TRX518 is a differentiated, humanized non-depleting IgG1 GITR agonist mAb.

GITR agonist without FcR binding signals to and does not deplete GITR expressing T cells.
Combination with PD-1 or PD-L1 Immunotherapy

Advanced solid tumors with labeled indications either as new combination therapy or add-on to best response of SD after 4 cycles

- First 2 patients treated at higher dose demonstrated clinical benefit
  - PR (-77%) esophageal squamous cell carcinoma
  - SD (-23%) ocular melanoma

- 1 patient at lower dose responded
  - PR (-39%) urothelial carcinoma previously treated with Keytruda

- Enrolling higher dose group

Combination with Gemcitabine

Advanced solid tumors where gemcitabine indicated

- 4 of 6 patients at higher dose demonstrated clinical benefit
- No dose limiting toxicity
- Expansion cohort (N=20) will be fully enrolled in Q4 2018
PR with TRX518 in Combination with Opdivo
Urothelial Carcinoma (previously treated with Keytruda)

- 75 year old male diagnosed in 2017
- PD-L1 positive tumor with baseline disease (at study entry) in lungs, lymph nodes, bones, retroperitoneum
- Prior therapy included radical nephrectomy followed by Keytruda (initial partial response, developed acquired resistance with progressive disease after 8 months)
- TRX518/Opdivo Response
  - PR at end of cycle 2 scans (39% reduction)
  - PR confirmed at end of cycle 4 scans, remains on therapy in cycle 5
- Increased infiltration of CD8+ T cells post-Rx
- Increased Granzyme B staining post-Rx
Two Target lesions (TL): Pre-treatment vs. EOC2 Scans

May 7, 2018 scan – Sum of TL* lesions: 38 mm

July 27, 2018 scan – Sum of TL* lesions: 23 mm

Per RECIST V1.1, a -39% reduction from baseline - Partial Response (PR)

*TL – Pre and para-aortic lymph nodes
• 86 year old female diagnosed in 2017

• Baseline disease in upper third of esophagus, supraclavicular lymph node

• Previously treated with concurrent carboplatin, paclitaxel and radiation therapy

• Microsatellite stable and PD-L1 positive tumor

• TRX518/Keytruda Response
  • PR at end of Cycle 2 scans (36% reduction)
  • Response deepened at end of Cycle 4 scans to a near CR (77% reduction)
**3000-0092 – esophageal cancer – PR at 6wk scan**

combination with pembrolizumab at 4 mg/kg load f/b 1 mg/kg 3 wks

Pre-Tx

Post-Tx (C1D21)
Leap Therapeutics | SD with TRX518 in Combination with Keytruda - Ocular Melanoma

• 45 year old male diagnosed in 2016

• Baseline disease in left choroid area of the eye and multiple liver metastases

• Previously treated with Ru-plaque radiation therapy and laser thermal therapy to eye

• TRX518/Keytruda Activity
  • SD at end of Cycle 2 scans (23% reduction)
  • SD with continued disease control and tumor reduction at end of Cycle 4 scans

• Ocular melanoma has known poor outcomes to anti-PD-1 therapy (Algazi 2016)
  • ORR: 3.6%
  • SD: 8.9%
  • PFS: 2.8 months
9349-0091 – ocular melanoma—SD at cycle 3 scan combination with pembrol at 4 mg/kg load f/b 1 mg/kg 3 wks

Pre-Tx

Post-Tx (C3D1)
Leap Therapeutics | CTX has Synergistic Activity with GITR agonist and modulates T cell ratios

Presented at AACR 2018 by Betof Warner, Hirschhorn, Wolchok, Merghoub (MSKCC)
B16 Melanoma Mouse Model
Tumor-Free Survival

Days post B16 injection

Tumor-free (%)

αGITR+αPD-1 Day 7
αGITR Day 4
αPD-1 Day 7
αGITR Day 7

Data from Zappasodi, Wolchok, Merghoub (MSKCC)
**PD1/PD-L1** therapy blocks CD8 exhaustion complementing GITR Therapy

**GITR**, as a costimulatory receptor, works best when antigen primed quiescent T cells are re-stimulated with appropriately processed antigen on APC bearing GITRL.

**CTX** promotes immunogenic cell death of tumors, enabling efficient tumor antigen presentation, complementing GITR therapy.

*Image from J Clin Invest DOI: 10.1172/JCI91190*
Stable Disease Achieved in Over 50% of Patients on TRX518 Multidose

Duration on Study (days)

Best Overall Response

<table>
<thead>
<tr>
<th>Response</th>
<th>Count (Percentage)</th>
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<tbody>
<tr>
<td>Stable Disease (SD)</td>
<td>24 (55.8%)</td>
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<tr>
<td>Progressive Disease (PD)</td>
<td>11 (25.6%)</td>
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<tr>
<td>Not Evaluable</td>
<td>8 (18.6%)</td>
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</table>

All Patients (N=43)
Leap Therapeutics | TRX518 Monotherapy Patient with Long-Term Stable Disease

- Hepatocellular carcinoma patient
- Currently in Cycle 20 with 15% reduction in liver lesion
- Failed prior CTLA4/PD-L1 therapy

Tumor Biopsy Analysis

- Reduction in Treg cells
- Increase in CD8/Treg ratio

Quadruple staining analysis

<table>
<thead>
<tr>
<th>Tregs (% of total cells)</th>
<th>CD8+ T cells (% of total cells)</th>
<th>CD8/Tregs ratio</th>
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<tbody>
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<td>PRE</td>
<td>POST</td>
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Cell frequency or ratio