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BIOMUNEX PHARMACEUTICALS

PRODUCT / SOLUTION
General Information: Biopharmaceutical company developing a disruptive immunotherapy approach based on the redirection of MAIT cells, a unique non-conventional T cell subset, creating a new class of T Cell Engagers, MAIT engagers, and the unique best-in-class BiXAb® bi- and mlti-specific antibody platform technology

Company Name: BIOMUNEX PHARMACEUTICALS

Product/Solution Name: BiXAb® MAIT engagers

Date of Approval (If FDA approved): NA

Sub-Categories (Digital Health /Medtech / Biotech): Galien biotech start-up prize

Therapeutic Categories: Immunotherapeutics based on bispecific antibodies

Document upload: ***Galien Biomunex Deck1: General Information***

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BACKGROUND
Background information and need for solution/product

Cancer immunotherapy has made real progress in the past decade and redefined the treatment of certain cancer indications. Among the different options, bispecific antibodies (BsAbs) are considered as a hot field for next-generation drug development with a focus on T-cell engaging BsAbs (TCEs, i.e., T cell engagers). However, there are still many challenges to be solved with the use of immunotherapies and TCEs including safety (e.g. dose limiting toxicities, such as cytokine release syndrome), efficacy (lack of activity in solid tumors), therapeutic window and production costs. The first BsAb drugs have been approved for the treatment of haematological malignancies (ie. Blincyto, Lunsumio, Tecvayli), but rarely in solid tumors. So today, most cancers are not addressed by these treatments. The potential of immunotherapy is out of reach for millions of patients with advanced or metastatic disease whilst the treatments administered today remain suboptimal and detrimental to patients, representing a large healthcare burden.

There are currently about 100 ongoing clinical trials to evaluate the efficacy and safety of TCEs for cancer treatment. This modality has shown great promise in the treatment of haematological malignancies, but still severe adverse events such as such as neurotoxicity and cytokine release syndrome are common. However, the picture for classical TCEs in solid tumors is still bleak. To date, no TCE for the treatment of solid tumors has shown meaningful clinical benefit for these Patients in Phase 3 (only the first BsAb, Removab, was approved for Ovarian cancer (ascite) many years ago but withdrawn from the market for strategic reasons). Many challenges still exist for TCEs due to the fact that they activate all T-cell subsets. Activation of all T-cells leads to cytokine release syndrome which has become the major toxicity that limits the use of these treatment or higher doses . Another issue is that TCEs also activate an immunosuppressive subset of T-cells in the tumor microenvironment, the regulatory T-cells (Tregs), and these cells can suppress the activity of the cytotoxic T-cells that are trying to kill the tumor.

To overcome those challenges, Biomunex has developed the world first Mucosal Associated Invariant T-cells (MAIT) redirection platform technology and will push the clinical development of the first two MAIT engagers targeting colorectal and lung cancers with the potential to treat several other solid tumors (especially in mucosal and barrier tissues, notably bladder, small intestine, prostate but also liver and pancreas). They will rapidly be followed by other MAIT engagers targeting further tumor associated antigens (TAA) and cancer indications.

This multi-patented approach is mediated by the BsAb produced by our best-in-class platform BiXAb®. MAIT engagers promise to achieve what no other T cell engagers can do today: to show efficacy in solid tumors with limited toxicity (reduced cytokine release syndrome) and reduced immunosuppression leading to increased therapeutic window. The game-changing products coming out of the BiXAb-MAIT platform will make Biomunex a global leader in the discovery and development of new immuno-therapeutics focused on unmet medical needs in oncology.

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See ***Galien Biomunex Deck2: Background information and need for solution/product***

DEVELOPMENT, CLINICAL & PRECLINICAL EVIDENCE

History of the development of the solution/product

There has been growing attention on the role of MAITs in inflammation and infection since their discovery in the 1990's. Up until recently, MAITs were not studied in cancer because they were mistaken for classical cytotoxic T-cells, but recently they have been defined a huge potential as a cutting-edge cancer immunotherapy. Biomunex is leading the way with the BiXAb-mediated MAIT engagers used as a novel cancer immunotherapy. The approach was invented with the Institut Curie, a leading French cancer institute, notably Dr. Lantz, who discovered the MAIT cells more 20 years ago (now a scientific adviser to Biomunex). To bring the first MAIT engagers to the clinic will be a game-changer and a new chapter in immunotherapy after immune checkpoint inhibitors, T Cell engagers (including gamma/delta), CAR-T and cytokine therapies. Evolution of the platform to trispecificity will push it further in terms of safety/specificity and efficacy rendering this project a gateway to a new era in immuno-oncology.

Biomunex has generated and validated a robust BsAb format, BiXAb®, which has tetra-valency. This format, based on an IgG1 antibody, with a second bivalent Fab tethered on top, lends itself to be modified to incorporate three, and eventually four, different binding domains. Several mutation pairs have been devised that permit the correct light and heavy chain pairing in the bi-specific format. The general architecture of the BiXAb has been shown to have excellent drug-like properties and biomanufacturing properties. The proprietary BiXAb antibody platform is a plug and play best-in-class platform that has all the characteristics needed in a robust drug-like format and enables the rapid production of bivalent, BsAb with very rapid assembly of BiXAbs using any two Fabs (less than 2 months), high solubility, no aggregation, thermal stability, high expression/production, cost effective. Proprietary mutation pairs ensure correct light/heavy chain pairing. Proprietary, non-immunogenic, linkers permit efficient binding of both Fabs to their targets.

The BiXAb-MAIT platform originates from the Biomunex best-in-class BiXAb platform (> 300 BiXAbs generated) and the MAIT redirection approach, developed by Biomunex and the Institut Curie over the last 3 years. The BiXAb platform has been validated by deals with Sanofi in 2019 regarding the platform and Onward Therapeutics in 2021 regarding the first BiXAb development candidate, that should enter Phase 1 clinical trial in Q2 2023. The BiXAb-MAIT platform feasibility was validated with the generation of several BiXAb-MAIT engagers targeting more 6 different TAAs to date. Biomunex has generated a robust preclinical data package showing that BiXAb-mediated MAIT cell redirection can potently kill cancer cells. The BiXAb-MAIT HER2 engager when bound to both MAIT cells and HER2+ cancer cells induces MAIT cell activation, proliferation, degranulation, cytokine release and directed killing of the bound cancer cell.

The first two BiXAb-MAIT engagers will enter regulatory preclinical (incl. CMC and IND enabling studies) in June 2023 for BMX-501 and October 2023 for BMX-502/503, for a first in man study planned in Q1 2025 for both programs targeting colorectal and lung cancers with the potential to also treat pancreatic, bladder, small intestine and prostate cancers.

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See ***Galien Biomunex Deck3: Development, clinical & preclinical evidences***

INNOVATION

Why this solution/product is innovative, the broad implications for future research, and/or how it will improve the human condition

Biomunex has developed the world first MAIT cell redirection platform and will push the clinical development of the first two MAIT engagers targeting colorectal and lung cancers with the potential to also treat pancreatic, bladder, small intestine and prostate cancers. They will be rapidly followed by other MAIT engagers targeting further tumor associated antigens (TAA) and cancer indications. This multi-patented approach is mediated by the BsAb produced by best-in-class platform BiXAb®. BiXAb-MAIT engagers promise to achieve what no other T cell engagers can do today: efficacy in solid tumors with limited toxicity and reduced immunosuppression leading to increased therapeutic window.

MAIT is a sub-population of non-conventional cytotoxic T-cells (up to 20% in blood) that are naturally tissue resident in many organs and solid tumors (e.g., in liver, up to 50% of all T cells, colorectal, in lung, gastric, ovarian, prostate, esophageal tissues and cancers). BiXAb-MAIT engagers activate only MAIT cells, unlike classical T-cell engagers which activate all T cell subsets including the helper and regulatory T cells that may contribute to toxicity and reduced efficacy. MAIT cells are the only T-cell subset resistant to certain chemotherapies (expressing Multi Drug Resistance gene). MAIT cell redirection can be considered for use in combination with chemotherapy.

BiXAb-MAIT engagers are a new class of non-conventional T cell engagers meaning a novel, disruptive modality in the field of T cell redirection in oncology giving birth to innovative therapies with a major impact on the treatment of many cancers leading to a major improvement in the medical service rendered. Theoretically there is no limit to the type and number of TAAs targeted by MAIT engagers and thus to the scope of cancer indications addressed by the BiXAb-MAIT platform.

The BiXAb-MAIT engagers may not only change the paradigm of immunotherapy treatment and dramatically improve overall survival, safety and quality of life of cancer patients:

- increased efficacy on solid tumors, with consequence on overall survival expected
- significantly improved therapeutic window in the treatment of solid tumors

- safer therapy with reduced side effects compared to other therapies, including immunotherapies, with potential concomitant use of chemotherapeutic agents
- improved quality of life of cancer patients and families
- simple treatment administration (simple injection every 2-4 weeks)

They may also optimize drug discovery process and accelerate early stages of R&D:

- potential to increase the speed of drug discovery by using the BiXAb format as common underlying element enabling the design of new immunotherapeutics in less than 2 months (from design to characterization).
- option to develop a broad pipeline of BsAb that can expand to a broader range of cancer indications
- encourage collaborative drug discovery and new pharmaceutical ecosystem with faster and more consistent translation to efficient cancer treatment
- reduced socio-economic costs for the society at large

Eventually Biomunex' innovative immunotherapy may profoundly change clinical practice, providing oncologists and patients with therapeutics that may dramatically improve treatment of advanced and metastatic cancer patients, by majorly increasing efficacy and safety of cancer treatments

Document upload
See ***Galien Biomunex Deck4: Innovation***

REFERENCES

Please provide appropriate references (ie Pubmed links)

- See ***Galien Biomunex Reference1****: Article Rabia et al (2023) Design and selection of ptimal ErbB-targeting bispecific antibodies in pancreatic cancer. Front. Immunol. 14:1168444. doi: 10.3389/fimmu.2023.1168444*
- See ***Galien Biomunex Reference2****: Poste AACR #2954, May 2023 Orlando, FL, USA: MAIT Engagers: an efficacious novel modality in the field of T-cell engagers for the treatment of solid tumors.*

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