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Caki-1 Preclinical Characterization of ARX305, a Next-Generation Anti-CD70 Antibody Drug Conjugate for the Treatment of CD70-Expressing Cancers


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RESULTS

<table>
<thead>
<tr>
<th>Table 2. CD70-Selective In Vitro Cytotoxicity in Tumor Cells</th>
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<td>Cell line</td>
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<td>786-O</td>
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<tr>
<td>Caki-1</td>
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<tr>
<td>U251MG</td>
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<tr>
<td>U266</td>
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<tr>
<td>Raji</td>
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<td>REC-1</td>
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<td>HiS676</td>
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<td>NCI-H929</td>
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ARX305 potently inhibited CD70-expressing tumor cell line growth in vitro, and exhibited minimal activity in CD70-negative tumor cell cultures.

CONCLUSION

- The ARX305 preclinical data demonstrated:
  - Stability in the circulation and mAb-like PK of the ADC
  - ARX305 outperforming sunitinib
- ARX305 was tolerated in cynomolgus monkeys at exposures well within the pharmacologically active dose in mice showed a clear therapeutic index.
- ARX305 was administered to male and female cynomolgus monkeys once every 3 weeks for a total of 3 doses followed by a 5-week recovery period.
- Comparison of the ARX305 concentration-time curve at the middle dose (identified as the HNSTD) in monkeys versus the concentration-time curve at a pharmacologically active dose in mice showed a clear therapeutic index.

REFERENCES


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Figure 3. Stability in Circulation

Figure 4. Cynomolgus TK & Therapeutic Index

ARX305 was administered to male and female cynomolgus monkeys once every 3 weeks for a total of 3 doses followed by a 5-week recovery period. Comparison of the ARX305 concentration-time curve at the middle dose (identified as the HNSTD) in monkeys versus the concentration-time curve at a pharmacologically active dose in mice showed a clear therapeutic index.

Samples collected from CD1 mice dosed with 1 mg/kg ARX305 or Unconjugated Antibody were measured in Total Antibody (TA) and Intact ADC (DA2-specific) PK methods. ARX305 TA and Intact ADC curves were overlaid, confirming high ADC stability in circulation and a long terminal half-life of 16.5 days. ARX305 showed a higher similarly PK profile as Unconjugated Antibody, demonstrating ADC clearance is not impacted by conjugated AS269.

CONCLUSION

- The ARX305 preclinical data demonstrated:
  - Stability in the circulation and mAb-like PK of the ADC
  - Strong anti-tumor activity in two RCC xenograft models, with ARX305 outperforming sunitinib
  - A single dose of 1.5 mg/kg ARX305 significantly increased survival in a multiple myeloma disseminated model
  - ARX305 was tolerated in cynomolgus monkeys at exposures well above the therapeutic exposure in mouse pharmacology studies, indicating a wide therapeutic window.
- The preclinical data support investigation of ARX305 in clinical trials targeting patients with CD70-positive cancers.
- ARX305 IND in the United States is open, and a Phase 1 dose escalation study in China is currently in progress.