The Blood Brain Barrier Delivery Company

Opening the door to large molecule biologic therapies for neurological diseases

August 2019

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.
### Bioasis Strategy

#### xB³™ Platform:

**Best-in-class technology for BBB drug delivery**

- 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 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

#### 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 xB³-001- xB³ + Herceptin® for HER2+ breast cancer brain metastases; Favorable FDA pre-IND meeting completed June 2019, FIH 2020; potential for accelerated approval
- **Second program xB³-007 - xB³+Cerezyme® for the treatment of Gaucher’s Type 2**: pre-clinical POC study will demonstrate CNS efficacy and confirm translational endpoints for human studies (2019); FDA pre-IND meeting anticipated date 4Q20, FIH 4Q21, potential for accelerated approval

#### Strategic partnering broadens uptake of the technology

- Partners are using the Bioasis xB³ platform to deliver antibodies and siRNA therapeutics
  - Licensing agreement with Prothena
  - A new research alliance with a major global pharma company
  - xB³ peptide can penetrate the lymphatic system and non-CNS tissues, expanding opportunities

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Achievement of the indicated timelines is conditional upon the company securing the capital necessary to achieve the milestones as set out.
## Bioasis Pipeline: Robust and Low-Risk

*Opening the door to large molecule biologic therapies for neurological diseases*

<table>
<thead>
<tr>
<th>Program</th>
<th>Discovery</th>
<th>Preclinical POC</th>
<th>IND Enabling</th>
<th>Ph 1</th>
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</thead>
<tbody>
<tr>
<td><strong>CNS Oncology</strong></td>
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<tr>
<td>xB³-001 (Herceptin®): HER2+ Breast cancer and brain mets</td>
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<td>xB³-003 (DOX): Glioma</td>
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<td>xB³-002 (Avastin®): Glioblastoma</td>
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<td><strong>Lysosomal Storage Disorders</strong></td>
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<td>xB³-007 (Cerezyme®): Gaucher’s Disease Type 2, Parkinson’s Disease</td>
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<td><strong>Inflammatory CNS Disorders and Pain</strong></td>
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<tr>
<td>xB³-004 (anti-IL1RA): Neuropathic pain</td>
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Herceptin® is a registered trademark of Genentech, Inc., Avastin® is a registered trademark of Genentech, Inc., Cerezyme® is a registered trademark of Genzyme Corporation.
Criteria for Internal Program Prioritization

- Approved Therapy
- Orphan Indication or Rare Disease
- Potential to Expand Use to a Broad Patient Population or Patient Subset
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.
The Bioasis Platform Technology
Active Transport Across the BBB via the LRP1 Receptor

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, 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
xB³ Platform is Superior to Transferrin

Greater CNS Transport Efficiency demonstrated in vivo

xB³ 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 (xB³ to Transferrin comparison)
n=8 for xB³, n=6 for Transferrin
Mice perfused with 10 nM xB³ or Transferrin

The xB³ Platform Technology
Outperforms Competing BBB Technologies

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

<table>
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<tr>
<th>Features</th>
<th>Bioasis xB³ Platform</th>
<th>Denali</th>
<th>Genentech</th>
<th>Roche</th>
<th>Armagen</th>
<th>Angiochem</th>
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<tr>
<td>% injected dose in brain</td>
<td>4-6%</td>
<td>1-1.5%</td>
<td>1-1.5%</td>
<td>1-1.5%</td>
<td>1-1.5%</td>
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<td>Mode of Action</td>
<td>LRP1</td>
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<td>TFR</td>
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<td>TFR and IR</td>
<td>LRP1</td>
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<td>siRNA</td>
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References:
9. *Bioasis internal data*
The xB³ 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
**xB³ 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
Independent validation of the xB³ 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 41-45 for detail)

**Small molecule** – Preclinical POC in the treatment of intracranial tumors – University of British Columbia
(see Appendix slides 46 for detail)
The Blood Brain Barrier Company

Lead Program : xB³-001
(xB³ - Trastuzumab) for the Treatment of HER2+ Breast Cancer and Brain Metastases
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**
The majority of HER2+ mBC patients receive Herceptin in all lines of therapy

Market Share for HER2-Targeting Agents by Line of Therapy

1L
- ~85% receive Herceptin
- 49%
- 38%
- 7%
- 5%

2L
- ~55% receive Herceptin
- 40%
- 32%
- 15%
- 13%

3L+
- ~55% receive Herceptin
- 51%
- 31%
- 13%
- 5%

Source: Kantar Treatment Architecture
Datamonitor expects continued growth of the US HER2+ breast cancer market, reaching >$6B by 2025

US HER2+ Breast Cancer Market
Datamonitor Forecast

Source: Datamonitor
**xB³-001 (xB³ - Trastuzumab) Summary**

<table>
<thead>
<tr>
<th>Indication</th>
<th>TREATMENT OF HER2+ BREAST CANCER AND BRAIN METASTASES</th>
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| 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 |

| Recent Development Milestones | • 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 Clinical Milestones | • IND submission, safe to proceed letter and initiation of Phase 1b component of trial (4Q20)  
|                               | • Completion of dose escalation phase and EOPI meeting (4Q21)  
|                               | • Completion of Phase 2 expansion cohort (4Q22) |
xB³-Herceptin Retains Peripheral Anti-Tumor Efficacy in the BT474 Xenograft Model

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

BT2111 = xB³-001 (xB³-Herceptin)
Ip injection 2x/wk for 5 weeks; 10mg/kg molar equivalent; n=10

Herceptin® is a registered trademark of Genentech, Inc.
xB³-001 Demonstrates Significantly Increased Localization in Brain Parenchyma Compared to Herceptin®

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

xB³-Herceptin

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

Herceptin

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

Work performed at National Research Council of Canada – Research Facility
**HER2+ Human Breast Cancer Brain Metastasis Mouse Model**

**Intracardiac injection**

MDA-MB-231-BR<sup>HER2/eGFP<sup> (Brain targeting HER2+ human breast cancer cells

5 weeks

Following establishment of brain metastases single IV injection of ¹²⁵I labeled test articles (10 mg/kg molar equivalent; n=3)

2h

Autoradiography
Quantification of brain radioactivity via microcomputer image device

5 weeks post breast cancer cell administration

3 weeks

Following establishment of brain metastases biweekly IV injection of test articles (10 mg/kg molar equivalent; n=8-9)

2 weeks

Efficacy assessment
- Tumor number
- Tumor size

xB³-001 in Human HER2⁺ Brain Metastasis Mouse Model
Target Engagement and Biological Effects

Metastases localization 5 weeks Post Inoculation

Concentrations of xB³-001 within Brain Regions at 2hrs post dose

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

Single injection of $^{125}$I-xB³-001 administered 5 weeks after initial intracardiac injection of cells and establishment of brain metastases.

**xB³ Platform Delivers 10-Fold Higher Herceptin® to Brain Metastases**

Mean ± SD; n = 61 (TZM), n = 77 (xB³-001); single dose; up to 8 hrs post dose.

Mean ± SD; n = 336 (TZM), n = 213 (xB³-001); single dose; up to 8 hrs post dose.


Herceptin® is a registered trademark of Genentech, Inc.
xB³ Platform Delivers Herceptin® (Trastuzumab, TZM) to Brain Metastases and Reduces Both Tumor Number and Size

xB³-001: Significant Tumor Reduction

<table>
<thead>
<tr>
<th>Group</th>
<th>Tumor size based on pooled data from all individual values in group</th>
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<tbody>
<tr>
<td></td>
<td># of tumor</td>
</tr>
<tr>
<td>Saline control (n=9)</td>
<td>765</td>
</tr>
<tr>
<td>xB³-001 (n=8)</td>
<td>223</td>
</tr>
<tr>
<td>TZM (n=13)</td>
<td>962</td>
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</tbody>
</table>

¹. xB³-001 group vs. TZM group P<0.001

xB³-001 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

TZM: Trastuzumab; n=13 for xB³, TZM groups; n=8-9 for xB³-001, 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


Herceptin® is a registered trademark of Genentech, Inc.
### Key Milestones:
1. IND submission and safe to proceed letter (4Q20)
2. Completion of dose escalation phase and EOPI meeting (4Q21), prior to expansion phase
3. Completion of expansion phase (4Q22)
xB³ – 001 Path to Market

- If clinically active, xB³-001 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

- xB³ – 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 xB³, p97, fusion proteins of p97 or xB³ with antibodies, including trastuzumab, bevacizumab, and other payloads
- Key xB³ 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 xB³-trastuzumab (xB³-001) - 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/xB³ conjugates including xB³-001, Bioasis’ lead product in development for the treatment of HER2+ breast cancer brain metastases.

**Additional patents pending for other xB³-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/xB³ 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.
A peptide derived from melanotransferrin delivers a protein-based interleukin 1 receptor antagonist across the BBB and ameliorates neuropathic pain in a preclinical model


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 utilise a simple 12 amino-acid peptide originating from the melanotransferrin (MFTI) 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 MFTI peptide or full-length MFTI protein. Measurement of plasma kinetics demonstrated the MFTI peptide fusions had very similar kinetics to an unmodified NIP228 control antibody, whereas the fusion to MFTI proteins led significantly reduced plasma exposure most likely due to a higher tissue distribution in the periphery. Brain exposure for the MFTI peptide fusions was significantly increased for the duration of the study, exceeding that of the fusions to full length MFTI 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 MFTI-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

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

MedImmune, Cambridge, UK
Bioasis Bioclonics Corp., Garfield, CT, USA
Novozymes A/S, Bagsvaerd, Denmark
Novozymes A/S, Bagsvaerd, Denmark
Corresponding author: Mei-Mei Tian, Bioasis Bioclonics Corp., 14 Water Street, Garfield, CT 07026, USA
Email: marcel@bioasis.ai
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)
xB³ 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

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

xB³ Resulted in Significant Exposure in the Brain Without Negative Impact on Plasma PK

xB³ peptide-Ab Fusion show improved Plasma PK compared to xB³ full length-Ab fusion

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

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

Systemic administration of xB³ –IL1RA Fusion: Dose Dependent PD Effects in Neuropathic Pain Model

Effect of xB³-hlgG1-IL1RA on Reversal of PNL Induced Mechanical Hyperalgesia – Ipsi/Contra Ratio

- Sham + PBS 10ml/kg s.c.
- Op = xB³-hlgG1-IL1Ra 100mg/kg s.c.
- Op = xB³-hlgG1-IL1Ra 50mg/kg
- Op + xB³-hlgG1-IL1Ra 25mg/kg s.c.
- Op + hlgG1-IL1Ra 100mg/kg s.c.
- Op + PBS 10ml/kg s.c.

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 + hlgG1 vs. xB³-IL1Ra 50mg/kg; *** P<0.001 – Op + hlgG1 vs. Op + xB³-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.

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.
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
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’ xB³ peptide-I2S fusion molecule increased I2S uptake into the brain and was accompanied by cellular and biochemical changes characteristic of enzyme activity.*
xB³-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
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
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 xB³ 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
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 xB3-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
xB³-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
Small Molecule: Doxorubicin Conjugate Achieves Significant Increase in Survival in Intracranial Tumor Mouse Models

- Treatment with xB³-DOX raised the mean and median survival to 77% and 40% respectively.
- 2/10 mice in xB³-DOX treatment group survived to over 50 days and were tumor-free at autopsy.

**A Unique Carrier For Delivery Of Therapeutic Compounds**

<table>
<thead>
<tr>
<th>Model</th>
<th>Compound (Total ADR dosed)</th>
<th>Mean survival (Days)</th>
<th>% change in mean survival</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial Zr-75-1 mammary tumors¹</td>
<td>PBS</td>
<td>10</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>DOX (20mg/kg)</td>
<td>9.24</td>
<td>-7.6</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>xB³-DOX (5.5 mg/kg)</td>
<td>17.7</td>
<td>77</td>
<td>P&lt;0.005</td>
</tr>
<tr>
<td>Intracranial C6 glioma tumors²</td>
<td>PBS</td>
<td>20.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>xB³-DOX (0.49 mg/kg)</td>
<td>28.3</td>
<td>40</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

¹ N = 10; dosing schedule D3,4,5,6,7,10,11,12,13,14; ² N = 10; dosing schedule 1,3,7,10,14
Neuro-oncology Applications Beyond $x\text{B}^3-001$

$x\text{B}^3-002$ for the Treatment of Glioblastoma
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>
<thead>
<tr>
<th>Expression</th>
<th>Normal (%)</th>
<th>Glioblastoma (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>21 (91)</td>
<td>7 (9)</td>
<td>28 (29)</td>
</tr>
<tr>
<td>Low</td>
<td>2 (9)</td>
<td>17 (23)</td>
<td>19 (19)</td>
</tr>
<tr>
<td>Moderate</td>
<td>0 (0)</td>
<td>30 (40)</td>
<td>30 (31)</td>
</tr>
<tr>
<td>High</td>
<td>0 (0)</td>
<td>21 (28)</td>
<td>21 (21)</td>
</tr>
<tr>
<td>Total</td>
<td>23 (100)</td>
<td>75 (100)</td>
<td>98 (100)</td>
</tr>
</tbody>
</table>

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).

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, xB³-bevacizumab (xB³-002) 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 xB³-002 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

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

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

Caroline Dircks, Ph.D.
Chief Operating Officer
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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