SPEARHEAD-1: A Phase 2 Trial of ADP-A2M4 SPEAR T-Cells in Patients with Advanced Synovial Sarcoma or Myxoid/Round Cell Liposarcoma

**Background**
- ADP-A2M4 T-cells target MAGE-A4 tumors (Figure 1).
- MAGE-A4 is highly expressed in synovial sarcoma and myxoid round cell liposarcoma (MRCLS) in the context of HLA-A*02 (Figure 2).
- This Phase 2 trial was initiated based on the favorable benefit/risk profile of ADP-A2M4 observed in a Phase I trial (NCT03132922), which demonstrated compelling clinical responses in patients with synovial sarcoma.

**Synovial Sarcoma**
- ~800–1000 new cases/year in the United States
- Often occurs in patients aged <40 years
- High metastatic potential

**MRCLS**
- ~750 new cases/year in the United States
- Typically presents at 35–55 years of age
- One-third MRCLS become metastatic

**SPEARHEAD-1 trial (NCT04044768)**
- Recruiting 45 patients from North America and Europe
- Advanced synovial sarcoma or MRCLS, prior chemotherapy, HLA-A*02 and MAGE-A4 positive

**Soft tissue sarcomas**
- >50 subtypes, including liposarcoma and synovial sarcoma
- Prognosis in advanced disease remains unfavorable

**Synovial Sarcoma MRCLS**

**Trial Details**
- Primary objective is to evaluate the efficacy of ADP-A2M4 in patients with synovial sarcoma or MRCLS
- Determined by the Overall Response Rate, defined as incidence of complete or partial responses as assessed by independent RECIST v1.1 review
- We are currently recruiting trial participants
  - Total of 20 sites open: 14 in the US, 1 in Canada, 2 in France, and 3 in Spain
- Trial design and engineered T-cell pathway are shown below (Figure 3 and Figure 4)

**Abbreviations**
- HLA: human leukocyte antigen
- IHC: immunohistochemistry
- MAGE-A4: melanoma-associated antigen-A4
- MRCLS: myxoid/round cell liposarcoma
- RECIST: response evaluation criteria in solid tumors
- SPEAR: specific peptide engineered antigen receptor
- TCR: T-cell receptor

**SPEARHEAD-1 trial design**

**Translational Studies**
- Analysis of targeted antigens in sarcoma biopsies
- Identification of novel targets
- Pre-clinical models

**Trial Assessments**
- Interim analysis after 20 patients
- Final analysis after 45 patients
- Safety assessed via grade 3/4 toxicity

**Apheresis**
- Leukapheresis
- Wash cells in automated device
- Positive selection of engineered TCRs

**Manufacturing**
- Fresh apheresis collection
- Apheresis in automated device
- Stores at <–130°C prior to manufacturing facility

**Quality Control**
- Release testing
- Release criteria in solid tumors
- SPEAR, specific peptide engineered antigen receptor

**SPEAR T-cell pathway**
- Fresh apheresis collection
- Harvest of cells in automated device
- Cryomedia and cryopreserve
- Store at <–130°C

**SPEAR T-cell infusion**
- Infusion center receives manufactured product and stores at <–130°C
- Infusion
- Tumor site
- More common
- Less common

**Patient cell journey**
- Harvest of cells in automated device
- Cryomedia and cryopreserve
- Store at <–130°C
- Infusion center receives manufactured product and stores at <–130°C
- Infusion

**Figure 1. MAGE-A4 expression (IHC analysis)**

**Figure 2. MAGE-A4 antigen-A4 TCRs**

**Figure 3. SPEARHEAD-1 trial design**

**Figure 4. Patient cell journey**

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1077x1559

41

1077x1581

1

1077x1616

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More common    Less common

Tumor site

Sarcoma

Cancer cell

TCR is the T-cell's natural receptor construct

Access to broader spectrum of extra- and intra-cellular proteins

More options for targeting cancers by enhancing the natural immune system:

MAGE-A4 antigen

Engineered TCRs

SPEAR T-cell mechanism of action video can be viewed by clicking here:
https://youtu.be/zdI8IGXoQd0

Full trial details from ClinicalTrials.gov

ASCO Annual Meeting, May 29-June 2, 2020 (Virtual Format)