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The Blood Brain Barrier Delivery Company

Opening the door to large molecule biologic therapies for neurological diseases

29 June 2020

BTI.V (TSX), BIOAF (OTCQB)

Forward Looking Information

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and forward-looking information within the meaning of Canadian securities legislation. This information and these statements, referred to herein as "forward-looking statements", are made as of the date of this presentation or as of the date of the effective date of information described in this presentation, as applicable. The forward-looking statements herein relate to predictions, expectations, beliefs, plans, projections, objectives, assumptions or future events or performance (often, but not always, using words or phrases such as "expects", "anticipates", "plans", "projects", "estimates", "envisages", "assumes", "intends", "strategy", "goals", "objectives" or variations thereof or stating that certain actions, events or results "may", "can", "could", "would", "might" or "will" be taken, occur or be achieved, or the negative of any of these terms and similar expressions).

All forward-looking statements are based on current beliefs as well as various assumptions made by, and information currently available to Bioasis. By their very nature, forward-looking statements involve inherent risks and uncertainties, both general and specific, and risks exist that estimates, forecasts, projections and other forward-looking statements will not be achieved or that assumptions do not reflect future experience. For a description of some of the risks that could cause our actual results to vary from those anticipated by forward-looking statements, please refer to the risk factors described in our filings with Canadian securities regulators, available at www.sedar.com. We caution any person reviewing this presentation not to place undue reliance on these forward-looking statements as a number of important factors could cause the actual outcomes to differ materially from the beliefs, plans, objectives, expectations, anticipations, estimates assumptions and intentions expressed in such forward-looking statements.

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Bioasis Strategy

xB^3 TM Platform : ***Best-in-class technology for BBB drug delivery***	**Delivery of Therapeutics Across the BBB Using Our Proprietary xB^3 Platform Technology** • Enables delivery of a variety of therapeutics across the BBB, including enzymes, siRNA, antibodies and other biologics (also small molecules) • 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 xB^3 delivery vector**, xB^3 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
Internal pipeline is focused on lower risk, expedited opportunities	**Initial Focus on Orphan Indications & Rare Genetic Diseases with High Unmet Medical Need Where Proof-of-Concept Exists** • **Lead program xB^3-001- xB^3 +Herceptin® for HER2+ breast cancer brain metastases**; Favorable FDA pre-IND meeting completed June 2019; potential for accelerated approval • **Second program xB^3-007 - xB^3+Cerezyme® for the treatment of Gaucher's Disease**; pre-clinical POC study will demonstrate CNS efficacy and confirm translational endpoints for human studies; potential for accelerated approval
Strategic partnering broadens uptake of the technology	**Partners are using the Bioasis xB^3 platform to deliver antibodies and siRNA therapeutics** • New licensing agreement with **Chiesi Group**, 4 undisclosed Lysosomal Storage Disease targets • Licensing agreement with **Prothena,** undisclosed neurodegeneration targets • Research agreement with **a major global pharma company**

Achievement of the indicated timelines is conditional upon the company securing the capital necessary to achieve the milestones as set out.

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Partnership with Chiesi Group

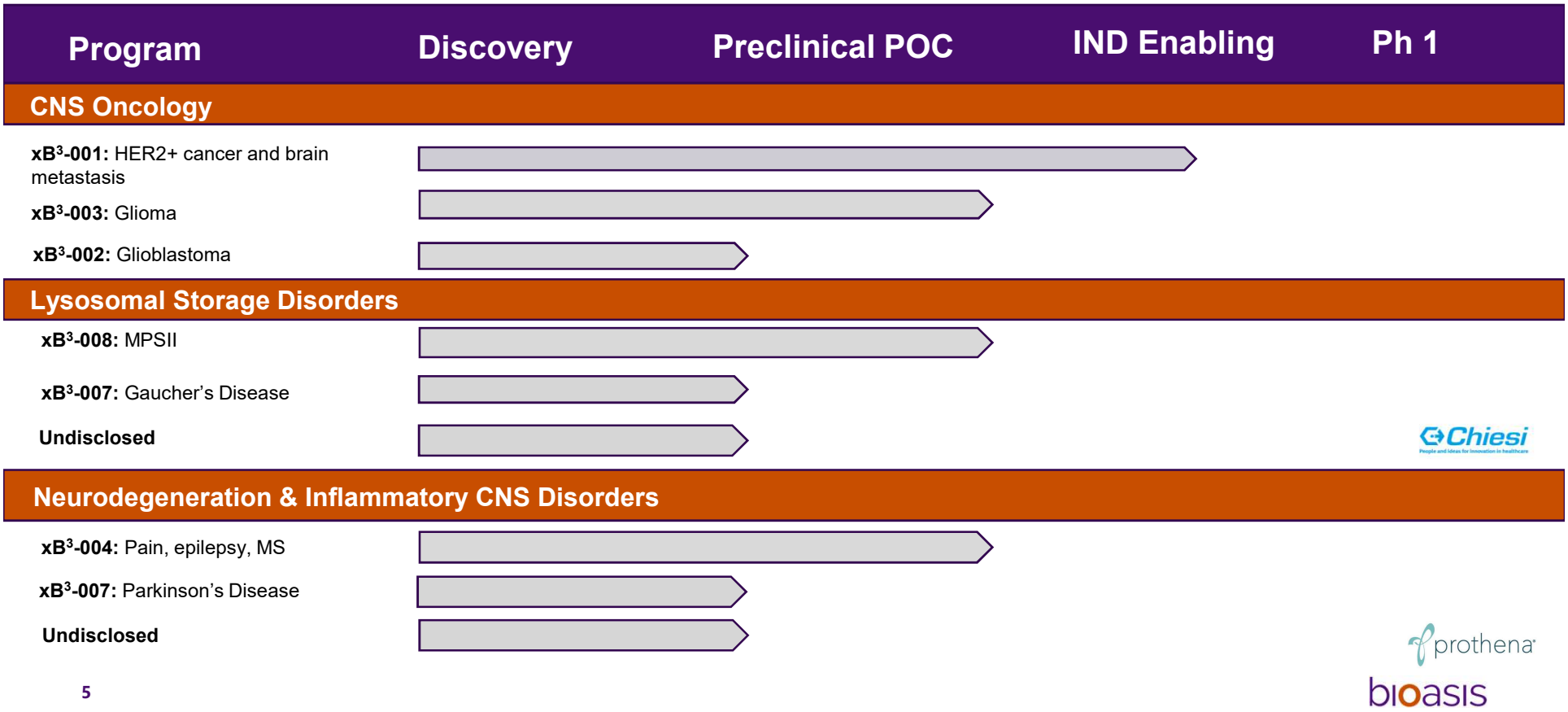
Bioasis and Chiesi Group Announced Rare Diseases Strategic Alliance on 29 June 2020

- Deal provides Chiesi Group with worldwide, exclusive license to use Bioasis xB^3 TM platform for delivery of undisclosed enzymes in treatment of four lysosomal storage disorders.
- Under terms of the agreement, Bioasis will receive an upfront payment of US$3 million, additional potential milestone payments of up to US$138 million and royalties on net sales from licensed products.
- Chiesi Group will be responsible for all costs associated with research, development and commercialization of the four undisclosed LSD programs.
- Giacomo Chiesi, Head of Chiesi Global Rare Diseases, a business unit of Chiesi Group: *"The unique delivery method of their xB^3 platform has the potential to overcome a significant challenge in the treatment of many neurological disorders, which is the ability to cross the blood brain barrier".*

Chiesi Global Rare Diseases bioasis

Bioasis Pipeline

Opening the door to large molecule biologic therapies for neurological diseases



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
- Significant market potential

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 xB^3 Platform Generating Multiple Inflection Points

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Partnering Provides External Validation of our xB^3 Platform

- Strategic Alliance with Chiesi Group in Rare Diseases
  - Upfront payment of US$3 million, additional potential milestone payments of up to US$138 million and royalties on net sales from licensed products.
- xB^3 ™ Platform Technology Licensing Agreement with Prothena
  - US$1M upfront, up to US$33M in milestones, additional royalty on product sales
- Agreement With Leading Pharmaceutical Company for Pre-Clinical Research Using the xB^3 Platform Technology
  - US$500,000 upfront, up to US$3M in R&D costs
- Publication of Independent Validation of the Company's xB^3 ™ Platform Technology
  - MedImmune collaboration

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Investment Highlights

- Best in class technology for delivery of drugs into the brain:
  - Outperforms other delivery technologies, able to deliver diverse payloads into the brain
  - Protected by a well-developed patent portfolio and intellectual property strategy
- Significant commercial potential in de-risked pipeline:
  - Lead product xB^3-001 targets HER2+ breast cancer and brain metastases
    - Worldwide peak revenue potential $440m (brain metastases) to $3.7b (standard of care)
    - Potential for accelerated approval
  - Robust pipeline includes non-opiod treatment for pain and inflammation, enzyme replacement therapy for Gaucher's Disease and Parkinson's disease, and treatments for brain cancers
- Partnerships with **Prothena** in neurodegeneration and **Chiesi Group** in Lysosomal Storage Disorders

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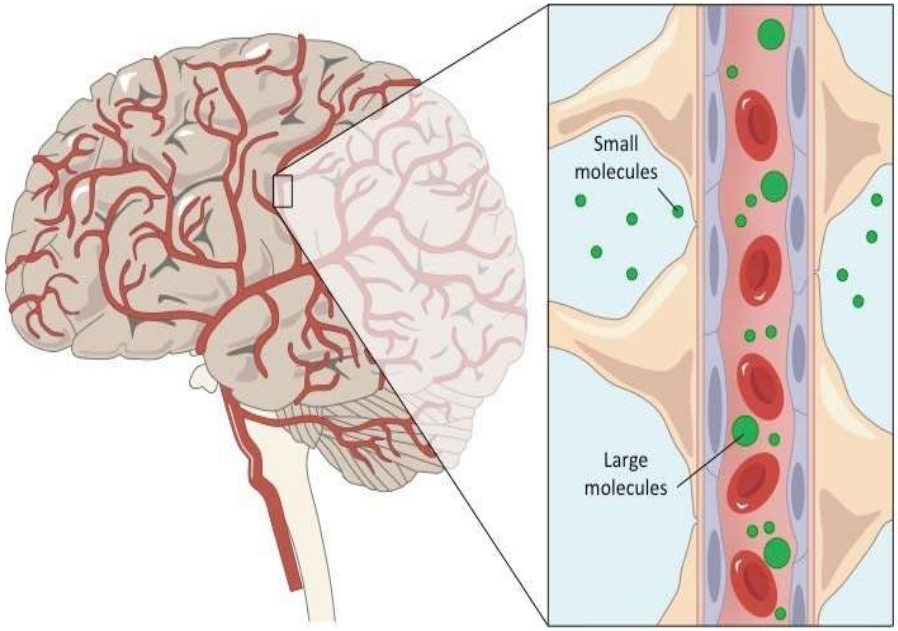
xB³ Platform Technology

The Blood Brain Barrier

- The blood-brain barrier (BBB) is a highly selective barrier that separates circulating blood from the brain and extracellular fluid in the CNS.
- The BBB functions to prevent the movement of bacteria, large molecules and most small molecules into the brain.
- The purpose of the blood-brain barrier is to protect the brain; however brain diseases are difficult to treat as the BBB significantly hinders the delivery of therapeutics to the brain.
- The ideal method for transporting drugs across the BBB should be controlled and should not damage the barrier in order to maintain its protective effects.



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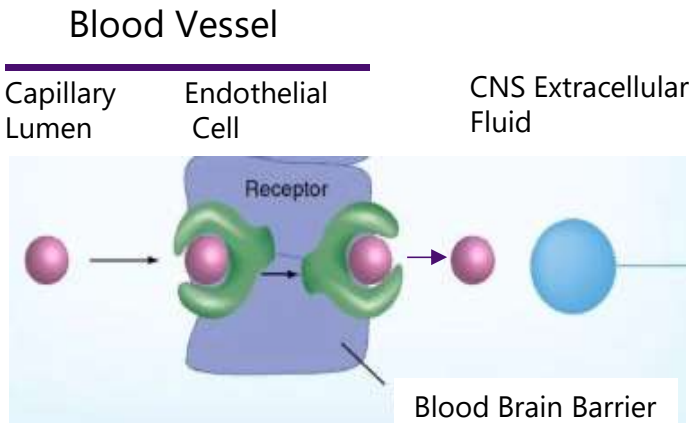
The Bioasis Platform Technology
Active Transport Across the BBB via the LRP1 Receptor



xB^3 Peptide

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

- xB^3 has been optimized by Bioasis' scientists to its key constituents (12 amino acids)
- xB^3 has shown improved brain penetration over the full-length protein

Mechanism of Action (MOA)

xB^3 binds to, and moves into cells via receptor-mediated endocytosis/transcytosis involving 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

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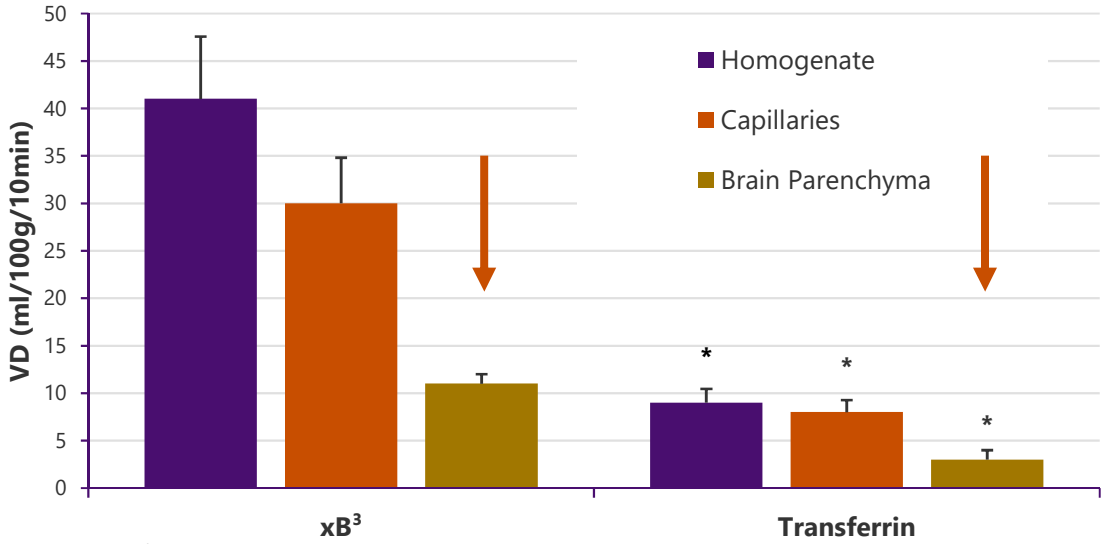
xB^3 Platform is Superior to Transferrin

Greater CNS Transport Efficiency demonstrated in vivo

xB^3 platform demonstrates superior volume of distribution in the brain compared to Transferrin as measured by *in situ* brain perfusion



Mean ± SE * $p<0.01$ Student's *t*-test (xB^3 to Transferrin comparison)
n=8 for xB^3, n=6 for Transferrin
Mice perfused with 10 nM xB^3 or Transferrin

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

Demeule et al. (2002). J. Neurochem. 83, 924-933.

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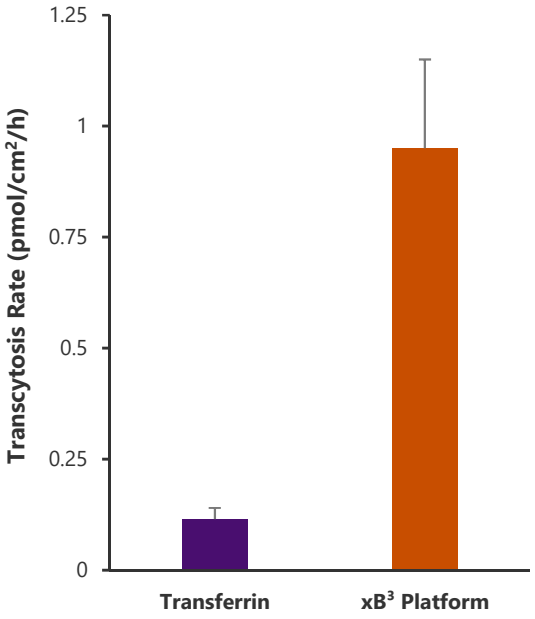
The xB³ Platform Technology
Outperforms Competing BBB Technologies

xB³ demonstrates superior transcytosis across *in vitro* BBB model (BBCEC)



** Bioasis internal data **

Features	Bioasis xB³ Platform	Denali	Genentech	Roche	Armagen	Angiochem
% injected dose in brain	4-6%	1-1.5%	1-1.5%	1-1.5%	1-1.5%	~1.5%
Mode of Action	LRP1	TfR	TfR	TfR	TfR and IR	LRP1
Payload Modalities						
Antibodies	✓	✓	✓	✓	✓	✓
Enzymes	✓	✓			✓	
siRNA	✓					
Small molecules	✓					✓

References: %ID/g brain based on 24 hr timepoint whenever available
[1]Thom G. et al. (2018) J Cereb Blood Flow Metab. ePub May 30, 2018.
[2]Extrapolated from data in Denali therapeutic annual report on form 10-K; Mar 2018
[3]Bien-Ly N, Yu YJ, Bumbaca D, et al. J Exp Med. 2014;211(2):233–244.
[4]Lajoie JM, Shusta EV. Annu Rev Pharmacol Toxicol. 2015;55:613–631.
[5]Weber F. et al., Cell reports. 2018; 22(1): 149-162
[6]Boado R., Pardridge WM., Mol Pharm. 2017 Apr 3; 14(4):1271-1277
[7]Zhou et al., Mol Pharm. 2010 Dec 6; 7(6):2148-2155
[8]Lu F, Pang Z, Zhao J, et al. Int J Nanomedicine. 2017;12:2117–2127
[9]Van Rooy I. et al., Pharm Res. 2011 Mar;28(3):456-471.

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The xB^3 Platform Technology

Key Advantages

Enables the delivery of large molecule therapeutics across the BBB into the CNS

- Improved brain uptake over competing technologies
- Enables targeting of previously unreachable CNS targets

Capable of delivering large and small molecules across the BBB

- Antibodies
- siRNA
- Enzymes
- Proteins
- Small molecules

Does not impact either PK, binding, or activity of payload

- Herceptin

Nounou et al. Pharm Res. December 2016, 11 33(12); 2930-2942

- IL1-RA

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

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xB^3 Platform Validation

Brain penetration

- Confocal microscopy to demonstrate brain uptake of labelled payload
- Brain PK
- Target engagement
  - Target, payload co-localization

Pharmacodynamic biomarkers

- Target engagement
  - Modulation of target activity
- Downstream biomarker modulation

Preclinical POC

- Brain tumor models
  - Metastasis & primary tumor models
- Pain
- Lysosomal Storage Disorder (LSD) models
- Stroke

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Independent validation of the xB^3 platform

Antibodies and Cytokines – IL-1RA preclinical POC in neuropathic pain-Medimmune collaboration

Enzymes – Preclinical POC in Hunters Syndrome – University of Padova

siRNA – Preclinical POC in ischemic induced stroke mouse model – National Research Council of Canada (see Appendix slides for detail)

Small molecule – Preclinical POC in the treatment of intracranial tumors – University of British Columbia (see Appendix slide for detail)

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The Blood Brain Barrier Company

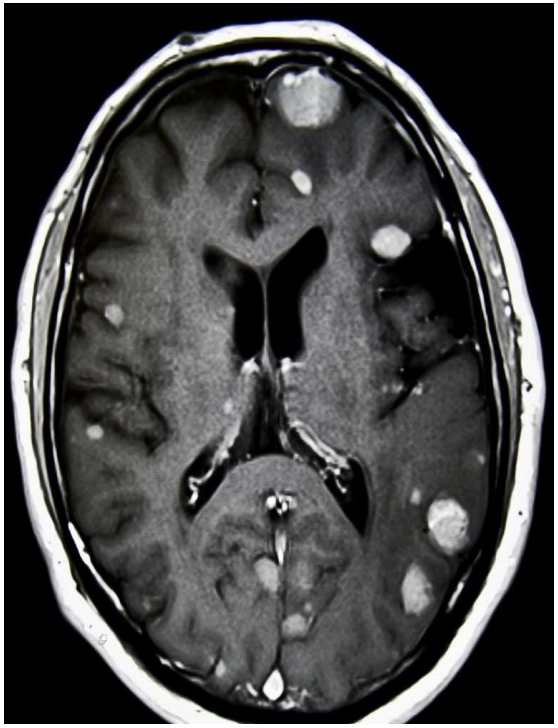
Lead Program : xB^3-001 (xB^3 - Trastuzumab) for the Treatment of HER2+ Breast Cancer and Brain Metastases

xB^3-001 (xB^3 - Herceptin) Summary

Indication	**TREATMENT OF HER2+ BREAST CANCER AND BRAIN METASTASES**
Preclinical Evidence	• Confocal microscopy demonstration of enhanced brain uptake in normal murine brain • Autoradiographic demonstration of co-localization with brain metastases, higher calculated brain concentrations associated with brain metastases compared to concentrations in brain regions distal to metastases, overall 10-fold higher drug levels in brain • No adverse effects on peripheral efficacy or PK, peripheral efficacy equal to TZM in murine HER2+ breast cancer model • ***Reduced both the number and size*** of established brain metastases in a HER2+ murine breast cancer model
Development Milestones Achieved	• Pre-IND filing, favorable response from the FDA to IND enabling studies and clinical plan • Pilot manufacture completed by WuXi with demonstration of brain penetrance of manufactured material by confocal microscopy • Assay development advanced for IND enabling studies
Anticipated Development & Clinical Milestones	• Completion of GMP manufacture • Completion of toxicology • IND submission (2021) and initiation of Phase 1b component of trial (2022) • Completion of dose escalation phase and EOPI meeting (2023) • Completion of Phase 2 expansion cohort (2023)

Breast Cancer Brain Metastases: Unmet Clinical Need

- Brain metastases are among the most common form of brain cancer in adults, with an estimated 200,000 patients newly diagnosed each year in the United States.
- Breast cancer is the second most common cause of brain metastases and is associated with increasing mortality rates and poor quality of life.
- HER2(+) breast cancers often show faster growth and metastasis compared to HER2 (-) breast cancers, with up to 50% of HER2+ patients developing brain metastases over time.
- ***Most systemic treatments do not penetrate the BBB***
- ***Current treatment options are limited***
- ***Safer and more effective treatment for brain metastases are needed***



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xB^3-001 is Designed to Improve upon the Efficacy of Herceptin, Improving upon CNS Disease Control and Potentially Development of CNS Metastases

xB^3-001 in HER2+ mBC

xB^3-001	Product Attribute
✓	Utilizes the most widely used HER2-targeting agent, trastuzumab
✓	Does not impact the PK, binding, or activity of the trastuzumab payload
✓	Localizes in the brain better and shows 10-fold higher concentration of trastuzumab in metastases
✓	Retains peripheral disease control in xenograft models
✓	Safety profile that should allow for use in combination with other agents

xB^3-001 could launch as HER2-targeted therapy of choice in 2L+ patients with CNS metastases

Demonstrating superiority to Herceptin in CNS disease prevention would position for broad use

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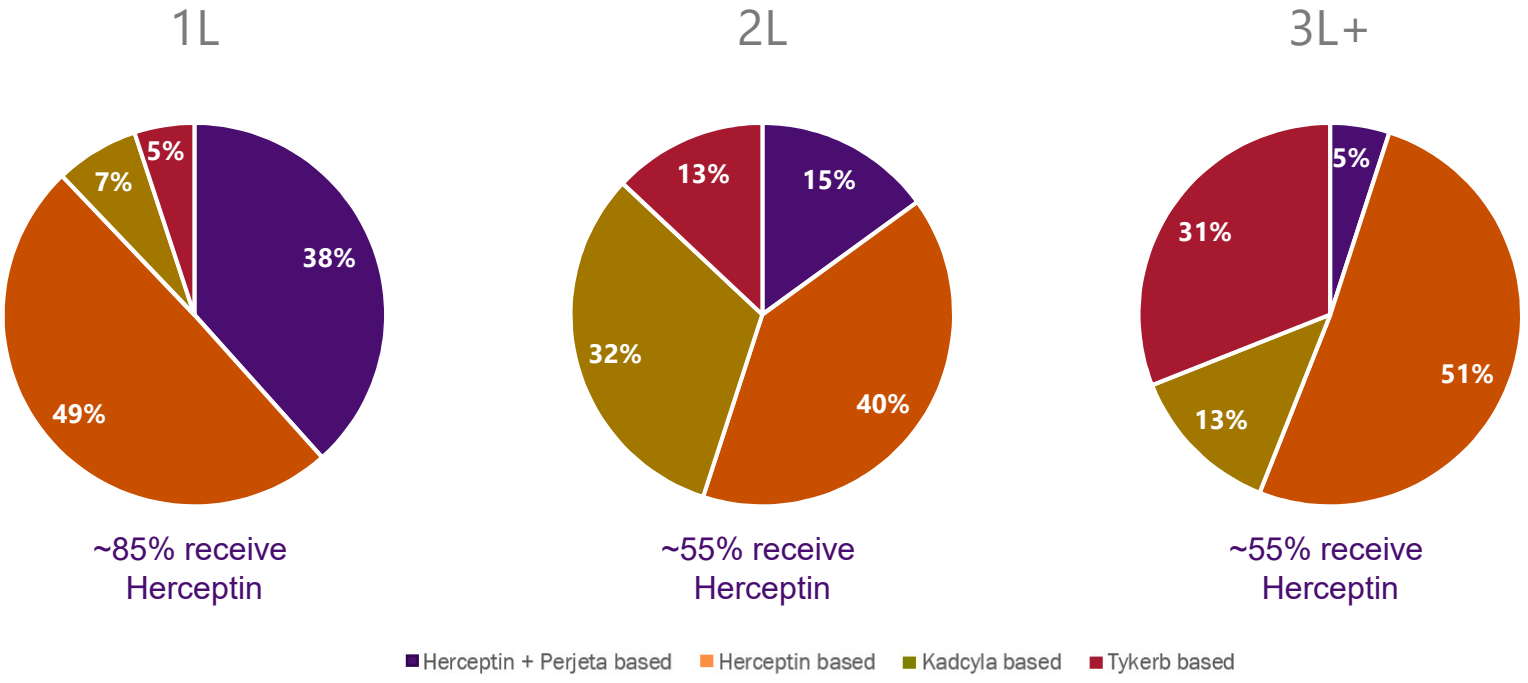
The Majority of HER2+ mBC Patients Receive Herceptin in all Lines of Therapy

Market Share for HER2-Targeting Agents by Line of Therapy



Source: Kantar Treatment Architecture

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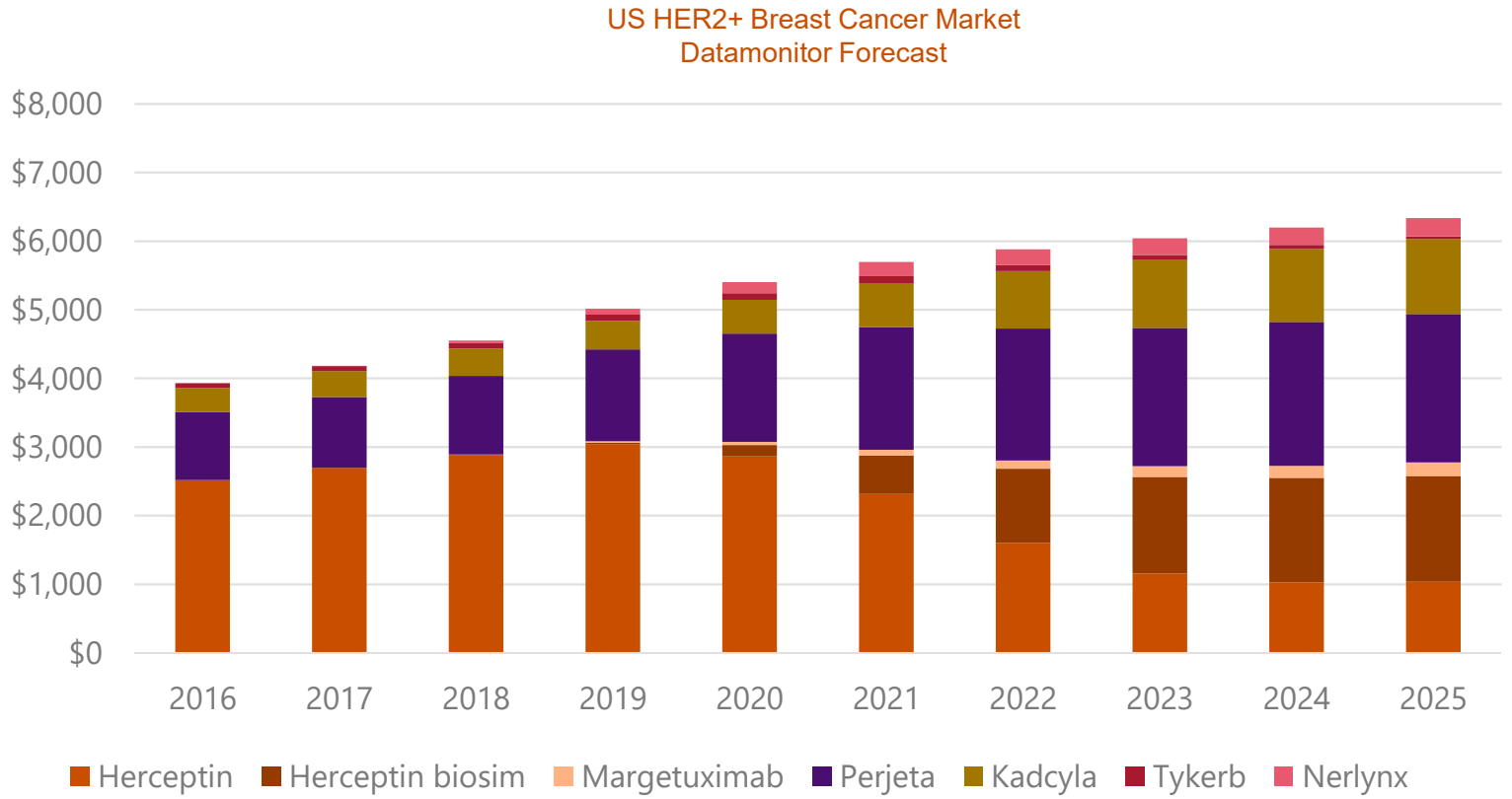
Datamonitor Expects Continued Growth of the US HER2+ Breast Cancer Market, Reaching >$6B by 2025



Source: Datamonitor

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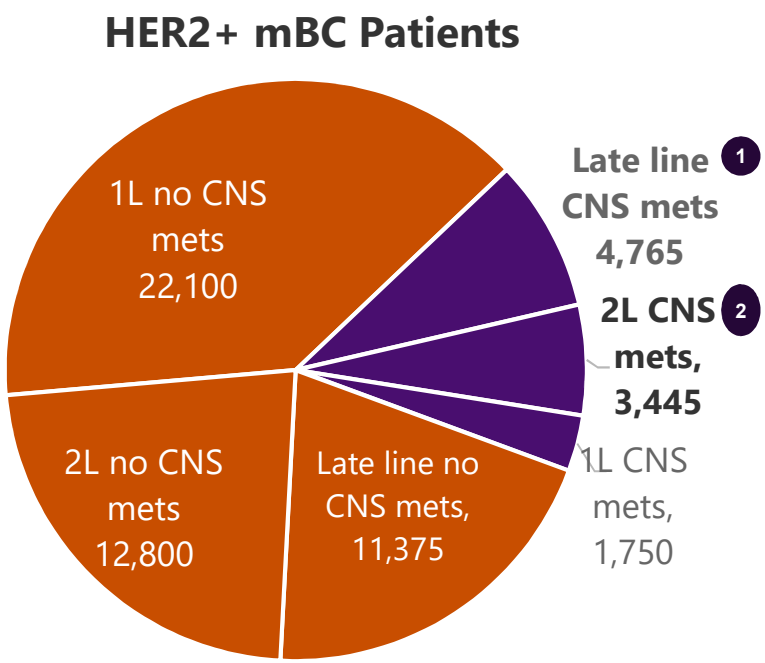
xB^3-001 Revenue Potential for 2L+ Patients with CNS Metastases is ~US$440M Worldwide

Market Potential – xB^3-001 CNS Metastases Treatment



CNS Metastases Treatment

Late Line

Improved CNS disease control in 3L+ patients
~4,765 candidates (1)
8 mos median duration of therapy

Market Potential
$380M US/$760M WW

xB^3-001 Potential (@ 30% share)
$115M US/$230M WW

2L+

Superior to Kadcyla in 2L+ patients with CNS mets
~8,210 candidates (1) (2)
10 mos median duration of therapy

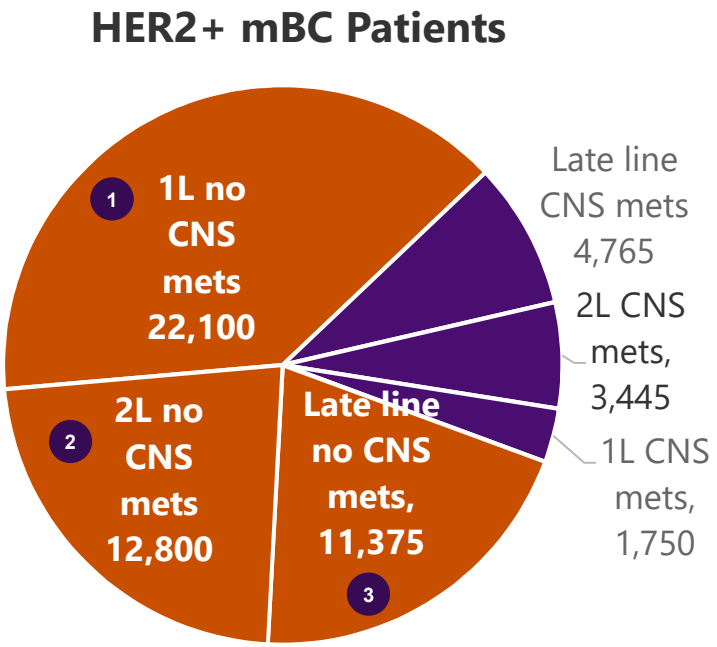
Market Potential
$725M US/$1.45B WW

xB^3-001 Potential (@ 30% share)
$220M US/$440M WW

Source: NCI SEER; Kantar Patient Metrics and Treatment Architecture; Datamonitor

Assumptions: Price of $10,000 per month, in between Herceptin and Kadcyla; US accounts for 50% of WW sales

Market Potential – xB^3-001 CNS Metastases Prevention



CNS Metastases Prevention

2L+ Patients without CNS Metastases

~24,000 candidates (2) (3)

8-10 mos median duration of therapy

Market Potential

$2.2B US/$4.4B WW

xB^3-001 Potential (@ 30% share)

$660M US/$1.32B WW

1L+ Patients without CNS Metastases

~46,000 candidates (1) (2) (3)

8-18 mos median duration of therapy

Market Potential

$6.2B US/$12.4B WW

xB^3-001 Potential (@ 30% share)

$1.85B US/$3.7B WW

Bluestar BioAdvisors

Source: NCI SEER; Kantar Patient Metrics and Treatment Architecture; Datamonitor

Assumptions: Price of $10,000 per month, in between Herceptin and Kadcyla; US accounts for 50% of WW sales

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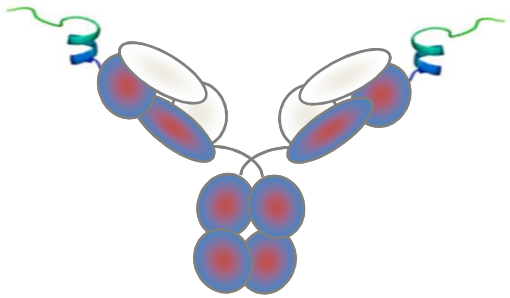
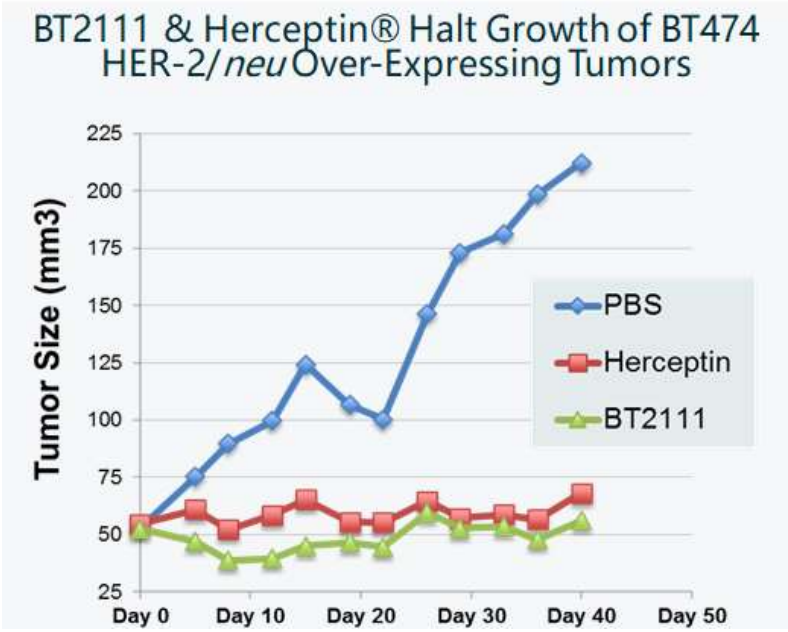
xB^3-Herceptin Retains Peripheral Anti-Tumor Efficacy in the BT474 Xenograft Model

xB^3 can be added to a therapeutic through chemical conjugation or fusion





BT2111 = xB^3-001 (xB^3-Herceptin)
Ip injection 2x/wk for 5 weeks; 10mg/kg molar equivalent; n=10

Work performed at Biopharmaceutical Research Inc.

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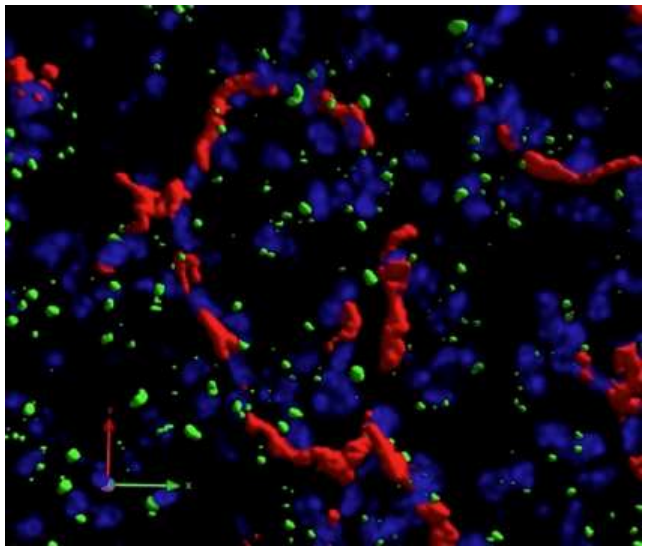
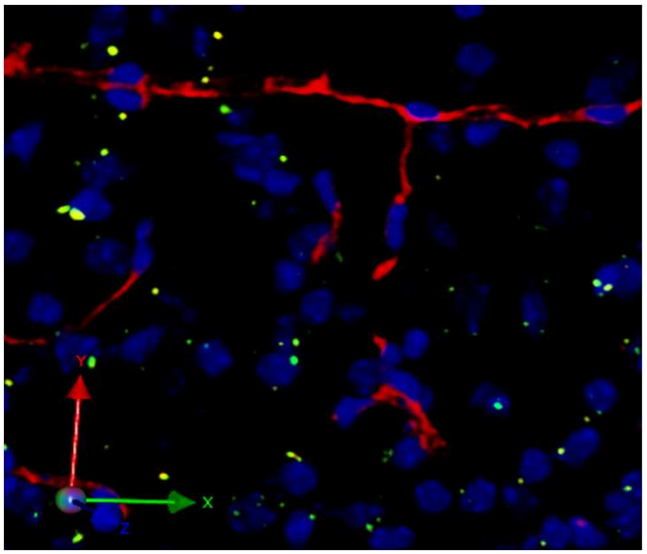
xB^3- 001 Demonstrates Significantly Increased Localization in Brain Parenchyma Compared to Herceptin®

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



xB^3-Herceptin

Red: Brain capillaries
Blue: Brain Nuclei
Green: xB^3-Herceptin in brain



Herceptin

Red: Brain capillaries
Blue: Nuclei
Green: Herceptin in brain

Work performed at National Research Council of Canada – Research Facility

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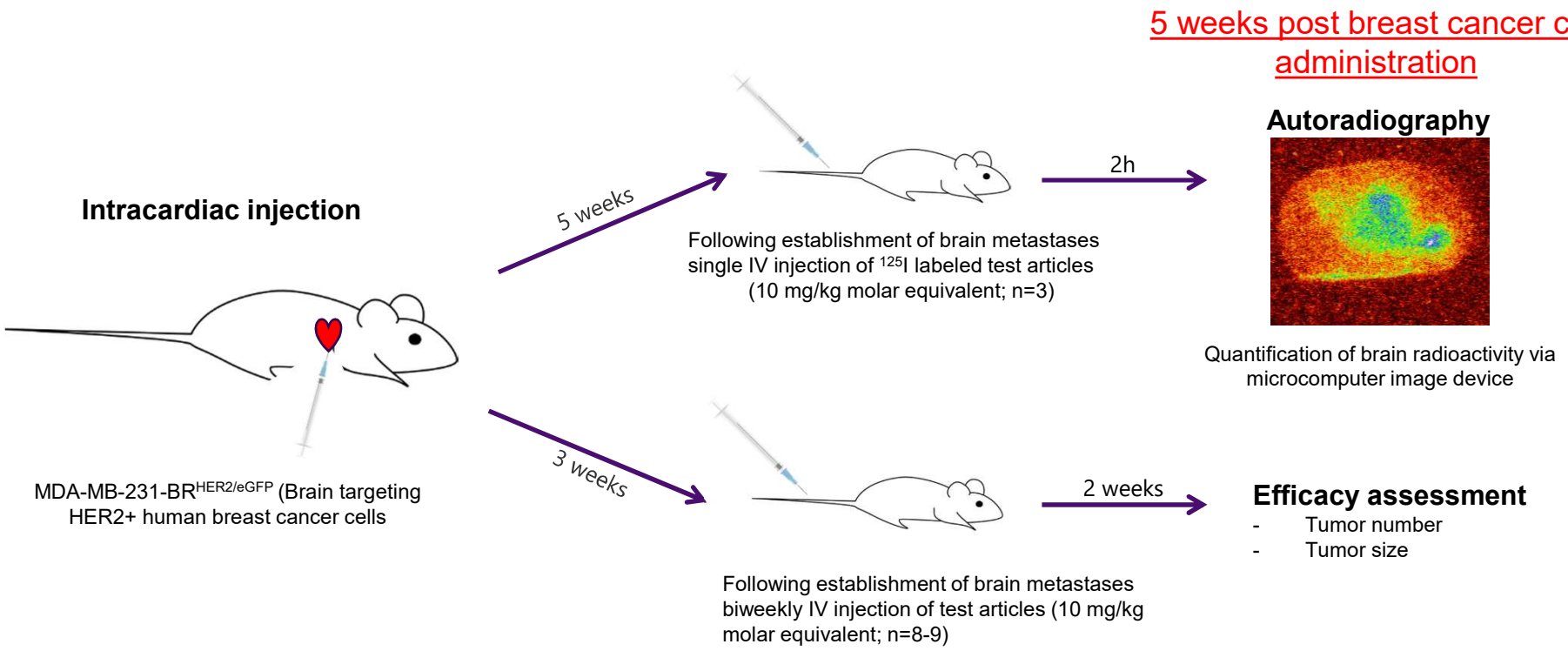
HER2+ Human Breast Cancer Brain Metastasis Mouse Model



Nounou, MI, et al. Pharm Res. 2016 Dec;33(12):2930-2942. Epub 2016 Aug 15

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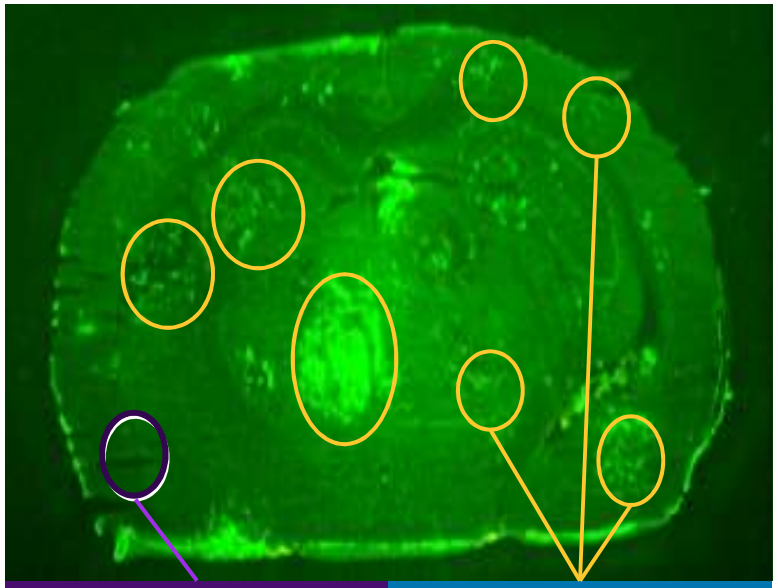
xB^3-001 in Human HER2+ Brain Metastasis Mouse Model

Target Engagement and Biological Effects

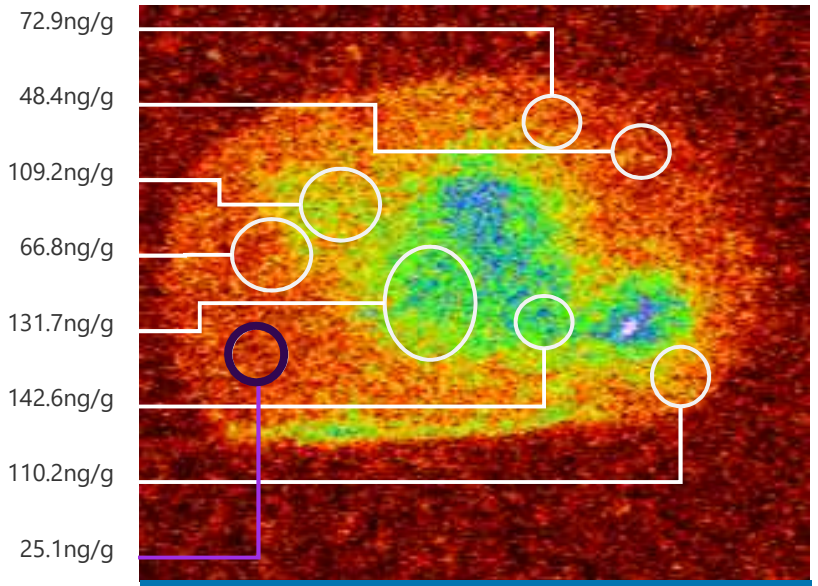
Metastases localization 5 weeks Post Inoculation



Brain tissue distal to tumors (BDT) | **Breast cancer metastasis distributed throughout the brain**

MDA-MB-231-BR$^{HER2/eGFP}$ breast cancer cell line injected in the left cardiac ventricle of mice.

Concentrations of xB^3 -001 within Brain Regions at 2hrs post dose



Preferential uptake of radio-labeled xB^3-001 conjugate into tumors compared with BDT

Single injection of ^{125}I-xB^3 -001 administered 5 weeks after initial intracardiac injection of cells and establishment of brain metastases.

Nounou, MI, et al. Pharm Res. 2016 Dec;33(12):2930-2942. Epub 2016 Aug 15

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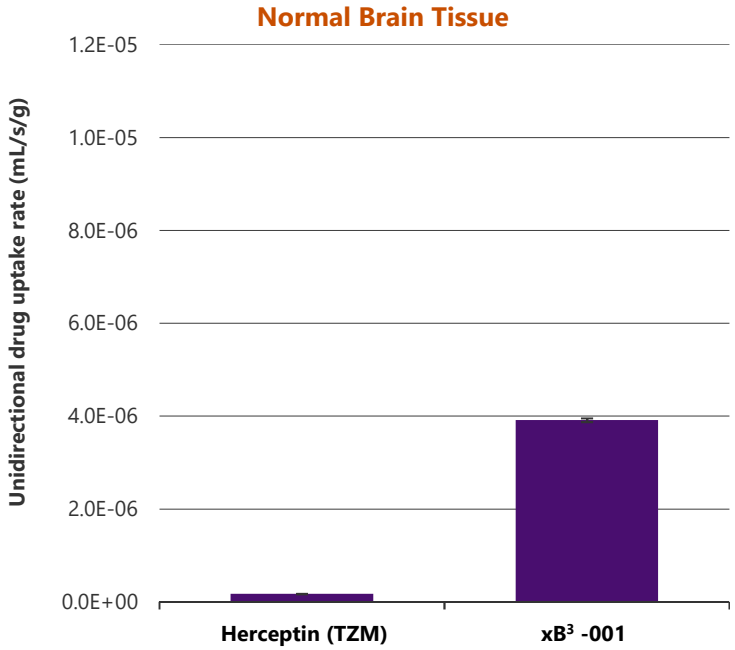
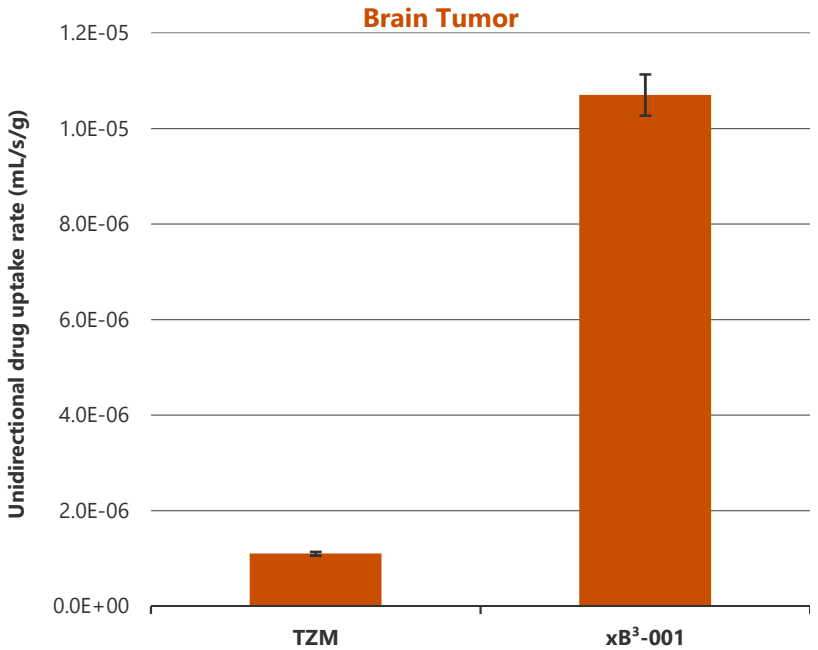
xB^3 Platform Delivers 10-Fold Higher Herceptin® to Brain Metastases



Mean ± SD; n = 61 (TZM), n = 77 (xB^3 -001); single dose; up to 8 hrs post dose.



Mean ± SD; n = 336 (TZM), n = 213 (xB^3 -001); single dose; up to 8 hrs post dose

Nounou, MI, et al. Pharm Res. 2016 Dec;33(12):2930-2942. Epub 2016 Aug 15

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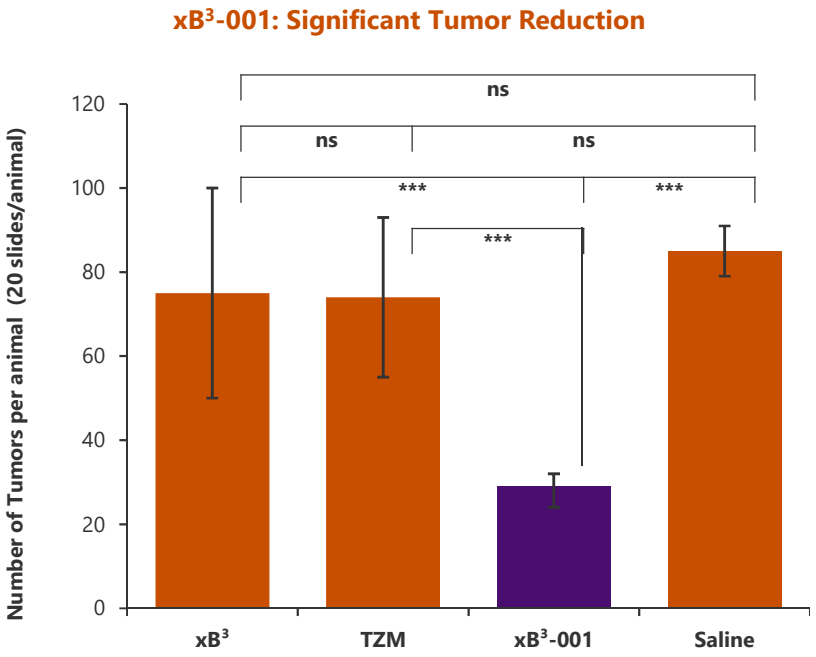
xB^3 Platform Delivers Herceptin® (Trastuzumab, TZM) to Brain Metastases and Reduces Both Tumor Number and Size



TZM: Trastuzumab; n= 13 for xB^3, TZM groups; n=8-9 for xB^3 -001, Saline groups. Biweekly IV treatment for 2 weeks. 10mg/kg molar equivalent. One-way ANOVA **P<0.001, ***P<0.001, ***P<0.0001 Mean+/-SEM

Group	Tumor size based on pooled data from all individual values in group	
	# of tumor	Tumor size (mm^2) Mean ± STDEV
Saline control (n=9)	765	1.654 ± 1.673
xB^3 -001 (n=8)	223	0.710 ± 0.727[1]
TZM (n=13)	962	1.402 ± 1.217

[1]. xB^3 -001 group vs. TZM group *P*<0.001

xB^3 -001 vs. TZM Treatment

- Reduced tumor number by 68%
- Tumors that remained after treatment were 46% smaller
- TZM treatment show no effect on reducing number of metastases with negligible reduction in tumor size

Nounou, MI, et al. Pharm Res. 2016 Dec;33(12):2930-2942. Epub 2016 Aug 15

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xB^3 – 001 Path to Market

- **If clinically active, xB^3-001 has the potential to be a candidate for accelerated approval:**
  - Addresses a serious or life-threatening condition.
  - Must demonstrate an effect on an intermediate clinical endpoint or surrogate endpoint, for example tumor shrinkage, in a way that is reasonably likely to predict clinical long-term benefit and can be measured earlier than that benefit. **As brain metastases determine the prognosis of HER2+ MBC patients they are a good surrogate for clinical benefit (survival).**
- **A non-inferiority study is not required as Herceptin is not effective in treating HER2+ brain metastases**
- **xB^3 – 001 accelerated approval study:**
  - The FDA have indicated that Bioasis should seek a meeting at the end of the Phase 1 component of the currently planned trial. At this time the company may have an opportunity to discuss an accelerated approval strategy and study design.

A Strong Patent Portfolio Underpins Bioasis' Platform and Products

Patent portfolio covers Bioasis' platform technologies (their uses and indications)

- Comprises over 120 patents and pending applications (10+ patent families) covering xB^3, p97, fusion proteins of p97 or xB^3 with antibodies, including trastuzumab, bevacizumab, and other payloads
- Key xB^3 patent granted in U.S. (expires in 2034; additional patent term extension up to 5 years)
- Patents have been filed in major geographic markets and have expiration dates in 2034-2035 (plus patent term extensions)

Patent pending for xB^3-trastuzumab (xB^3-001) - and uses/indications

- Patents have been filed in major geographic markets with expiration date in 2035 (plus patent term extensions)
- In June 2019, the European Patent Office issued allowance of a patent application relating to trastuzumab/xB^3 conjugates including xB^3-001, Bioasis' lead product in development for the treatment of HER2+ breast cancer brain metastases.

Additional patents pending for other xB^3-related innovations

- Enzyme Replacement, e.g., Gaucher disease
  - In June 2019, the U.S. Patent Office and Trademark and European Patent Offices issued allowances of patent applications relating to iduronate-2-sulfatase, or IDS, polypeptide/xB^3 conjugates for the treatment of Hunter Syndrome a Lysosomal Storage Disorder.
- Brain transport plus lymphatic engagement
- Innovations in the areas of combination therapies, fusion proteins with various antibodies, CNS-targeted conjugates, treatment of neuropathologies and pain, as well as other innovations. Generally, these patents, when granted, have expiration dates from 2023 to 2037.

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xB³ Platform Technology

MedImmune - Bioasis Collaboration

MedImmune

Original Article

JCBFM
Journal of Cerebral Blood Flow & Metabolism
0(00) 1–15

DOI: 10.1177/0271678X18772998
journals.sagepub.com/home/jcbfm
SAGE

A peptide derived from melanotransferrin delivers a protein-based interleukin 1 receptor antagonist across the BBB and ameliorates neuropathic pain in a preclinical model

George Thom[1], Mei-Mei Tian[2], Jon P Hatcher[3], Natalia Rodrigo[1], Matthew Burrell[1], Ian Gurrell[3], Timothy Z Vitalis[4], Thomas Abraham[5], Wilfred A Jefferies[6], Carl I Webster[1] and Reinhard Gabathuler[4]

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

Received 31 July 2017; Revised 23 March 2018; Accepted 26 March 2018

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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[5]Neural and Behavioural Sciences & Microscopy Imaging Core Lab, College of Medicine, The Pennsylvania State University, Hershey, PA, USA
[6]The Michael Smith Laboratories, University of British Columbia, Vancouver, BC, Canada; The Vancouver Prostate Centre, Vancouver General Hospital, Vancouver, BC, Canada; The Djavad Mowafaghian Centre for Brain Health, University of British Columbia, Vancouver, BC, Canada; Centre for Blood Research and Departments of Microbiology and Immunology, Medical Genetics, and Zoology University of British Columbia, Vancouver, BC, Canada

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MedImmune Collaboration:

Independent Validation of Bioasis Technology

Why

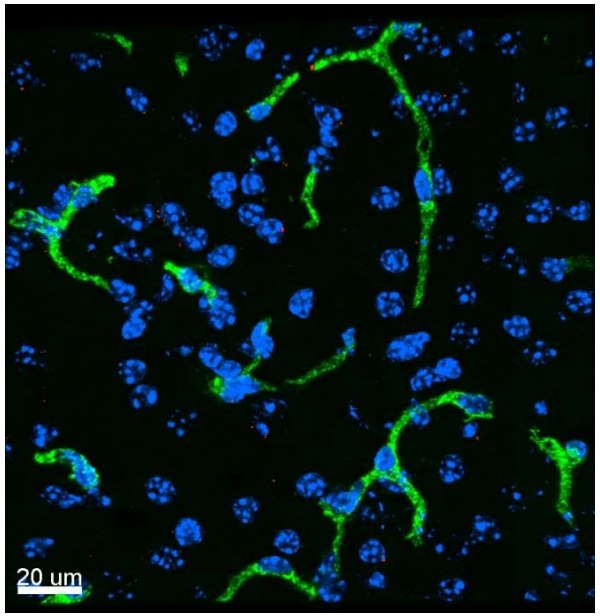
- MedImmune was evaluating blood-brain barrier platforms using test antibodies for brain delivery
- They evaluated **eight** blood-brain companies and selected Bioasis
- The selection was based on speed of delivery, superiority to transferrin and multi-modality potential

How – illustrative of the approach in a typical program

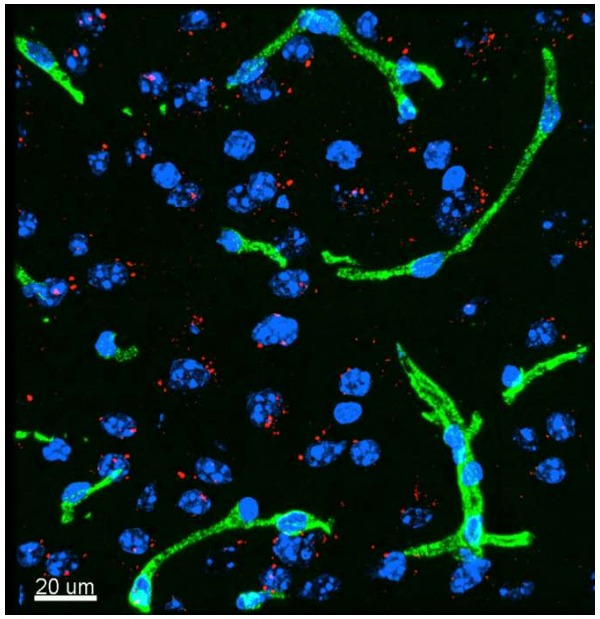
- Measured brain uptake by confocal microscopy
- Measured systemic and brain PK in wild-type mice (xB^3-hIgG1) , followed by a PD study in a mouse neuropathic pain model (xB^3-hIgG1-IL1RA)

xB^3 Facilitated the Penetration and Preferential Localization of Antibodies in the Brain Parenchyma

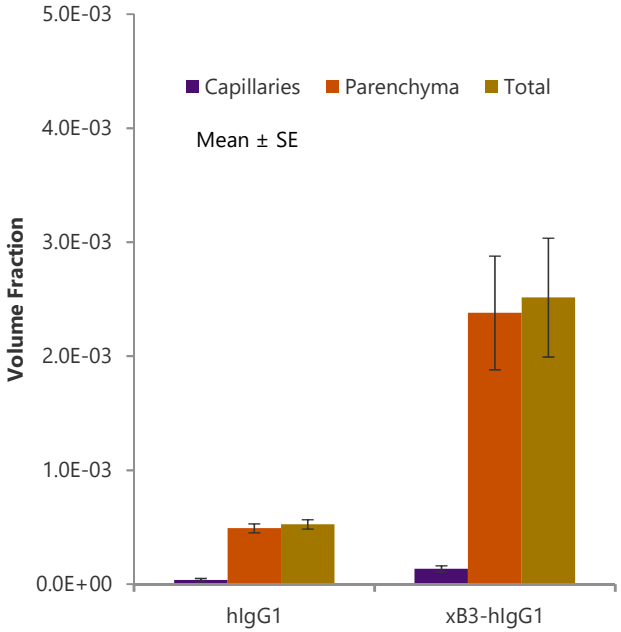
Confocal Images Two Hours Post Single IV Administration (10mg/kg) in Wild-type Mice



hIgG 1
Capillary
Nucleus



xB^3-hIgG1
Capillary
Nucleus



Mean ± SEM; n=3 mice/ molecule; single IV injection

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

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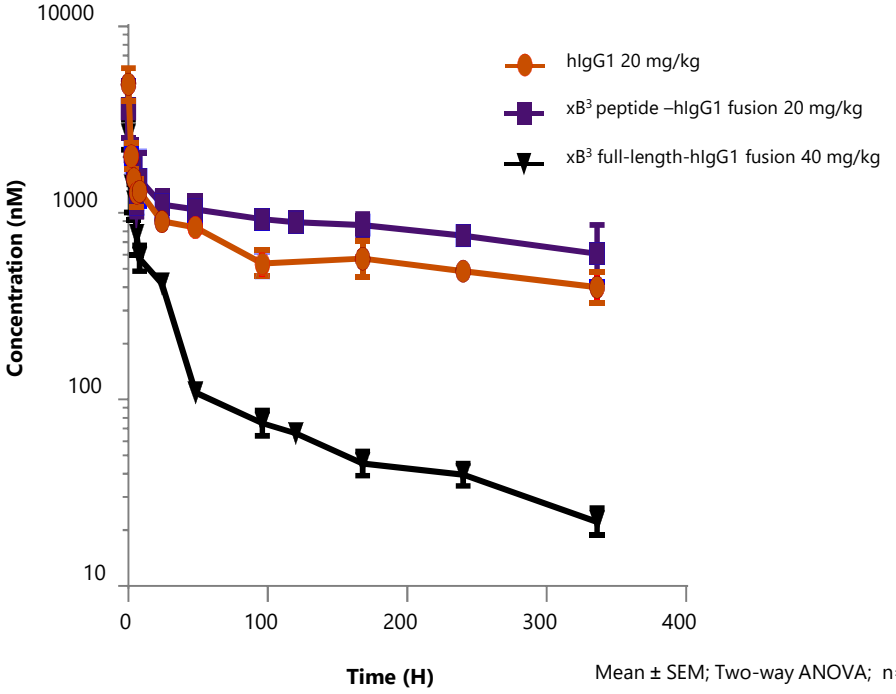
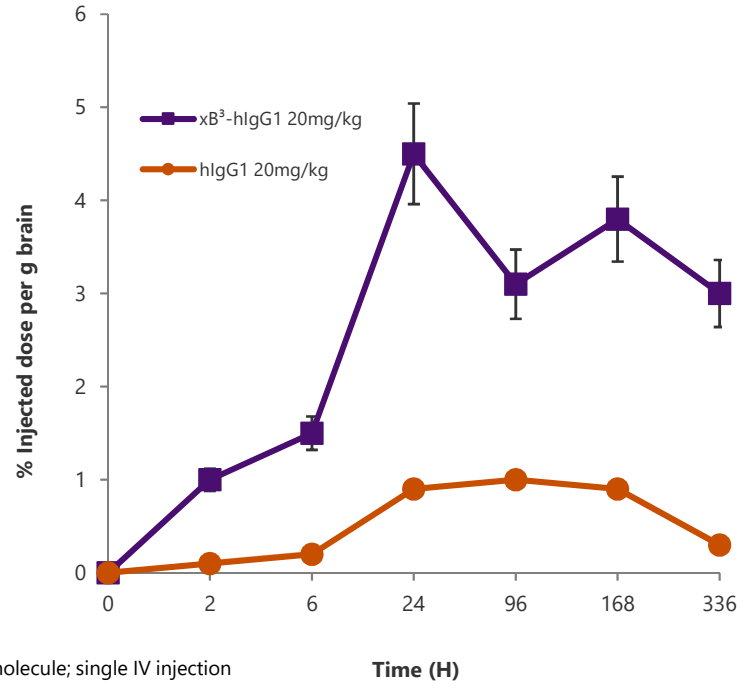
xB^3 Resulted in Significant Exposure in the Brain Without Negative Impact on Plasma PK

xB^3 peptide-Ab Fusion show improved Plasma PK compared to xB^3 full length-Ab fusion



xB^3-Ab Fusion significantly increased Brain Exposure over Ab alone



Mean ± SEM; Two-way ANOVA; n=6 mice/ molecule; single IV injection

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

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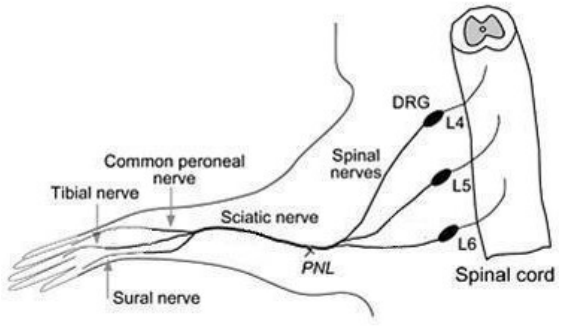
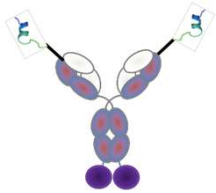
Efficacy Model: Neuropathic Pain Mouse Model

- Neuropathic pain model (Seltzer et al, 1990)
  - Sciatic nerve of one limb partially ligated
  - Results in mechanical hyperalgesia
- Neuropathic pain centrally mediated
  - Drug must reach CNS to relieve pain
- Analgesic drug will reduce pain if it reaches the CNS
  - IL-1 receptor antagonism has been implicated in relieving the symptoms of neuropathic pain (Gabay et al, 2011)
    - IL1RA (Kineret) can induce analgesia **only** when delivered intrathecally
    - Peripheral delivery of IL1RA or control IgG-IL1RA do not induce analgesia



hIgG1-IL1RA



xB^3-NH-hIgG1-IL1RA

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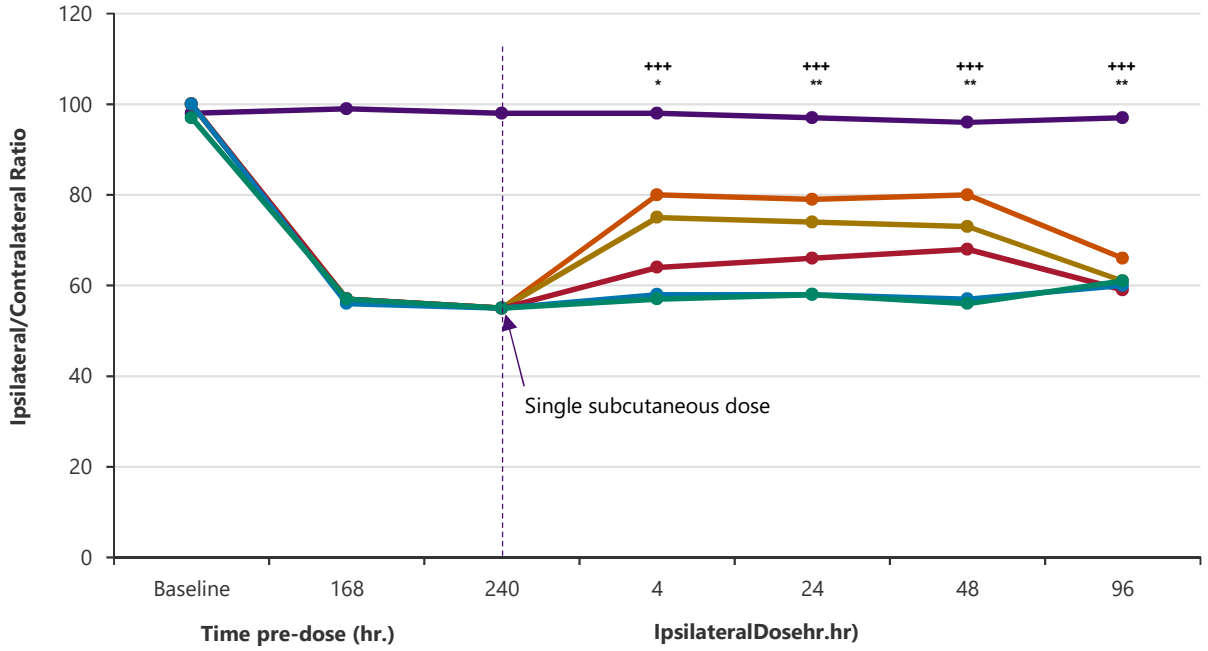
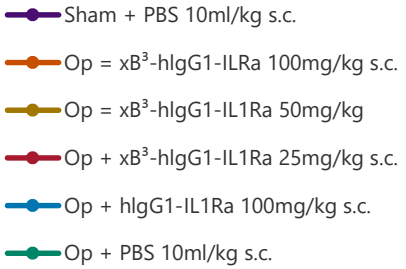
Systemic administration of xB^3 –IL1RA Fusion: Dose Dependent PD Effects in Neuropathic Pain Model

Effect of xB^3-hIgG1-IL1RA on Reversal of PNL Induced Mechanical Hyperalgesia – Ipsi/Contra Ratio





N=7-10 per group. Two way ANOVA with time and treatment as dependent factors. Subsequent statistical significance obtained using Tukey's Post Hoc test.

* P<0.05; ** P<0.01 – Op + hIgG1 vs. xB^3-IL1Ra 50mg/kg; +++ P<0.001 – Op + hIgG1 vs. Op + xB^3-IL1Ra.

Note: Baseline response were measured at Day 7 and 10 post surgery; mice were tested for mechanical hyperalgesia at 4hrs, 1, 2 and 4 days post dose.

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

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Neurodegeneration: Parkinson's Disease

The Need for Improved Delivery of Therapeutics to the CNS Continues to Increase

Prevalence of Parkinson's

- Nearly one million will be living with Parkinson's disease (PD) in the U.S. by 2020, which is more than the combined number of people diagnosed with multiple sclerosis, muscular dystrophy and Lou Gehrig's disease (or Amyotrophic Lateral Sclerosis)
- Approximately 60,000 Americans are diagnosed with PD each year.
- More than 10 million people worldwide are living with PD.
- Incidence of Parkinson's disease increases with age, but an estimated four percent of people with PD are diagnosed before age 50.
- Men are 1.5 times more likely to have Parkinson's disease than women.

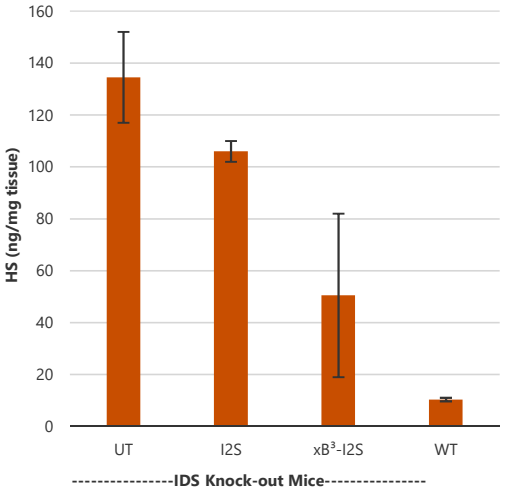
Estimated Cost of Parkinson's

- Medications alone cost an average of $2,500 a year and therapeutic surgery can cost up to $100,000 per person.
- The combined direct and indirect cost of Parkinson's, including treatment, social security payments and lost income, is estimated to be nearly $52 billion per year in the United States alone.

xB^3-007: 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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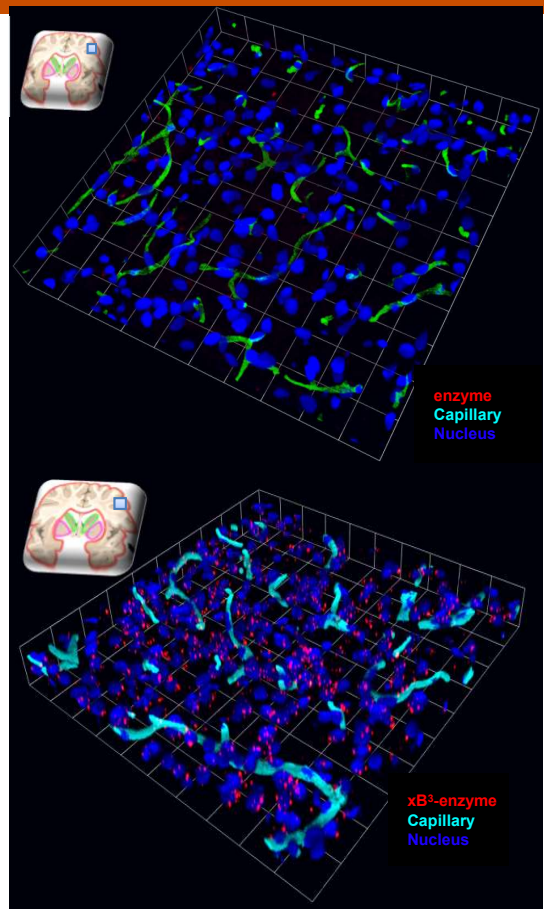
xB^3 is able to Effectively Deliver Enzymes to the Brain to Treat Lysosomal Storage Disorders

Hunter Syndrome (MPS II)

- Lysosomal Storage disease, MPS II is caused by an iduronate 2-sulfatase (I2S) enzyme deficiency
- Currently CNS effects are untreatable

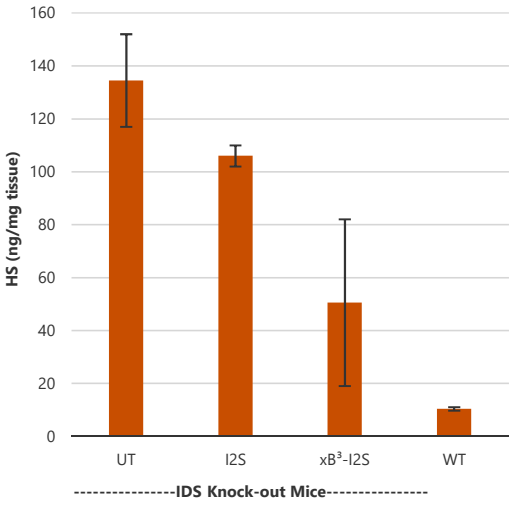
Bioasis' xB^3 peptide-I2S fusion molecule increased I2S uptake into the brain and was accompanied by cellular and biochemical changes characteristic of enzyme activity.



xB^3-I2S Treatment Facilitated the Reduction of Heparan Sulfate Levels, Reduced Number of Storage Cell Vacuoles & Reduction in Number of Lysosome Vesicles in the Brain

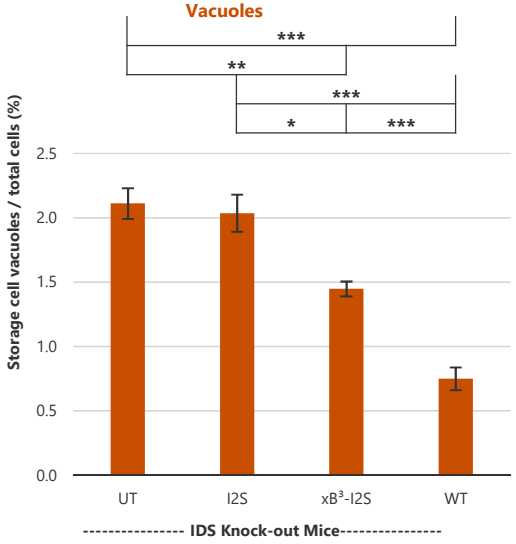
- Significant reduction in brain heparan sulfate accumulation, cell vacuolation and lysosome vesicles in a Hunter Syndrome mouse model
- Increase in brain heparan sulfate accumulation, cell vacuolation and lysosome numbers are hallmarks of Hunter Syndrome

Reduction in Heparan Sulfate Accumulation



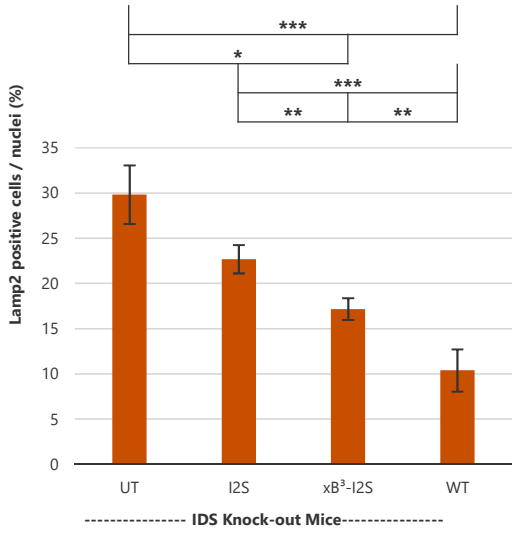
Mean ± SEM; n= 2-3

Reduction in Number of Storage Cell Vacuoles



Mean ± SEM (***P≤0.0001, **P≤0.001, *P≤0.01, One-way ANOVA); n=4-5

Reduction in Number of Lysosome Vesicles



Mean ± SEM (***P≤0.005, **P≤0.05, *P≤0.01, One-way ANOVA); n=5

Work performed at University of Padova, Italy

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Recent Achievements

- January 2019: Bioasis Announces Agreement With Leading Pharmaceutical Company for Pre-Clinical Research Using the xB^3 Platform Technology
  - $500,000 upfront, up to $3M in R&D costs
- October 2018: Bioasis Announces xB^3 ™ 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 xB^3 ™ Platform Technology
  - MedImmune collaboration

Appendix

Delivery of siRNA-based treatment to brain in an induced ischemic stroke

Why

- Utility of siRNA therapeutic approaches for CNS diseases has been limited by their distribution *in vivo*
  - Preferentially localize to the kidney and liver, unable to cross the BBB

Aim

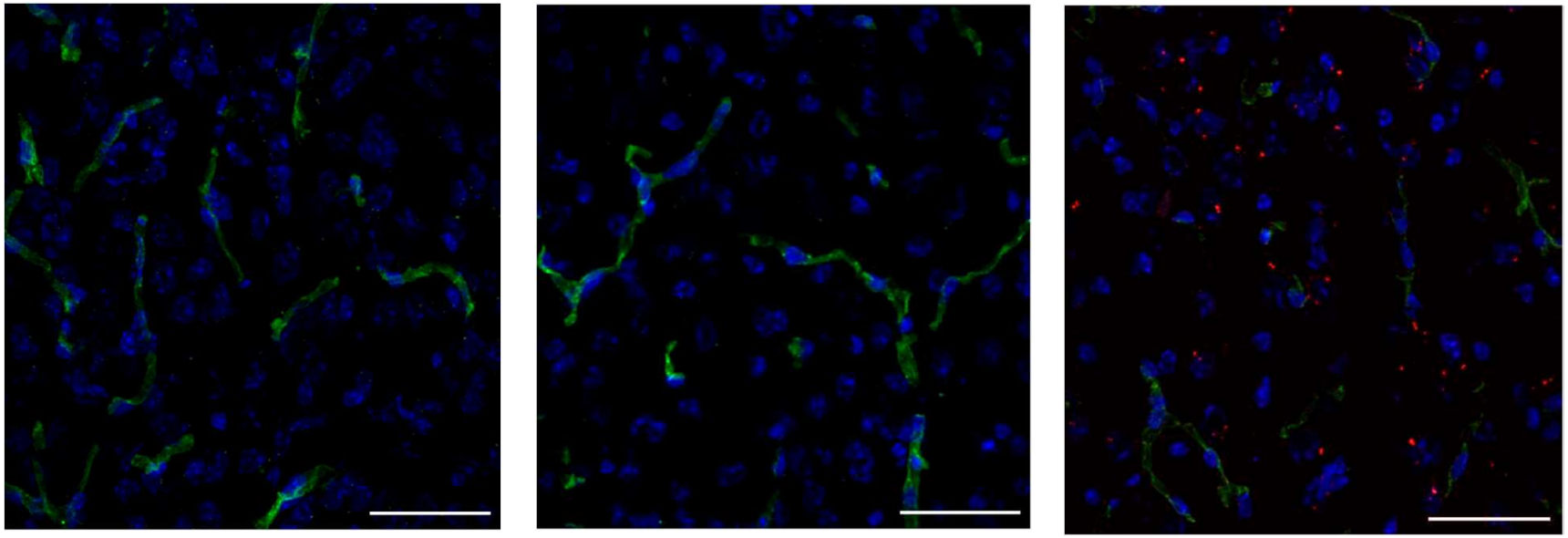
- Delivery of siRNA to brain to knock down gene targets associated with specific CNS disease / condition

Target

- NADPH oxidase (NOX) enzyme gene in ischemic stroke
  - Stroke is one of the leading causes of death in North America, with majority result from blockage of blood vessels in the brain (ischemic stroke)
  - NOX4 has been identified in neurons, astrocytes and microglia
  - NOX4 is thought to be responsible for majority of oxidative stress observed in acute traumatic brain injury[1]
  - Animal deficient in NOX4 are strongly protected from ischemic stroke[2,3]

Conjugation to xB^3 Facilitated the Transport of siRNA Across the BBB into Brain Parenchyma of Wild Type Mice

Confocal Images One Hour Post Single IV Administration (10mg/kg) in Wild-type Mice



siRNA / xB^3-siRNA
Capillary
Nucleus

PBS | siRNA | xB^3-siRNA

Work performed at National Research Council of Canada – Research Facility

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Stroke Induction Via Middle Cerebral Artery Occlusion

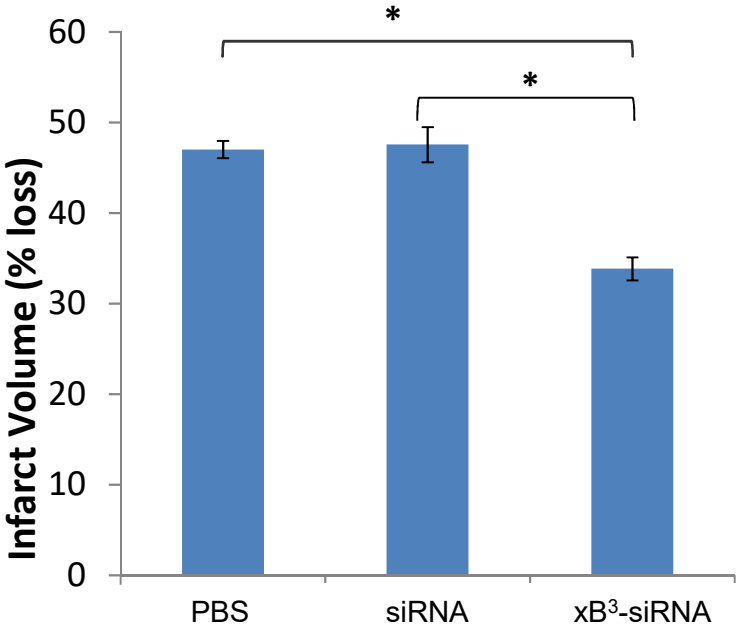
Model:

- Middle cerebral artery occlusion via filament
- Duration of occlusion: 60 min
- Animal sacrificed 24 hrs post reperfusion
- Dose: 30 mg/kg
- Administration: i.v. prior to stroke induction

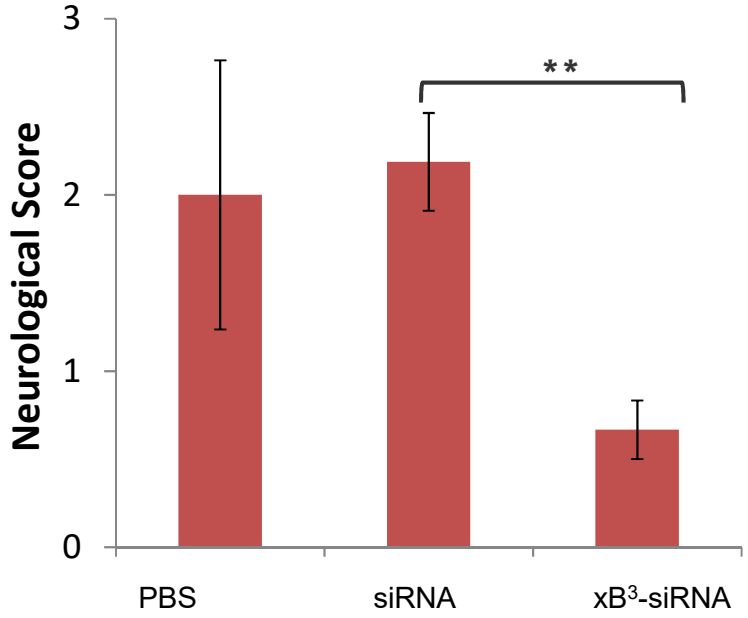
Analysis>

- Cerebral infarction – via 2,3,5-triphenyltetrazolium chloride colorimetric staining
- Neurological deficit – blinded behavioral assessment base on scale of 0 (best) - 5 (worst)
- Knock-down quantification (mRNA level) – Quantitative PCR

Pretreatment with xB^3-siRNA Conjugates Significantly Reduced the Infarct Volume and Improved Neurological Deficit



* P ≤ 0.05 (1 way Anova); n=4



** P ≤ 0.01 (1 way Anova); n=4

Work performed at National Research Council of Canada – Research Facility

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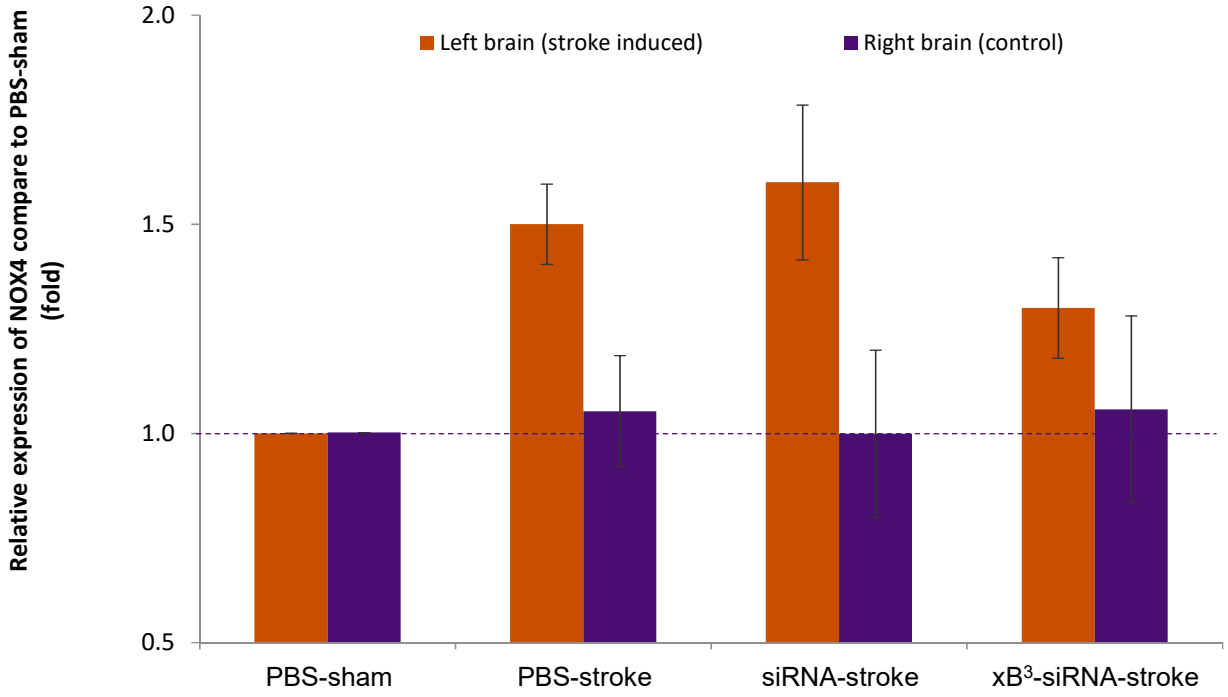
xB^3-siRNA Pretreatment Reduced NOX4 Expression Compared to siRNA or PBS in Stroke Induced Brain at mRNA Level



Mean ± SEM; n=4; data obtained from a separate set of animal as those used for the analysis of infarct volume/neurodeficit

Work performed at National Research Council of Canada – Research Facility

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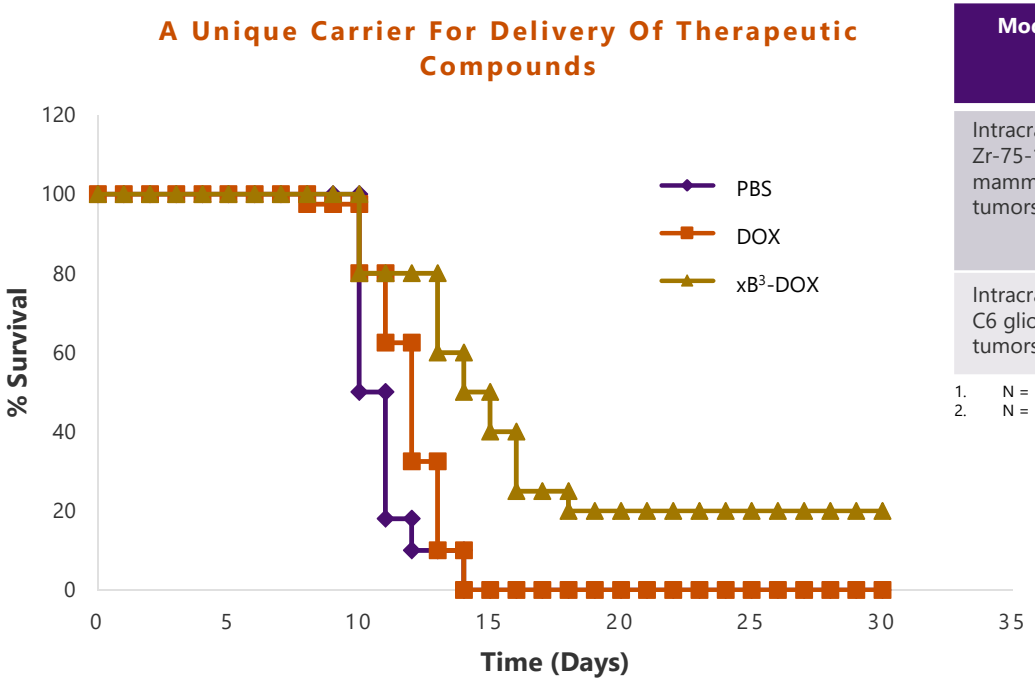
Small Molecule: Doxorubicin Conjugate Achieves Significant Increase in Survival in Intracranial Tumor Mouse Models



N = 10; total in DOX group = 20mg/kg, total ADR in xB^3-DOX group = 5.5mg/kg; dosing schedule D3,4,5,6,7,10,11,12,13,14

Model	Compound (Total ADR dosed)	Mean survival (Days)	% change in mean survival	Significance
Intracranial Zr-75-1 mammary tumors[1]	PBS	10	-	-
	DOX (20mg/kg)	9.24	-7.6	P<0.05
	xB^3-DOX (5.5 mg/kg)	17.7	77	P<0.005
Intracranial C6 glioma tumors[2]	PBS	20.2	-	-
	xB^3-DOX (0.49 mg/kg)	28.3	40	P<0.001

1. N = 10; dosing schedule D3,4,5,6,7,10,11,12,13,14;
2. N = 10; dosing schedule D1,3,7,10,14

- Treatment with xB^3-DOX raised the mean and median survival to 77% and 40% respectively
- 2/10 mice in xB^3-DOX treatment group survived to over 50 days and were tumor-free at autopsy

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Neuro-oncology Applications Beyond xB^3-001

xB^3-002 for the Treatment of Glioblastoma

xB^3-002 Program for the Treatment of Glioblastoma:

One of the Most Aggressive Cancers Originating from the Brain

- **Approximately 80% of all diagnosed primary malignant brain tumors are malignant gliomas (GBM).**
- **The deadliest form of brain cancer due to the high infiltration of the tumor with surrounding brain tissues**
- **GBM tissues show moderate to high expression level of LRP1**
  - **68% of GBM brain slice specimens showed moderate to high LRP-1 expression**
  - **0% of normal brain slice specimens showed moderate to high LRP-1 expression**

Table 1. Distribution of LRP1 expression in normal and GBM specimens.

Expression	Normal (%)	Glioblastoma (%)	Total (%)
Negative	21 (91)	7 (9)	28 (29)
Low	2 (9)	17 (23)	19 (19)
Moderate	0 (0)	30 (40)	30 (31)
High	0 (0)	21 (28)	21 (21)
Total	23 (100)	75 (100)	98 (100)

Histopathological scoring is as follows: negative staining (0), weak staining (1), moderate (2–3), and strong (4–5). Fisher's exact test suggests a strong association between sample type and LRP1 expression level ($p<0.001$).

Gopal U, et al. (2011) A Novel Extracellular Hsp90 Mediated Co-Receptor Function for LRP1 Regulates EphA2 Dependent Glioblastoma Cell Invasion. PLoS ONE 6(3): e17649

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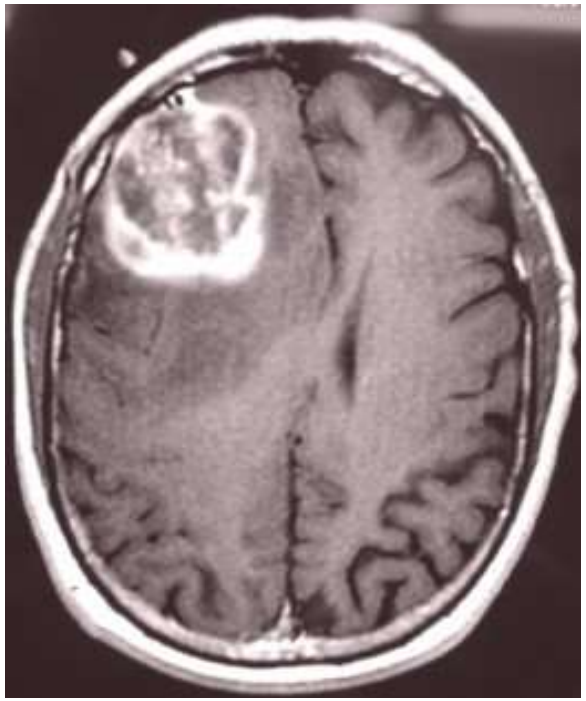
Avastin and Glioblastoma



Antiangiogenic compounds such as bevacizumab (Avastin, BEV) has been shown to prolong progression-free survival in glioblastoma, with no overall survival benefit.

Due to a higher expression of LRP1 on glioblastoma, xB^3-bevacizumab (xB^3-002) therapy may provide advantages over bevacizumab alone:

- **Potential to significantly increase brain levels of Avastin**
- **LRP1 receptors on glioblastoma may act like a "sink," targeting more xB^3-002 to the glioblastoma sites**

  Bevacizumab is known to have negative impacts on CNS function, therefore targeting Avastin and minimizing localization to other brain areas may result in lower dose needed for efficacy and less negative impact to the CNS.

Our Management Team

Deborah Rathjen, Ph.D., MAICD, FTSE

Chief Executive Officer & Executive Chair

Previous Chief Executive Officer and Managing Director, Bionomics, Head BD, Peptech (acquired by Cephalon/Teva)

Christine Antalik

Chief Financial Officer

25+ years of experience in accounting & finance, including role of CFO at multiple corporations

Mei Mei Tian, Ph.D.

VP, Head of External Research

15 years of experience in xB³-related research

Joined Bioasis in 2012

Dr. May Orfali

Consultant Chief Medical Officer

Extensive background in drug and clinical development programs spanning two decades in multiple therapeutic areas, with a focus on rare diseases and oncology.

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Our Board of Directors

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Previous Chief Executive Officer and Managing Director, Bionomics, Head BD, Peptech (acquired by Cephalon)

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Director

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John E. Curran, CPA

Director

Former Partner, Deloitte & Touche LLP

David M. Wurzer, CPA

Lead Director

Executive Vice President and Chief Investment Officer, Connecticut Innovations

Medical Advisory Board

Dr. May Orfali, Chairperson of the Advisory Board in her role of consultant Chief Medical Officer, has an extensive background in drug and clinical development programs spanning two decades in multiple therapeutic areas, with a focus on rare diseases and oncology. Her career includes senior positions at Oncology and Rare Disease Consulting, CANbridge , Pfizer, Wyeth, Artisan Pharma, Aeris, Cubist and Boston Scientific Corporation.

Dr. Hope S. Rugo is Professor of Medicine at the University of California San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center, where she is also the director of Breast Oncology and Clinical Trials Education.

Dr Javier Cortés is Head of Breast Cancer and Gynecological Tumors at Ramon y Cajal University Hospital in Madrid and Clinical Investigator of the Breast Cancer Research Program at Vall d'Hebron Institute of Oncology, Barcelona.

Dr. John de Groot is a Professor, and Chairman ad interim, in the Department of Neuro-Oncology at The University of Texas MD Anderson Cancer Center.

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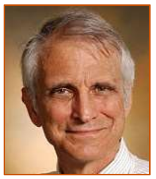
Vice President, Innovation & Strategic Initiatives
Bionomics Ltd.



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