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Xentria: redefining collaborative approaches to advance R&D

Xentria is taking an innovative approach leveraging in vitro and pharmacokenitic models and the power of partnerships to co-develop accessible treatment options for patients with unmet needs.

Based in Chicago, Xentria is offering a new collaborative way to move molecules from concept to clinical trials to market, all while adding value and finding solutions. By working with biotech partners like Xentria, scientists can progress challenging research and development (R&D) projects—leveraging their partners' expertise and capabilities while retaining their own agency. Xentria validated this model in its lead rare-disease drug candidate by leveraging early community engagement, exploring innovative regulatory and clinical strategies, and deploying novel approaches to de-risk future clinical trials and commercialization. These efforts allowed Xentria to add value to the asset early in development and identify a commercialization partner.

Xentria was established in 2020 to develop a new way to collaborate to solve unmet clinical needs for suffering patients. The biotech leverages internal experience and relationships across the pharmaceutical industry and academia, while embracing the risk that comes with innovation, to turn challenging drug targets into promising clinical programs.

Validating the model

Xentria validated its approach in the development of an anti-tumor necrosis factor alpha (TNF-α) monoclonal antibody, XTMAB-16, which is currently in clinical trials as a potential treatment for the rare inflammatory disease pulmonary sarcoidosis (Fig. 1). Similar types of molecules have shown promise in this indication, but corticosteroids remain the only approved treatment. Chronic use of steroids can lead to side effects and decreased quality of life, leaving limited treatment options.

Sarcoidosis affects individuals differently, and companies have struggled to design successful drug trials, leading to disinvestment and limited treatment options. To manage this, Xentria took a collaborative risk and evidence-based approach to design an innovative trial for pulmonary sarcoidosis by working closely with key opinion leaders, advocacy groups, and scientists around the globe. The biotech took into account key physiologic and quality-of-life outcomes, and worked with regulators to align outcomes considered meaningful for patients and their physicians.

Xentria deployed novel scientific strategies to account for disease heterogeneity by simulating the suspected propensity of XTMAB-16 at different doses to reach pulmonary granulomas. These efforts helped to bolster scientific rationale and identify potentially safe and effective doses to study. The biotech described the novel approach in a paper published in the journal *Frontiers in Pharmacology*[1].

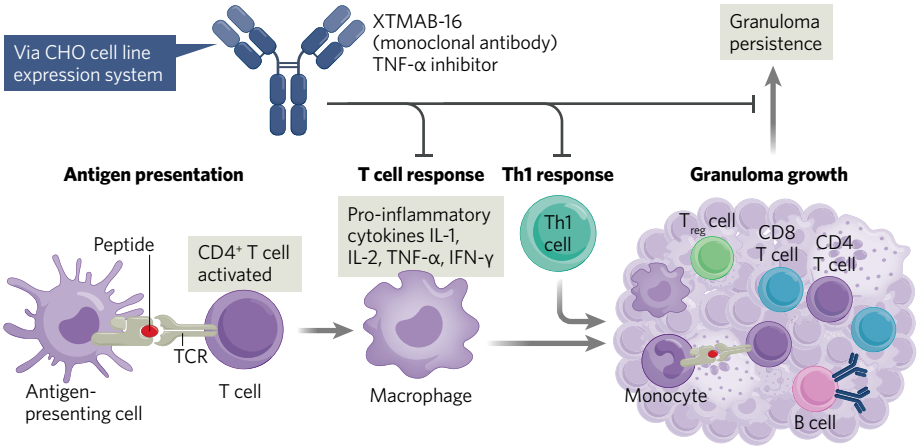

Fig. 1 | The proposed mechanism of action of XTMAB-16. XTMAB-16 aims to inhibit key pro-inflammatory cytokines to reduce activation of inflammatory pathways implicated in pulmonary sarcoidosis.

The team identified a potentially efficacious dose range in an in vitro model while concurrently exploring XTMAB-16 in its first-in-human clinical trial. Xentria used these combined data to develop a population pharmacokinetic model. The model enabled Xentria to evaluate sources of pharmacokinetic variability and guided its dose level and frequency assumptions.

The project marked the first time that bio-simulation modeling had been used to influence dosing strategy in a sarcoidosis trial, de-risking future development and providing a translational framework for selecting a safe and effective dose for patients.

In parallel, Xentria worked to understand the patient journey for sarcoidosis and made sure the patient's voice was heard early in development. The biotech considered race, gender, and socioeconomic disparities as it designed future trials of the candidate. The team also worked to provide equitable inclusive criteria and a trial design that was not overly burdensome to patients or researchers. In addition, the team weighed diversity and inclusion as a core tenet when selecting strategic partners for XTMAB-16 trials.

The team is working to complete enrolment for studies in patients living with pulmonary sarcoidosis while continuing to engage with patients and regulators, and is exploring new scientific collaborations to further support XTMAB-16 for sarcoidosis.

Forging new partnerships

The XTMAB-16 project culminated in a commercialization licensing agreement for the North American market with Meitheal Pharmaceuticals[2] in 2023. Having shown that its approach can bring challenging R&D programs to value inflection points, Xentria is looking to partner on new projects that enable it to work with like-minded researchers to accelerate the development of potentially life-changing early-stage drug candidates.

Xentria is interested in co-development partnerships that build its pipeline and increase the possibility of providing accessible treatment options to patients with unmet needs. The biotech is open to collaborations with researchers with preclinical or clinical-stage assets or those looking to advance investigational products to the next phase of drug development.

As new projects advance, Xentria will support the growth and development of its partners alongside the Chicago life sciences sector that it calls home. In doing so, the biotech and its partners will continue to advance their shared mission to take on big challenges in drug development, combining knowledge and capabilities to create patient-focused R&D programs that address major unmet medical needs and lead to promising advancements for all stakeholders.

1. Offman, E. et al. *Front. Pharmacol.* **14**, 1066454 (2023).
2. Licensing Agreement to Commercialize XTMAB-16 in Sarcoidosis | XENTRIA & Meitheal Pharmaceuticals Announce Exclusive Licensing Agreement for XTMAB-16 In North America. https://xentria.com/news/11 (2023).

XTMAB-16 is currently under investigation. The safety and effectiveness for its uses have not yet been established.

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