Monobody-Linker Technology as a Catalyst to Transform Access to Organ Transplantation

Nanoparticle (NP) Core

Inert Coating

Drug cargo

Targeting Ligand

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Blavatnik Proposal
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Our Motivation: Improving Access to Organ Transplant

Comparative Survival Without Transplant:
- Kidney – ~30% survival for typical 6-8 year wait
- Liver – 27% Survival at 3 months

Data from:
Cooper et al. Clinical Transplant 33 e13419 (2019).
Our Approach:
Vascular-targeted nanomedicines delivered ex vivo

Characteristics of Ideal Therapy for Ex Vivo Organ Repair:

- Potential for sustained effect
- Modular adaptability for different drugs
- Capacity for robust retention on vascular-endothelium throughout organ

Ex Vivo Organ Perfusion has Emerged as a Clinical Platform for Organ Repair

Our Comprehensive Team of Experts

**Transplant/Vascular Immunology**

- **Jordan Pober MD/PhD, Yale University**: World leader in human translational immunology with decades of experience in defining biologic pathways of injury related to organ transplant

**Targeted Nanomedicine Development**

- **Mark Saltzman PhD, Yale University**: World leader in nanomedicine based drug delivery, member of two national academies (Medicine, Engineering), founder of Yale CBIT, several patents & startup co.
- **Shohei Koide, PhD, NYU**: World leader in protein engineering, Inventor of Monobody Technology, extensive experience with therapeutic Ab development (1 Ab nearing IND), 19 issued patents
- **Greg Tietjen, PhD, Yale**: Emerging leader in therapeutic delivery during ex vivo human organ perfusion, built a robust pipeline for preclinical research in non-transplanted human organs

**Clinical Organ Transplant and Ex Vivo Organ Perfusion**

- **Peter Friend, MD, Oxford University**: Pioneer of normothermic liver perfusion, scientific founder of OrganOx and co-inventor of best-in-class liver perfusion device
- **Mike Nicholson, MD, Cambridge University**: Pioneer of normothermic kidney perfusion, currently running largest multi-center randomized control of kidney machine perfusion
The Problem: Getting Nanomedicines to the Cells that Need Them

Achieving effective NP-targeting in a petri dish is easy!

Translating this to a complex vascular network in a human organ is really hard!

Targeted PLA-PEG NP Delivered in Human Kidney Ex Vivo

The Problem:
Getting Nanomedicines to the Cells that Need Them

Human Organs are Very Complex and Competitive Environment!
Our Solution: Monobody-Linker Technology

Benefits of our technology:

• Optimal antibody orientation dramatically improves targeting
• Highly adaptable to different Abs and payloads
• Can use existing Abs without need to re-engineer or produce bespoke Abs
• Current version binds IgG1 FC, but adaptable to other Abs species/isoforms (e.g. humanized Abs)

Monobody Binding Protein (invented by Shohei Koidei)

Lack of disulfides allows for engineered terminal cysteine
Market Opportunity

**Phase I: Ex Vivo Organ Delivery**
- Transplant Market ~$3 billion
- Cost per transplant:
  - Kidney: $418,400
  - Liver: $812,500
- Current # on Wait list:
  - ~114,000 patients
- Current # of Transplants/year
  - ~30,000

**Phase II: In Vivo Delivery**
- Pre-clinical validation in human organs could enable targeted in vivo delivery
- Diagnostic and Therapeutic possibilities in wide array of indications
- Nanomedicine market projected to be ~$350 billion by 2025

How We Intend to Use Blavatnik Funds

- Requesting $300k for preclinical validation to enable clinical trials
- CRO for large scale production of Monobody-NP and in vitro validation
- Ex Vivo validation in human liver and kidney (Tietjen and Friend Labs) with CRO analysis of biopsies
  - Phase I: NP target and dose optimization
  - Phase II: Evaluation of Therapeutic Efficacy
- Candidate therapeutic encapsulants:
  - Small Molecule: Rapamycin
  - siRNA: MHC knockout

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