZM) to the Target Brain Tissues

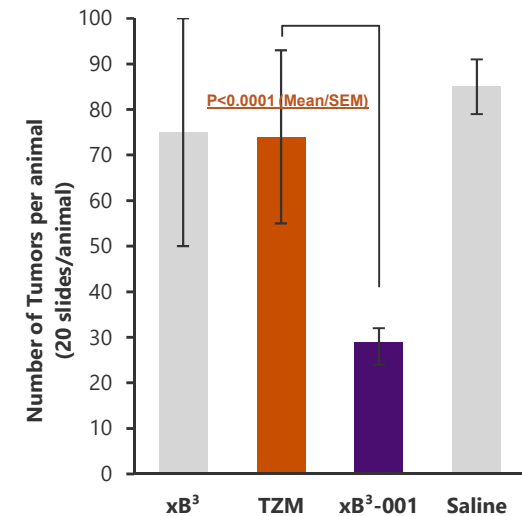
1. xB³ Increases the Brain Exposure of Approved Medicines - Herceptin® (trastuzumab, TZM)



2. xB³ Enables Target Engagement of Relevant Brain Target Tissues



3. xB³ Drives Biological Effect; 68% Reduction in HER2+ Brain Metastases with xB³-001



TZM: Trastuzumab; n=13 for xB³, TZM groups; n=8-9 for xB³-TZM, saline groups.
One-way ANOVA **P<0.001, ***P<0.001, ***P<0.0001 Mean±SEM

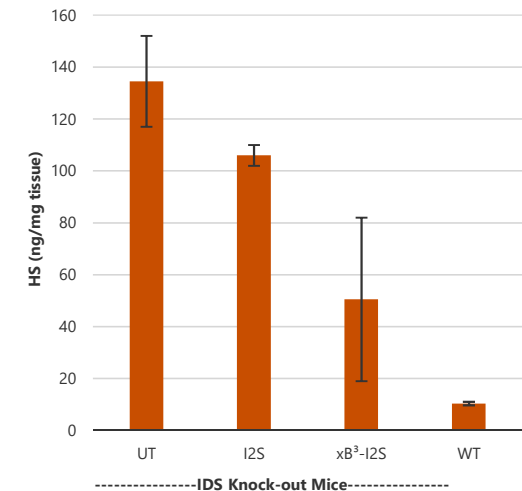
xB³-007: Glucocerebrosidase

Untreated Neuropathic Gaucher's Disease Type II

- Gaucher's disease (GD) results in the deficiency in an enzyme, causing a portion of old cells to be stored in areas such as the liver, spleen, lungs, lymph system, and bones instead of being expelled from the body. It is caused by mutations in GBA1 gene that encodes glucocerebrosidase enzyme
 - **Type II is an acute, infantile, neuropathic form of the disease, associated with severe brain damage: No effective treatments are currently available**
 - **Early onset (3-6 months), severe, rapidly progressing, fatal within two years**
 - **Pathologies: seizures, spasticity, enlarged spleen & liver, poor development**
- Cerezyme[®] (glucocerebrosidase) is used as an **enzyme replacement therapy** for patients with Gaucher's Disease Type I. Cerezyme robustly treats the peripheral symptoms of Type I (non-neuropathic), however, is not able to cross the BBB and is not effective in Types II and III
 - Bioasis scientists have preliminary data demonstrating the ability of an enzyme to cross the BBB with an associated decrease in heparin sulfate as well as glycosaminoglycans in the central nervous system

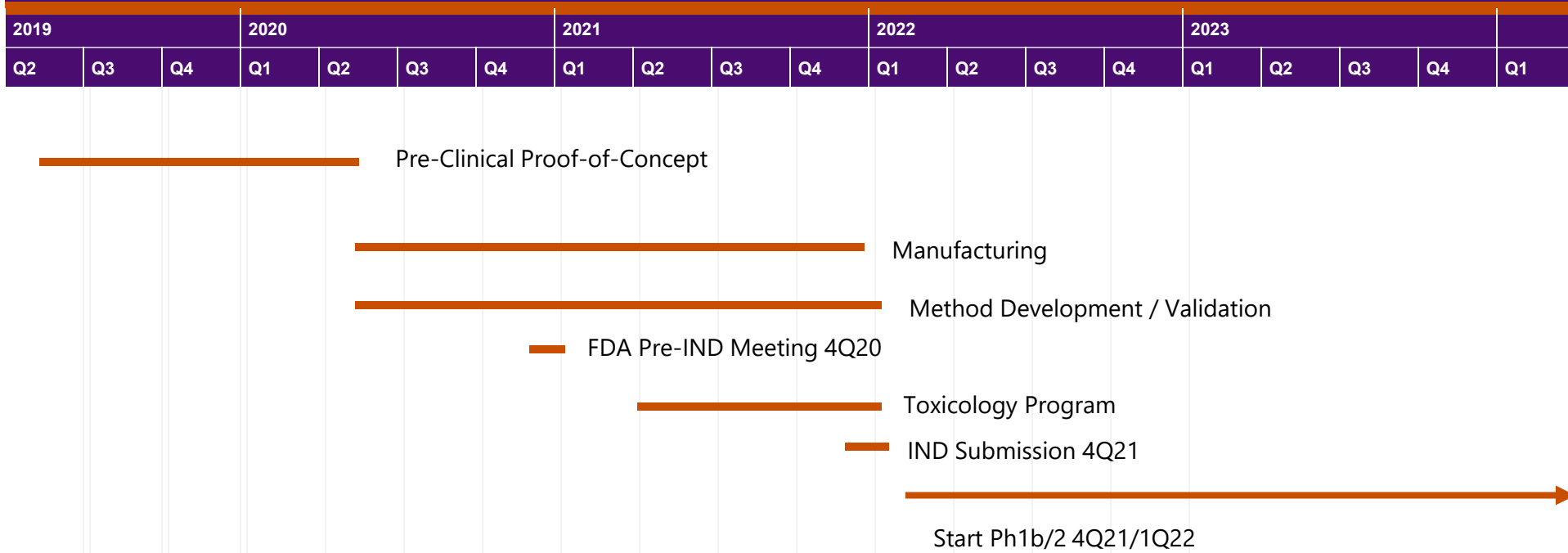


Reduction in Heparan Sulfate Accumulation



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xB³-007 for the Treatment of Gaucher's Disease Type II



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xB³ Platform Technology

MedImmune - Bioasis Collaboration

 MedImmune

Original Article

JCBFM

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SAGE

A peptide derived from melanotransferrin delivers a protein-based interleukin I receptor antagonist across the BBB and ameliorates neuropathic pain in a preclinical model

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Abstract

Delivery of biologic drugs across the blood–brain barrier is becoming a reality. However, the solutions often involve the assembly of complex multi-specific antibody molecules. Here we utilize a simple 12 amino-acid peptide originating from the melanotransferrin (MTF) protein that has shown improved brain delivery properties. 3D confocal fluorescence microscopic analysis demonstrated brain parenchymal localisation of a fluorescently labelled antibody (NIP228) when chemically conjugated to either the MTF peptide or full-length MTF protein. Measurement of plasma kinetics demonstrated the MTF peptide fusions had very similar kinetics to an unmodified NIP228 control antibody, whereas the fusion to MTF protein had significantly reduced plasma exposure most likely due to a higher tissue distribution in the periphery. Brain exposure for the MTF peptide fusions was significantly increased for the duration of the study, exceeding that of the fusions to full length MTF protein. Using a neuropathic pain model, we have demonstrated that fusions to interleukin-1 receptor antagonist (IL-1RA) are able to induce significant and durable analgesia following peripheral administration. These data demonstrate that recombinant and chemically conjugated MTF-based brain delivery vectors can deliver therapeutic levels of drug to the central nervous system.

Keywords

Blood–brain barrier, central nervous system, interleukin-1 receptor antagonist, melanotransferrin peptide, pharmacokinetic

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Introduction

Although protective in design, the blood–brain barrier (BBB) presents a constant challenge to effectively deliver therapeutic drugs directed at the treatment of brain diseases. Efficient drug delivery across the BBB is most important in the treatment of neurophysiological disorders (including neuropathic pain, Alzheimer's disease

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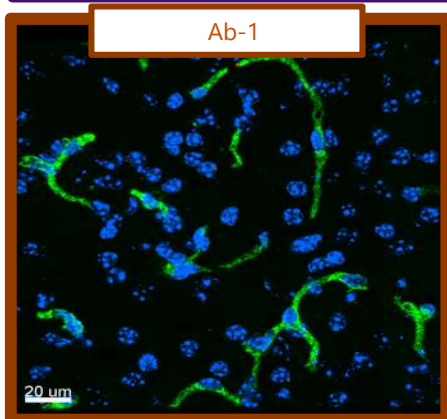
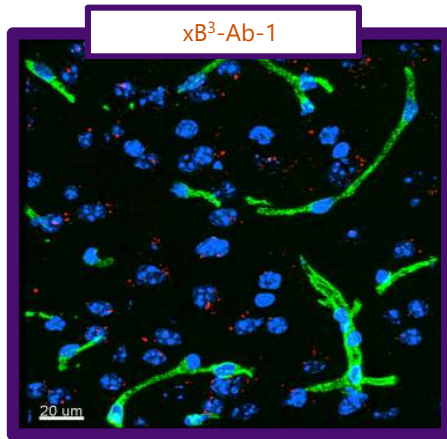
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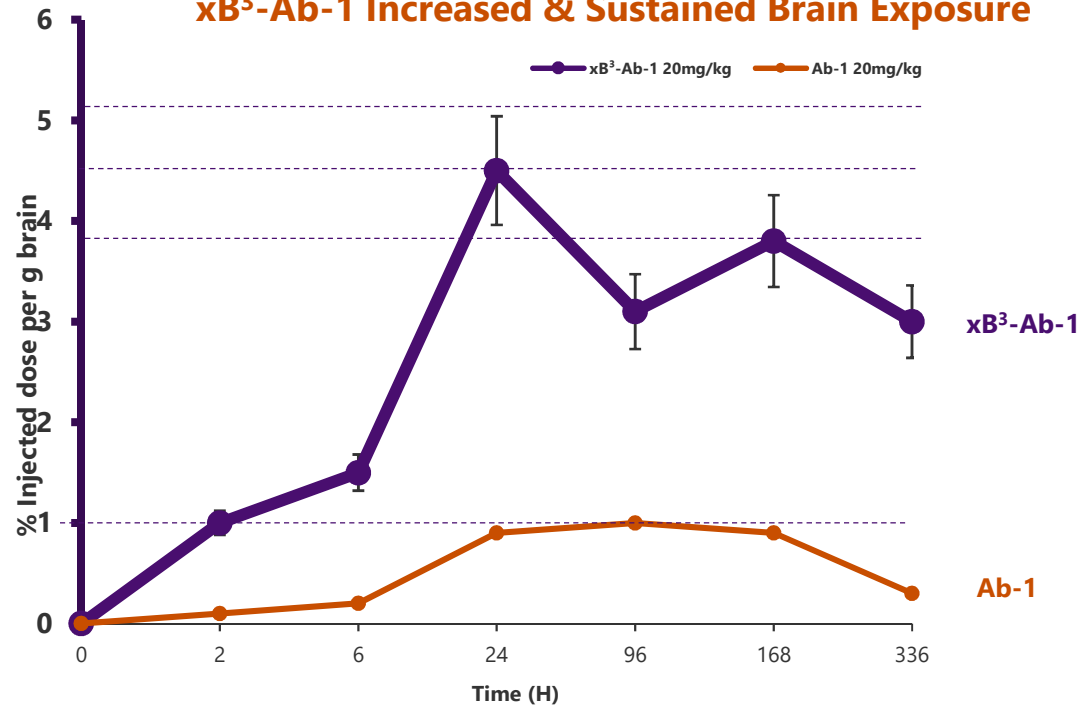
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Antibody Delivery: xB³-mAb Demonstrates Superior Brain Delivery



Antibody, Capillary, Nucleus

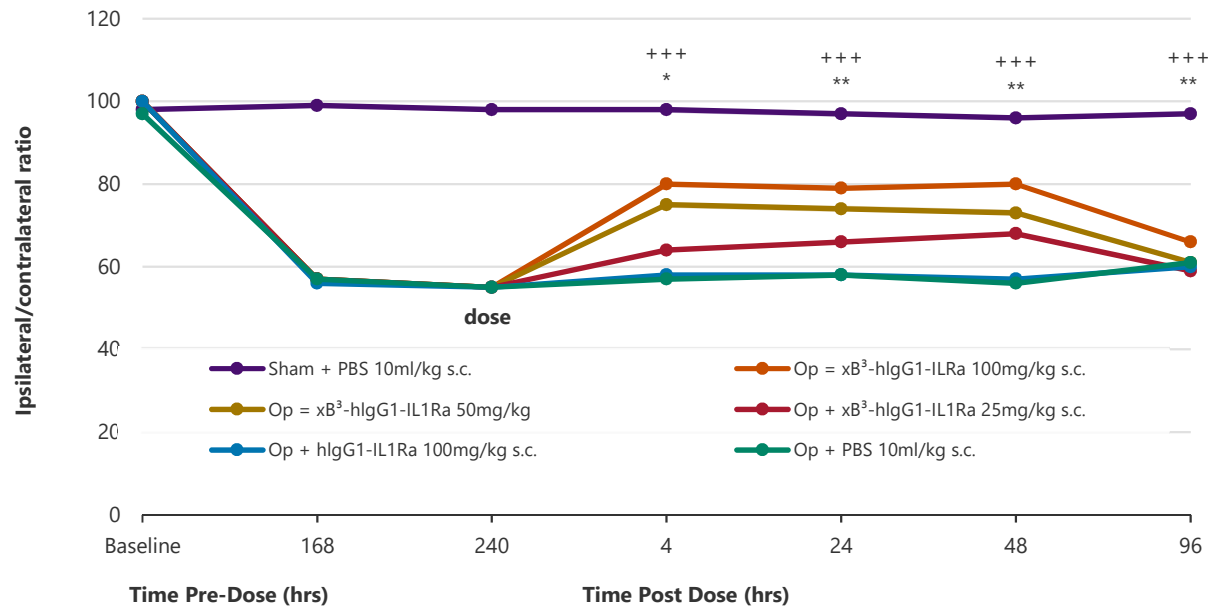
xB³-Ab-1 Increased & Sustained Brain Exposure



Mean ± SEM; n=6 mice/ molecule; single IV injection

Thom G. et al. (2018) *J Cereb Blood Flow Metab.* ePub May 30, 2018.

Antibody Delivery: αB^3 -IL-1RA Demonstrates Dose Dependent Therapeutic Efficacy in a Neuropathic Pain Mouse Model



Mean \pm SEM; n=7-10 mice/ molecule; single s.c. injection

Recent Achievements

- January 2019: Bioasis Announces Agreement With Leading Pharmaceutical Company for Pre-Clinical Research Using the xB³ Platform Technology
 - \$500,000 upfront, up to \$3M in R&D costs
- October 2018: Bioasis Announces xB³™ Platform Technology Licensing Agreement with Prothena
 - \$1M upfront, up to \$33M in milestones, additional royalty on product sales
- May 2018: Bioasis Announces Publication of Independent Validation of the Company's xB³™ Platform Technology
 - MedImmune collaboration

Strategic Approach:

Two Pillar Strategy to Maximize Value and Success

**Pipeline Programs:
Well-established medicines, fast path to BLA/NDA**

- De-risked programs
- Approved drugs, well-established with regulatory agencies, physicians and patients
- Orphan indications, including CNS cancers and rare genetic diseases with fast and cost effective paths to BLA/NDA submission

**Business Development:
Novel targets & drug candidates**

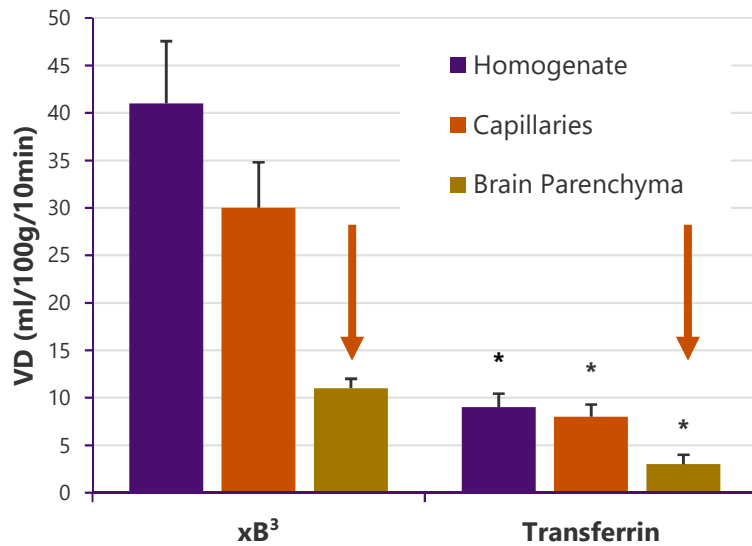
- Higher risk taken on by partner novel targets and new chemical entities
- Strategic partnering with selected Pharma
- Broaden utility and use of technology across multiple CNS disorders and treatment modalities
- Retain upside for Bioasis

Maximizing Value and Success of xB³ Platform

Appendix

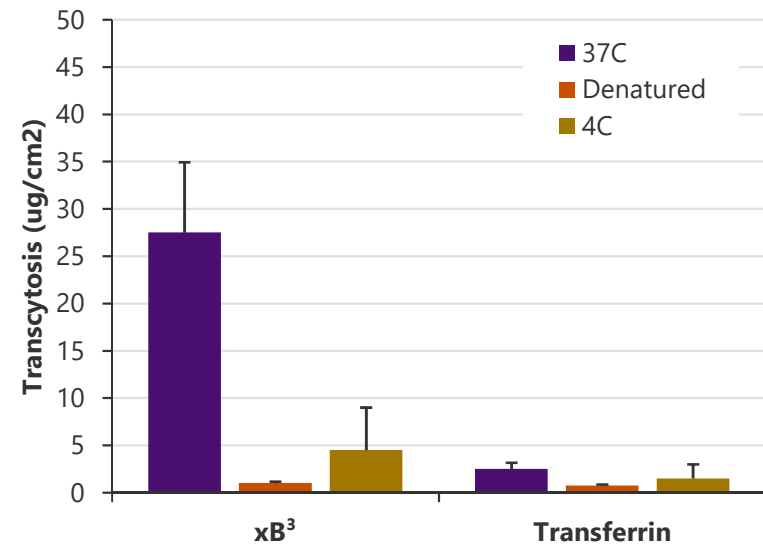
xB³ Platform is Superior to Transferrin

Greater Transport Efficiency



Mean ± SE * $p < 0.01$ Student's *t*-test (xB³ to Tf comparison) ; n=8 for xB³, n=6 for Tf

- xB³ platform shows superior volume of distribution in the brain compared to Tf as measured by in situ brain perfusion
- Mice perfused with 10 nM xB³ or Tf



Mean ± SE ; n=4 for 37C and 4C, n=2 for denatured

- xB³ platform shows superior transcytosis efficiency across BBB
- temperature-dependent and conformational-dependent process
- *In vitro* BBB transcytosis assay

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Cephalon)*



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Operations*

*Former BMS head
of specialty and
regional R&D
operations,
covering discovery
through life cycle
management*



**Mei Mei Tian,
Ph.D.**

*VP, Head of
External Research*

*15 years of
experience in xB³-
related research
Joined Bioasis in
2012*



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