This presentation contains “forward-looking statements” Forward-looking statements reflect our current view about future events. When used in this presentation, the words “anticipate,” “believe,” “estimate,” “expect,” “future,” “intend,” “plan,” or the negative of these terms and similar expressions, as they relate to us or our management, identify forward-looking statements. Such statements, include, but are not limited to, statements contained in this presentation relating to our business strategy, our future operating results and liquidity and capital resources outlook. Forward-looking statements are based on our current expectations and assumptions regarding our business, the economy and other future conditions. Because forward–looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. Our actual results may differ materially from those contemplated by the forward-looking statements. They are neither statements of historical fact nor guarantees of assurance of future performance. We caution you therefore against relying on any of these forward-looking statements. Important factors that could cause actual results to differ materially from those in the forward-looking statements include, without limitation, our ability to raise capital to fund continuing operations; our ability to protect our intellectual property rights; the impact of any infringement actions or other litigation brought against us; competition from other providers and products; our ability to develop and commercialize products and services; changes in government regulation; our ability to complete capital raising transactions; and other factors relating to our industry, our operations and results of operations. Actual results may differ significantly from those anticipated, believed, estimated, expected, intended or planned. Factors or events that could cause our actual results to differ may emerge from time to time, and it is not possible for us to predict all of them. We cannot guarantee future results, levels of activity, performance or achievements. Except as required by applicable law, including the securities laws of the United States, we do not intend to update any of the forward-looking statements to conform these statements to actual results.
A Next Generation immunology company

- Two product platforms targeting innate immune dysfunction
- Programs in cancer, AD and NASH
  - Resistance to cancer immunotherapy in the TME
  - Neuroinflammation as a cause of neurodegenerative disease
  - Chronic inflammation as a cause of NASH
- Platform technologies provide multiple strategic opportunities
- Experienced management team
- Multiple programs provide sum-of-parts value
Financial Highlights

- **Nasdaq:** INMB
- **Cash 6/30/19:** $9.4 million
- **Debt:** $0
- **Common Shares O/S:** 10.8 million

**Insider ownership:** ~50%

**Notable Shareholder:** Xencor (XNCR)

**XNCR licensing fee:** Option to buy 10% of INMB for $10m at $100m valuation
Our Vision: Become the Leader in Reprogramming the Innate Immune System for the Treatment of Diseases
<table>
<thead>
<tr>
<th>Platforms - Therapeutic Areas</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>POC Phase 2</th>
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<tbody>
<tr>
<td><strong>Immune Priming Platform</strong></td>
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<tr>
<td>INKmune MRD ovarian cancer</td>
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<tr>
<td>INKmune high risk MDS</td>
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<tr>
<td>INB03 MDSC/CPI</td>
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<tr>
<td>INB03 trastuzumab resistance</td>
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<tr>
<td><strong>DN-TNF Platform</strong></td>
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<tr>
<td>XPro1595 AD</td>
<td></td>
<td></td>
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<tr>
<td>NeuLiv NASH</td>
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</tr>
</tbody>
</table>

Clinic ready: INMB non-confidential3Q19.v4
Market Opportunity: announced programs

- **XPro1595 - Alzheimer’s/dementia market***
  - 2019 est cost to care for US AD patients $280B
- **INKmune - Cancer residual disease market **
  - 1,735,350 new cases and 609,640 people will die
- **INB03 - Resistance to Cancer Immunotherapy market***
  - Cancer immunotherapy market est. >$119B in 2021
- **NeuLiv – NASH market†
  - Market size >$7B

DN-TNF Platform
TNF – the “master” cytokine

Pro-inflammatory

IL-6

Anti-inflammatory

TNF

IL-1

TNF-R

IL-1ra

IL-10
DN-TNF: novel inhibitor of soluble TNF

- 17 kDal mutated protein +10 kDal linear PEG
- Identical to human TNF except for 6 amino acid substitutions
- Once a week dosing by subQ injection

Receptor binding, "small" domain (subunit A)

Mutation A145R

Receptor binding, "large" domain (subunit C)

Mutation R31C (for 10kD PEGylation)

Mutation Y87H

Receptor binding, "DE loop" domain (subunit A)
DN-TNF: how does it work

**Normal sTNF activity**

Active TNF + TNFR → sTNF bind TNFR → Inflammation

**No sTNF activity**

Active TNF + Inactive heterotrimer or XPro1595 → Heterotrimer cannot bind TNFR → NO Inflammation
How is DN-TNF Different?

**Normal TNF Biology**

- TNFR1
  - sTNF (bad)
- TNFR2
  - tmTNF (good)

**Approved TNF inhibitors**

- TNFR1
  - X
- TNFR2
  - X

Prevent function of sTNF and tmTNF

**DN-TNF**

- TNFR1
  - X
- TNFR2
  - X

Neutralizes sTNF allowing normal of TM TNF
**DN-TNF: Next Generation TNF inhibitor**

**Differences: selective vs non-selective TNF inhibition**

<table>
<thead>
<tr>
<th></th>
<th>Non-selective TNF inhibitor</th>
<th>DN-TNF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inflammation</strong></td>
<td><strong>Decreases inflammation</strong></td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td><strong>Immuno-suppression</strong></td>
<td><strong>Increased risk of infection</strong></td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Increased risk of cancer</strong></td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td><strong>CNS</strong></td>
<td><strong>Causes demyelination</strong></td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Neuroprotective</strong></td>
<td><strong>NO</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Enhances neuroplasticity</strong></td>
<td><strong>NO</strong></td>
</tr>
</tbody>
</table>
INB03 for treatment of cancers resistance to immunotherapy
MDSC Predict Resistance to CPI

• INB03 targets MDSC
• CPI + INB03 should overcome MDSC based resistance by eliminating MDSC so CPI become effective

Stage IV Melanoma treated with Ipilimumab (Wolchok 2016)

(n=209)

\( P = 6.7 \times 10^{-11} \)
Targeting sTNF: fibrosarcoma model

**↓MDSC in tumor**

Decreased sTNF decreases differentiation and proliferation of MDSC

**↑CD8+ lymphocytes in tumor**

tmTNF promotes NK/DC crosstalk that recruits CD+8 TILs

**↑112 day survival**

↓MDSC with ↑CD8+TIL results in better survival

from Vujanovic 2016
INB03 reverses trastuzumab resistance

JIMT-1 breast cancer into nude mouse

Tumor volume (mm³)

Time of treatment (days)

T=trastuzumab
DN=INB03

Fewer Myeloid Cells

More activated NK

from Schillaci 2018
Goals:
1. Determine safety
2. Determine Phase II dose
3. Demonstrate PD effect
4. Determine Phase II strategy

“Top-Line” Results
1. Safe and well tolerated
2. Phase II dose: 1mg/kg
3. Pharmacodynamic effect confirmed - ↓IL6
4. Planning Phase II study

"Top-Line" Results
1. Safe and well tolerated
2. Phase II dose: 1mg/kg
3. Pharmacodynamic effect confirmed - ↓IL6
4. Planning Phase II study

11 of 12 patients treated
- **Demographics**: age (median): 64 yo gender: 6M/5F
- **Disease**: ovary; mesothelioma; RCC; lung; prostate; colon, cholangio, other
  - **Previous lines of therapy**: 3 (range:2-5)
  - **INB03 duration**: 74 days (21-119d)
- No drug related SAE
- All discontinuation due to disease progression
XPro1595 (for the treatment of Alzheimer's Disease/dementia)
AD: the problem..

Nerve cell death

Synaptic dysfunction

Cognitive Decline
Alzheimer’s Association awards INmune Bio Part the Cloud Grant - $1M USD translational funding to study XPro1595 in Alzheimer's disease
### TNF: a validated target in AD

**The good:** targeting TNF decreases risk of AD

<table>
<thead>
<tr>
<th>TNF inhibitor</th>
<th>Odds Ratio</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enbrel</td>
<td>0.31</td>
<td>21,280</td>
</tr>
<tr>
<td>Humira</td>
<td>0.35</td>
<td>20,130</td>
</tr>
<tr>
<td>Remicade</td>
<td>0.54</td>
<td>10,320</td>
</tr>
</tbody>
</table>

Adapted from Xu, Zhu and Gurney AAIC 2019

**The bad:** ↑ risk of cancer, infection and MS when treated with currently approved TNF inhibitor

INMB non-confidential3Q19.v4
XPro1595 AD Development Program

Phase I biomarker directed trial of patients with inflammation and proven Alzheimer’s Diseases

18 patients in 3 cohorts

• Weekly XPro1595 subQ for 3 months
• Biomarkers of inflammation at 0, 6 and 12 weeks
  • Endpoints:
    – Safety
    – ↓ neuro-inflammation measured in: blood, cerebrospinal fluid, brain, breath and behavior
    – Measures of cognition, neuro-psychiatric symptoms and QOL
Immunologic biomarkers: AD

- MRI
- CSF
- Breath
- Blood

**Free Water content of white matter**

**Behavioral biomarkers of inflammation**
- Sleep disorders
- Depression
- Psychosis
- Apathy
- Aggression
NeuLiv for NASH
Three Principles of INMB NASH program

1. Fibrosis is a highly conserved wound healing response and represents the final common pathway of virtually all chronic inflammatory injuries. Prof. John Iresdale 2013

2. Chronic inflammation in the liver is caused by innate immune cells

3. Targeting chronic inflammation should prevent progressive fibrosis and allow liver to heal
3 cycles of chronic inflammation in NASH

Peripheral Inflammation
- Obesity
- Insulin Resistance

Regional Inflammation
- Intestinal Inflammation
- Mesenteric fat

Local Inflammation
- Lipotoxicity
- Innate immune activation
NAFLD: high fat/high fructose diet–13 weeks

**Weight Gain**

- Control/Saline
- Control/NeuLiv
- HSHF/Saline
- HSHF/NeuLiv

**Plasma Insulin (µg/mL)**

- Control
- HSHF

adapted from Rodriguez/Tansey 2016

INMB non-confidential3Q19.v4
NAFLD: high fat/high fructose diet–13 weeks

- Decreased insulin resistance
- Decreased hepatic steatosis
- No change in total body weight

adapted from Rodriguez/Tansey 2016
INMB non-confidential3Q19.v4
### STAM model: NAFLD Activity Score and Fibrosis Score

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>NeuLiv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sirus Red positive area (%)</td>
<td>0.96 ± 0.29</td>
<td>0.69 ± 0.23</td>
</tr>
</tbody>
</table>

**NAS (mean ± SD)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>NeuLiv</th>
</tr>
</thead>
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<td>Sirus Red positive area (%)</td>
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</tr>
</tbody>
</table>
INKmune for the treatment cancer
INKmune Primed NK Cells Kill Cancer

Human ovarian cancer cells plus patient’s own NK cells

Human ovarian cancer cells with patient’s NK cells after INKmune treatment
INKmune: “universal” cancer therapy

INKmune TpNK are active against many types of cancers:

- **Blood cancers**: AML, MM, lymphoma
- **Solid tumors**: breast, ovary, prostate, renal, lung

modified from Lowdell2007 and 2011
INMB non-confidential3Q19.v4
**Phase 1/2 study in relapsed/refractory CaOva**

Platinum resistant/refractory patients with residual disease

- Treatment: INKmune IP
- Endpoints:
  - Safety
  - ↑ NK activation and tumor killing
  - ↓ tumor burden*

**Phase 1/2 dose-finding study in high-risk MDS†**

Patients with high-risk MDS and measurable disease

- Treatment: INKmune IV
- Endpoints:
  - ↑ NK activation and tumor killing
  - ↓ blasts in marrow*

* in Phase II
† when resources available
INMB = Innate Immunity
Milestones

- February 1, 2019 – IPO closed
- February 4, 2019 – NASDAQ Capital Markets listing
- Feb19 – Part the Cloud award – Alzheimer’ Assoc
- 3Q19 – initial data on INB03 Phase I
- 3Q19 – announce NeuLiv NASH
- 3Q19 – first patient enrolled XPro1595 AD trial
- 4Q19 – first patient enrolled INKmune cancer trial
- 1H20 – initiate INB03 combination Phase II cancer trial
- 1H20 – initial data from INKmune Phase I
- 2H20 – XPro1595 AD Phase II trial and INKmune Phase II cancer
Intellectual Property

**DN-TNF**
- 2021 – composition-of-matter (licensed from Xencor)
- 2032 – Methods for treatment of neurologic disease
- 2035 – use for treatment of cancer (licensed from University of Pittsburgh)
- 2039 – use for treatment of NASH

**INKmune**
- 2035 – use for treatment of cancer
- 2039 – INB16 composition-of-matter IP

**Future**
- Other IP filed and/or in process
Experienced Leadership

Management

RJ Tesi, MD
Chief Executive Officer & Chief Medical Officer

Mark Lowdell, PhD
Chief Scientific Officer

David Moss
Chief Financial Officer

Board of Directors

J. Kelly Ganjei
CEO of Cognate

Timothy Schroeder
CEO and Founder of CTI

David Szymkowski, PhD
VP of Cell Biology

Scott Juda
Founder and Managing Member, Fossick Capital

Edgardo (Ed) Baracchini
BD and licensing professional

For complete biographies, visit www.inmunebio.com
INMB: summary

• Public clinical stage immunology company
• Two product platforms with multiple clinical programs
• Efficient use of capital and funding sources to maximize run-way
• Opportunity to add clinical programs as resources become available
INB03/XPro1595 MOA Appendix
Precision Therapy: Targets sTNF not tmTNF

Inflammatory soluble TNF eliminated:
No paracrine signaling through receptors

Immunoprotective transmembrane TNF unaffected:
Allows juxtacrine cell-cell signaling

Graphs show Caspase activity vs. Log [anti-TNF (µg/ml)] for different treatment groups:
- INB03
- etanercept
- infliximab
- adalimumab
- vehicle

Zalevsky et al., J. Immunol. 2007
How is DN-TNF Different?

**Normal TNF Biology**

<table>
<thead>
<tr>
<th>TNFR1</th>
<th>TNFR2</th>
</tr>
</thead>
<tbody>
<tr>
<td>sTNF (bad)</td>
<td>tmTNF (good)</td>
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</table>

**INB03 does not neutralize tmTNF**

INB03 does not neutralize tmTNF.

tmTNF binds TNFR with normal function.

**Approved TNF inhibitors**

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>sTNF (bad)</td>
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</table>

**XPro1595/INB03**

Neutralizes sTNF allowing normal of TM TNF.

Prevent function of sTNF and tmTNF.
Expected Dose: 1mg/kg/week

Repeat Dose Modeling of XENP1595 in Humans
1mg/kg Administered SC Every 5, 7, or 10 Days

Allometric scaling of cyno PK data suggests weekly dosing of 1 mg/kg SC in humans will sustain >1 μg/ml trough serum levels of INB03

V = 494.9 ml
k_{01} = 3.552/day
k_{10} = 0.25/day

Volume and k_{ab} are the same as for cyno. The k_{el} term is reduced by ~2x
Determining INB03 dose

1 to 1 ratio DN-TNF to TNF

<table>
<thead>
<tr>
<th>Flag</th>
<th>His</th>
<th>Flag</th>
<th>His</th>
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<tbody>
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4 DNs + 4 TNFs =

[wtTNF] = 50 μg/ml; [DN-TNF] = 50 μg/ml
Exchange at equilibrium in PBS + 0.1 mg/ml BSA
Separation & quantitation by native PAGE

Varying ratios DN to wt (native PAGE)

At equilibrium (binomial distribution):

- XPro1595 = TNF: Eliminates 75% TNF (1:3:3:1)
- 2x XPro1595 > TNF: Eliminates ~88.9% TNF
- 5x XPro1595 > TNF: Eliminates ~97.2% TNF
- 10x XPro1595 > TNF: Eliminates >99.2% TNF
- 100x XPro1595 > TNF: Eliminates >99.99% TNF
**Goal:** blood trough level at least 2 logs greater than blood TNF level

**Conclusion:**
- 1mg/kg dose provides adequate drug level
- Above 3 log target 8 hours after first dose

Patients below 3 log target drug level

<table>
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<tr>
<th></th>
<th>0.3mg</th>
<th>1.0mg</th>
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</thead>
<tbody>
<tr>
<td>day 8</td>
<td>2 of 3</td>
<td>0 of 3</td>
</tr>
<tr>
<td>day 15</td>
<td>2 of 3</td>
<td>1* of 3</td>
</tr>
<tr>
<td>day 22</td>
<td>2 of 3</td>
<td>0 of 3</td>
</tr>
<tr>
<td>day 29</td>
<td>1 of 2</td>
<td>0 of 3</td>
</tr>
<tr>
<td>day 43</td>
<td>1 of 2</td>
<td>0 of 2</td>
</tr>
<tr>
<td>day 57</td>
<td>0 of 1</td>
<td>0 of 2</td>
</tr>
</tbody>
</table>

3 log threshold = 3700ng

2 log threshold = 2600ng
RP-HPLC of INB03

- INB03 was engineered for single, site-specific clean pegylation (10kD PEG/monomer x 3 monomers)
- Unpegylated XENP550 is produced through E. coli expression
- INB03 is a nonglycosylated small (17 kD monomer) & stable homotrimeric protein, with superior manufacturing vs. mAbs & Fc fusions
- Current production yield = ~300mg/liter
- Yd improvement and new batch manufacturing planned for after IPO
INB03: Phase I in cancer

• Open label, biomarker directed, dose-escalation trial in patients with advanced solid tumors and elevated markers of inflammation

• Enrollment criteria:
  – Advanced solid tumors
  – hsCRP > 4 mg/L
  – Treatment: INB03 subQ once a week
  – 3 cohorts of 3: 0.3, 1.0, 3.0 mg/kg
**Phase I summary**

- Safe at all doses tested
  - No SAE, No DLT, Well tolerated
- 1mg/kg once a week will be carried into Phase II
  - Dose provides robust trough drug levels
- Pharmacologically active at all dose levels
  - >50% decreases IL6

**Phase II combination trial**

- Design variables:
  1. Combination with what!
  2. Which tumor type
  3. Interaction of efficacy and safety
  4. Partnering opportunities
  5. First line vs second line therapy
TNF – the “master” cytokine

• sTNF promotes translation of IL6 and other downstream cytokines
• CRP more durable than any cytokine signature
Resistance to immunotherapy case study: CPI

- Small cell Lung
- Melanoma
- RCC
- Bladder
- Ureothelial
- Merkel Cell
- NSCLC
- Gastric
- HNC
- HCC
- Microsatellite instability

Eligibility vs Benefit CPI
US patients 2018

INMB non-confidential3Q19.v4

JAMA Hasim2019
Eligibility vs Response to CPI - US

- 44% US cancer patients eligible for CPI
- 29% of cancer patients who receive CPI respond
Resistance to Immunotherapy: CPI

Cancers affected by immunology drugs
Respond to immunology drugs

Year from Haslam 2019

Percentage

0 10 20 30 40 50 60 70 80 90 100

47% 12%
Different Approach to Immuno-oncology

- Effector cells: T and NK cells
- Protector cells: MDSC, TAM, TAN, Treg, CAF
INB03 decreases MDSC by “starvation”

- **No pSTAT3** stops differentiation and proliferation of myeloid cells to MDSC
- ↑ NK/DC recruits CD8+ TIL to tumor
- ↓ MDSC causes ↓ TAM and Treg
- tmTNF required for NK/DC crosstalk
INB03 HER2/MUC4 Appendix
• ~30% of women with breast cancer are HER2+
• 30% - 50% patients have 1° or 2° resistance to trastuzumab
• MUC4 expression predicts trastuzumab resistance

![Disease-free survival probability graph](image_url)

- MUC4 negative n=31
- MUC4 positive n=47

P=0.0086
INB03 reverses trastuzumab resistance in JIMT-1 tumors

INB03 overcomes trastuzumab resistance in JIMT-1 tumors

MUC4 blocks trastuzumab binding

INB03 decreases MUC4 expression

T-trastuzumab
DN- INB03

Schillaci-SABCS2018
Alzheimer’s Disease Appendix
Soluble TNF: a validated target in AD

1. Risk of AD in RA patients 8 times higher*
2. Risk of AD in RA patients treated with anti-TNF therapy is 0.4* (60% lower)

* In RA patients compared to patients without RA

from Chou et al. 2016
INMB non-confidential3Q19.v4
AD is an expanding, expensive and intractable disease that defies a therapeutic solution

- **Problem**: synaptic pruning and nerve cell death
- **Solution**: reduce neuroinflammation
- **Drug**: XPro1595
- **Target**: activated glial cells in the brain
- **Status**: entering Phase I trial in patients with mild to moderate Alzheimer’s disease
Majority of genes associated with AD expressed in innate immune cells

<table>
<thead>
<tr>
<th>Cell type</th>
<th>-log10(p-value)</th>
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</thead>
<tbody>
<tr>
<td>Microglia</td>
<td></td>
</tr>
<tr>
<td>Hippocampal CA 1 pyramidal neurons</td>
<td></td>
</tr>
<tr>
<td>Endothelial cells</td>
<td></td>
</tr>
<tr>
<td>Prefrontal glutamergic neurons 2</td>
<td></td>
</tr>
<tr>
<td>Prefrontal glutamergic neurons 1</td>
<td></td>
</tr>
<tr>
<td>Oligodendrocytes</td>
<td></td>
</tr>
<tr>
<td>Astrocytes 2</td>
<td></td>
</tr>
<tr>
<td>Oligodendrocyte precursor cells 1</td>
<td></td>
</tr>
<tr>
<td>GABAergic interneurons 1</td>
<td></td>
</tr>
<tr>
<td>Neuronal stem cells</td>
<td></td>
</tr>
<tr>
<td>GABAergic interneurons 2</td>
<td></td>
</tr>
<tr>
<td>Oligodendrocyte precursor cells 2</td>
<td></td>
</tr>
<tr>
<td>Hippocampal CA 3 pyramidal neurons</td>
<td></td>
</tr>
<tr>
<td>Astrocytes 1</td>
<td></td>
</tr>
<tr>
<td>Dentate gyrus granule neurons</td>
<td></td>
</tr>
</tbody>
</table>

Jansen2019
Genetics implicates every aspect of the immune cell is dysfunctional

McQuade & Blurton-Jones, 2019
TNF in humans: the dark passenger of AD

• Elevated plasma TNF (Fillit et al. 1991)
• TNF co-localized with plaques (Dickson 1997)
• TNF levels correlate with disease progression (Paganelli et al. 2002)
• Elevated TNF in CSF (Tarkowski et al. 2003)
XPro1595 attenuates AD pathology and restores normal function.

**Synapse dysfunction**

- Saline
- XPro1595
- NTG
- TgCRND8

**Cognitive Impairment**

- Spatial Learning
- Swim distance (% first block)
- Training block

**Immune dysfunction**

- Activated Myeloid cells
- Brain T cell infiltration

**Amyloid pathology**

- Microglia
- Saline
- XPro\textsuperscript{1595}
- Hippocampus

*Efficacy has been shown in 3xTgAD, 5xFAD, TgCRND8 and aged mice*
Problem XPro1595 Addresses: Neuroinflammation, Linked to Every Aspect of Alzheimer’s Disease Pathology

XPro1595 is a protein biologic that targets soluble Tumor Necrosis Factor (sTNF) to decrease neuroinflammation linked to Alzheimer’s Disease.
Phase 1b Biomarker Directed, Proof of Biology Study in Mild to Moderate AD Patients

Key enrollment criterion
- Mild to Moderate Disease (N=18)
- Positive for Amyloid
- Blood hsCRP > 2mg/L

Baseline
- Safety
- Blood inflammation
- Brain inflammation
- Imaging (MRI)
- Cognition
- Psychiatric symptoms
- Quality of Life

Week 6
- Safety
- Blood inflammation
- Imaging (MRI)
- Cognition
- Psychiatric symptoms
- Quality of Life

Week 12
- Safety
- Blood inflammation
- Brain inflammation
- Imaging (MRI)
- Cognition
- Psychiatric symptoms
- Quality of Life

<table>
<thead>
<tr>
<th>Cohort (n=6)</th>
<th>Dose of XPro1595</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort 1:</td>
<td>0.3 mg/kg</td>
</tr>
<tr>
<td>Cohort 2:</td>
<td>1.0 mg/kg</td>
</tr>
<tr>
<td>Cohort 3:</td>
<td>3.0 mg/kg</td>
</tr>
</tbody>
</table>
INKmune Appendix
Problem: Minimal Residual Disease (MRD) causes relapse

Difference between survivors and relapsers is MRD
Residual disease is the cause of relapse and death in a majority of patients

- **Problem:** cancer remains after treatment
- **Solution:** eliminate residual disease
- **Drug:** INKmune
- **Target:** patient’s NK cells
- **Status:** entering Phase I/II trial in women with relapse/refractory ovarian cancer
What is MRD?

• Residual disease is the cancer that is left behind after treatment
• Two types:
  – Overt: visible by imaging studies
  – Minimal (MRD): invisible by imaging studies
• Natural Killer (NK) cells are responsible for eliminating MRD
• **Problem:** patient’s NK cells are inert
• **Solution:** INKmune primes the patient’s NK cells to attack MRD
**Survivor AML**

**Survivor NK cells**

Does Not Kill

**Relapser AML**

**Relapser NK cells**

Does not kill

**Kills**

**Conclusion:** AML mutates to evade NK cell killing.
Relapse due to Minimal Residual Disease

**Relapse due to MRD**

- rNK Cell
- Cancer Cell

Cancer down-regulates S1, "evading" NK cells, allowing cancer to grow.

**INKmune primes NK cells to eliminate MRD**

- TpNK Cell
- Dead-Cancer Cell

INKmune artificially replaces S1 allowing the NK to engage and kill cancer cells.

\[
\text{aNK Cell} = \text{Activated NK Cell} \\
\text{rNK Cell} = \text{Resting NK Cell}
\]
Results with 1st-Generation TpNK Therapy

AML Phase 1

2 Phase 1 clinical trials; 20 patients with high-risk AML using ex vivo, personalized TpNK therapy

Clinical Results

- *Prolonged* remissions with excellent quality of life
- Put chemo-resistant disease into remission
- 2 patients remain alive in complete remission after >3 years

Conclusions:

- TpNK biology translated to the clinic
- Most patients relapsed – need multiple treatments
- Personalized therapy cumbersome – need universal off-the-shelf solution
NK cells and INKmune in Ovarian Cancer

**SKOV3 killing by NK cells from healthy donor (HD) or CaOva patient ascites**

![Bar chart showing SKOV3 killing by NK cells](chart.png)

Patient ascites NK cells kill SKOV3

IL2 primed NK cells do not kill SKOV3
**INKmune MOA**

**INB16 vs cytokine priming – Differential protein expression @16h**

- Paradoxical decrease (not loss) in ligand expression associated with increased function
- INKmune priming fundamentally different than cytokine or antibody priming
INKmune Primed NK Cell Killing Assay

**Real-Time Cytolysis Plot**

- NK 1:1
- NK 2:1
- NK 5:1
- NK 20:1
- TP-NK 1:1
- TP-NK 2:1
- TP-NK 5:1

% Cytolysis vs. Time (hr Post-Treatment)

INKmune added

NK added
INKmune MOA

INB16

NK

CD15 epitope

CD2

CD16

NK

CD3ζ

INK signalling upon co-culture with CTV-1

% positive

pLAT

pZAP70

TpNK 4h

rNK

Lowdell2007

INKB non-confidential3Q19.v4
ALCAM - NK cell migration and adhesion
STAT5 – “molecular switch” essential for NK killing
CD70 – CD27L and NCR for B cell tumours
VEGFA – survival signal for NK
CXCL10 – chemoattractant for NK cells