BioMed Valley Discoveries, Inc.
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BIOMED VALLEY DISCOVERIES

Translational medicine: doing things differently

With a unique ownership structure and stable long-term funding, Biomed Valley Discoveries fuels a virtuous circle of investment, profit and research for the benefit of patients with unmet medical needs.

BioMed Valley Discoveries (BVD) is a clinical-stage biotech with a mission to address a wide range of diseases with novel treatments employing diverse therapeutic modalities, from small molecules to biologics. Headquartered in Kansas City, Missouri, BVD has created a pipeline of four oncology and immuno-oncology candidates, with two currently in clinical trials and two in preclinical development.

BVD's pipeline comprises Ulixertinib (BVD-523), a small-molecule ERK1/2 kinase inhibitor in phase 2 trials for cancers with MAPK pathway mutations; Clostridium novyi-NT (CNV-NT), a tumor-destroying bacteria in phase 1 trials for inoperable tumors; BVD-723, a small-molecule PI3Kγ inhibitor; and antibody–drug conjugates (ADCs) targeting TEM8 and CD276.

BVD's mission is supported by a unique ownership model. The company was created in 2007 by Jim and Virginia Stowers, both cancer survivors who wanted to help others through the wealth they accumulated as significant equity owners of American Century Investments (ACI), a global asset management firm Jim founded in 1958. In 1994, the couple launched the Stowers Institute for Medical Research (SIMR) in Kansas City to conduct research into the molecular drivers of disease. Today, SIMR is the controlling owner of ACI, and uses dividend payments from ACI to fund its research, which to date has totalled more than $1.5 billion.

SIMR also owns and finances BVD, a for-profit translational medicine company, under an arrangement giving BVD access to SIMR's intellectual property, while the fruits of BVD's commercial success are fed back into the SIMR funding pool. This arrangement provides BVD with stable, long-term financing, and allows the company to pursue programs that would be difficult in a more traditional biotech and enables more flexible financing partnerships that might otherwise not be possible.

Virtual dual strategy

As a virtual company, BVD pursues a dual development strategy. In the long term, it aims to initiate novel programs derived from knowledge about diseases and targets emerging from SIMR. In the shorter term, BVD has in-licensed assets that are being developed by R&D activities outsourced to CROs and other partners. Downstream plans include partnerships that either license BVD's assets or participate in collaborative development programs. BVD's streamlined infrastructure makes the company nimble and flexible, and able to adapt quickly to new opportunities and changing circumstances.

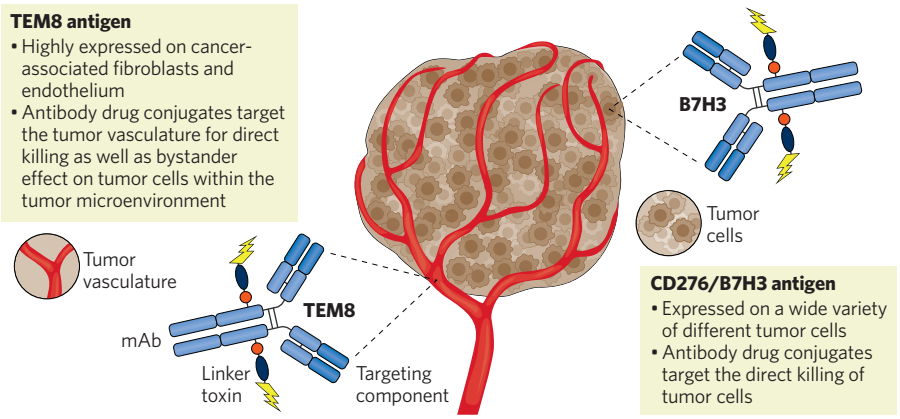

Fig. 1 | Antibody programs targeting cancer antigens. BVD has two different Antibody–drug conjugate programs, one targets CD276 and the other targets TEM8.

BVD's most advanced candidate, Ulixertinib, is a first-in-class/best-in-class small-molecule ERK1/2 kinase inhibitor in phase 2 trials, and a number of additional early trials (NCT04488003, NCT04145297, NCT03454035, NCT04566393, NCT03155620), for cancers harboring alterations in the MAPK pathway. Mutations in upstream components of the MAPK pathway occur in more than 40% of all cancers and there are a number of disease indications that Ulixertinib could address.

BVD's other clinical-stage candidate is a strain of the bacterium Clostridium novyi (CNV-NT), which lacks the alpha-toxin gene, in-licensed from Johns Hopkins University. When CNV-NT spores are injected intratumorally, the hypoxic regions of the tumor support germination and the bacterium destroys tumor cells by secreting lipases, proteases and other hydrolytic enzymes. This germination and the destruction of the tumor microenvironment also activates components of the immune system. BVD has completed a phase 1 monotherapy trial and is currently running a phase 1 combination trial with pembrolizumab (Keytruda), a monoclonal antibody that targets the PD-1 receptor (NCT034359520).

Antibody–drug conjugate assets

In addition to its clinical-stage assets, BVD has two pre-IND ADC candidates. The discovery of the antibody leads were made under a Cooperative Research and Development Agreement with the National Cancer Institute. BVD is now leading the therapeutic development effort.

One ADC targets the well-known anti-cancer antigen CD276, a member of the tumor necrosis factor receptor family, to deliver cytotoxic payloads directly to cancerous cells while the other targets tumor endothelial marker 8 (TEM8), which is overexpressed on cancer-associated fibroblasts and endothelium (Fig. 1). Preclinical work has shown robust anti-tumor activity with both ADCs across a wide variety of tumor types[1,2]. These antibodies have also shown activity when deployed as chimeric antigen T cell (CAR T) agents. In collaboration with a partner, BVD is currently developing different versions of these ADCs using a proprietary site-specific bioconjugation technology. BVD is open to discussions with potential partners interested in further development and commercialization of these antibodies, both as ADCs and CAR T agents.

1. Seaman, S. et al. *Cancer Cell* **31**, 501–515 (2017).
2. Szot, C. et al. *J. Clin. Invest.* **128**, 2927–2943 (2018).

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