The clinical benefit of CTLA-4 blockade to cancer patients has been well established.

However, efficacy of current therapies is impaired by dose limiting toxicity arising from systemic immune activation.

XTX101 is a tumor-selective anti-CTLA-4 mAb that is designed to improve upon the therapeutic index of existing anti-CTLA-4 therapies by overcoming potency and tolerability limitations.

XTX101 has improved potency.

• Higher affinity binding to the target CTLA-4.

• Enhanced Fc effector function.

• Reduced peripheral immune activation.

• Better in vivo circulation in the periphery due to masking of the CDR sequences.

• Activated by protease-dependent release of the masks.

• Active selectively in the tumor microenvironment and avoids toxicity associated with systemic immune activation.

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### RESULTS

**XTX101: Affinity and Fc enhancements combined with tumor selectivity for optimized TI**

- **α-CTLA4 mAb**
  - Increased specificity through improved affinity and enhanced ADCC to deplete Tregs.

- **Improved tolerability by adding tumor selectivity.**
  - Combining increased potency and improved tolerability to maximize opportunity for improved TI.

### BACKGROUND

**Ipilimumab data strongly validate potential for improved α-CTLA4 mAb**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Median OS</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mg/kg</td>
<td>11.5 mo</td>
<td>Treatment with higher dose resulted in increased OS but also increased AEs and discontinuations.</td>
</tr>
<tr>
<td>10 mg/kg</td>
<td>15.7 mo</td>
<td></td>
</tr>
</tbody>
</table>

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### RESULTS

**XTX101 shows potent TGI, superior to ipilimumab-analog**

A dose of 3 mg/kg of ipilimumab-analog is required to achieve similar peripheral PD.

The clinical benefit of CTLA-4 blockade is well established, but remains limited due to toxicities arising from systemic immune activation.

**XTX101 is a potent, tumor-selective anti-CTLA4 mAb with the potential to significantly expand the TI relative to ipilimumab and therefore potentially reduce toxicity while enhancing efficacy.**

**Functional characterization of XTX101 confirmed protease-dependent activity.**

- XTX101 binds to CTLA4 with high affinity in a protease-dependent manner.

- XTX101 inhibits protease-dependent inhibition of CD80/86 binding to CTLA4.

- XTX101 is more potent than ipilimumab-analog.

- XTX101 possesses protease-dependent ADCC activity.

**Conclusion:**

The broad potential for tumor selective XTX101 activity leads to opportunities in many indications.

Given the broad activity of XTX101 across diverse tumor types, Companion Diagnostic (CDx) biomarker for prostate activity or expression likely not required.

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**XTX101 demonstrates potent intratumoral PD, superior to ipilimumab-analog**

A dose of 0.3 mg/kg of ipilimumab-analog is required to achieve similar efficacy and CR rate as XTX101 at 0.3 mg/kg, suggesting XTX101 has 10x higher potency.

**Conclusion:**

**XTX101 is a potent, tumor-selective anti-CTLA4 mAb with the potential to significantly expand the TI relative to ipilimumab and therefore potentially reduce toxicity while enhancing efficacy.**

**Functional characterization of XTX101 confirmed protease-dependent activity.**

- XTX101 binds to CTLA4 with high affinity in a protease-dependent manner.

- XTX101 inhibits protease-dependent inhibition of CD80/86 binding to CTLA4.

- XTX101 is more potent than ipilimumab-analog.

- XTX101 possesses protease-dependent ADCC activity.

**Conclusion:**

The broad potential for tumor selective XTX101 activity leads to opportunities in many indications.

Given the broad activity of XTX101 across diverse tumor types, Companion Diagnostic (CDx) biomarker for prostate activity or expression likely not required.

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**XTX101 is activated broadly across multiple tumor indications based on ex vivo studies in fresh human tumor tissue.**

These data support evaluation of XTX101 in clinical studies.

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**CONCLUSION**

- XTX101 is a potent, tumor-selective anti-CTLA4 mAb with the potential to significantly expand the TI relative to ipilimumab and therefore potentially reduce toxicity while enhancing efficacy.

- Functional characterization of XTX101 confirmed protease-dependent activity.

- XTX101 binds to CTLA4 with high affinity in a protease-dependent manner.

- XTX101 inhibits protease-dependent inhibition of CD80/86 binding to CTLA4.

- XTX101 is more potent than ipilimumab-analog.

- XTX101 possesses protease-dependent ADCC activity.

- XTX101 is activated broadly across multiple tumor indications based on ex vivo studies in fresh human tumor tissue.

These data support evaluation of XTX101 in clinical studies.

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**XTX101 shows Treg depletion in the tumor and no effect on peripheral Treg levels.**

A dose of 0.3 mg/kg of ipilimumab-analog is required to achieve similar peripheral PD as XTX101 at 10 mg/kg, consistent with better tolerability of XTX101 in mice.

**Conclusion:**

- XTX101 shows Treg depletion in the tumor and no effect on peripheral Treg levels.

- XTX101 demonstrates 10x improvement in potency in tumor growth inhibition studies.

- XTX101 exhibited enhanced Treg depletion in tumors.

- XTX101 showed reduced peripheral immune activation by comparison to ipilimumab-analog.

- XTX101 is activated broadly across multiple tumor indications based on ex vivo studies in fresh human tumor tissue.

These data support evaluation of XTX101 in clinical studies.