Improving the Outcome of Stem Cell Transplants for Cancer Treatment Using Multivirus-Specific T Cells (Viralym-M)

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Co-Founder and Chief Scientific Officer
Severe viral infections can threaten the lives of anyone with a weakened immune system

VIRAL INFECTION AND STEM CELL TRANSPLANTS

- Approximately **30,000 patients** received an allogeneic hematopoietic stem cell transplant (allo-HSCT) in 2017 (US and EU).

- **Up to 70%** of allo-HSCT patients suffer a severe viral infection following transplant.\(^1\)

- Viral infections cause pain, extended hospital stay, transplant failure, and organ failure.

- Viral infections are the **leading cause of non-relapse mortality** after allo-HSCT.

- There are **no FDA approved drugs** or effective experimental therapies for treating most infections.

\(^1\) Slade et. al., Transplant Infect Dis, 2016
BACKGROUND AND INTRODUCTION

- ViraCyte was formed to commercialize novel T cell therapies developed at Baylor College of Medicine

- Why now?
  - **Mature therapy**: >20 years of R&D and clinical experience at Center for Cell and Gene Therapy, BCM
  - **Unmet medical need** among cancer patients, and increasing demand from transplant centers
  - Demonstrated **safety and efficacy** in >100 patients treated (BCM and ViraCyte INDs)
  - Clinically validated “off the shelf” availability of therapy
  - Simple, robust, and **scalable manufacturing**
**VIRACYTE: MANUFACTURING PLATFORM**

- **Validated, fully-GMP compliant manufacturing process**
- **One production (1 unit of blood) yields 300 adult T cell doses**
- **Depletion of alloreactive cells → minimal risk of GVHD**
- **Validated potency assay**
- **Product stability proven up to 5 years**

* Exclusively Licensed from Baylor College of Medicine
**VIRALYM-M PRODUCTION**

**Day 0**
- 250E+06 PBMCs
- Pepmix + cytokines
- 1 L of media

**Day 9-12**
- 4E+09 VSTs
VIRALYM-M EXPANSION

**T Cell Number**

```
Days
0 1 9
```

**Culture Monitoring**

```
Days
3 4 5 6 7 8 9
```

- Glucose
- Lactate

**Total number of cells (x10^9)**

```
0 1 2 3 4
```

**mMol/L**

```
0 5 10 15 20
```

**mg/dl**

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0 100 200 300 400
```
### SCIENTIFIC AND CLINICAL FOUNDATION

- “Off the shelf” T cells
- Multivirus specificity: BK, CMV, AdV, HHV6, EBV
- Current cell bank from 59 healthy donors
- Single arm Phase I/IIA Trial (ongoing) for allo-HSCT patients with one or more **refractory** viral infections
- 46 patients with 53 refractory infections

### PHASE I/IIA CLINICAL PROTOCOL

- Patients receive $2 \times 10^7$ multi-virus specific T cells per square meter of body surface area intravenously
- If less than a complete response is achieved, patients may receive additional doses at 2 week intervals following the initial infusion
VIRALYM-M T CELL PHENOTYPE

% positive cells

n=59

CD3  CD4  CD8  CD3/56  CD45RO

CD62L+

CCR7+

CD45RO

CD62L−
### 46 PATIENTS – 53 INFECTIONS

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<th>Viruses</th>
<th>CMV</th>
<th>EBV</th>
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**ViraCyte**

ADVANCING T CELL THERAPY
## VIRAYLM-M – OVERALL RR 94%

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Tzannou et al, JCO, 2017
VIRALYM-M: CLINICAL RESPONSE FOR PATIENT WITH CMV

CMV DNA copies / ml

Month -2  Month -1  pre-infusion  Week1  Week 2  Week 4  Week 6

T cells
Viral load

Viralym-M

SFC /5x10^5

Month -2  Month -1  pre-infusion  Week1  Week 2  Week 4  Week 6
VIRALYM-M: CLINICAL RESPONSE FOR PATIENT WITH EBV

![Graph showing T cells and Viral load over time.]

- **Viralym-M**
- **copies / ug DNA**
- **SFC /5x10^5**

- **T cells** vs **Viral load**
- **Pre-infusion**
- **Week 1**
- **Week 2**
- **Week 4**
- **Week 5**
- **Week 6**
17 of 42 patients enrolled in Viralym-M protocol suffered from severe, refractory BK-associated disease

- 15 BK Hemorrhagic Cystitis
- 2 BK nephritis

17/17 patients with BK disease had complete clinical resolution of disease following Viralym-M treatment
VIRALYM-M: VIROLOGIC RESPONSE FOR PATIENT WITH BKV

Viralym-M

- viral load plasma
- viral load urine

Tzannou et al, JCO, 2017
**BK VIRUS-ASSOCIATED HEMORRHAGIC CYSTITIS FOLLOWING HSCT**  
A Critical Unmet Clinical Need

- **BK virus** is a non-enveloped, DNA polyomavirus identified in the 1980s as a significant pathogen in HSCT patients

- **25% of allo-HSCT patients suffer BK hemorrhagic cystitis (HC)**\(^1\)
  - Severe, debilitating pain
  - Hemorrhage leading to 2X red blood cell transfusions; 3X platelet transfusions; average of 10 days extra hospital stay
  - BK-HC is strongly associated with the development of renal failure and increased non-relapse mortality
  - Each episode of BK-HC adds on average $71,000 - $231,000 in health care costs

- **Up to 65% of adult haplo-HSCT** on Post-Cy regimen develop BK-HC (Texas Transplant Institute, San Antonio, TX)

- There are **no FDA approved drugs to treat BK**; off-label or experimental drugs are ineffective, toxic, and generally avoided at major transplant centers

\(^1\)Abudayyeh et. al., Journal of Transplantation, 2016
<table>
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CONTACT INFORMATION:

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