

# BioCentury

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## EMERGING COMPANY PROFILE

# LEVERAGING CROSS-LINKING

BY SANDI WONG, STAFF WRITER

Lyvgen Biopharma Co. Ltd. is using its xLinkAb platform to develop mAbs that agonize T cell or dendritic cell co-stimulatory receptors with better safety and selectivity for tumors than competing mAbs.

According to founder and CEO Jieyi Wang, mAbs in clinical development that agonize co-stimulatory molecules, such as CD40 and TNF receptor superfamily member 9 (4-1BB; TNFRSF9; CD137), were primarily discovered by screening for strong agonism of the co-stimulatory receptors but not screened for specific activity in the tumor environment. Consequently, those mAbs have narrow therapeutic windows and toxicity issues, including liver toxicity and cytokine storm syndrome, due in part to lack of tumor selectivity.

To increase selectivity for tumor cells, Lyvgen develops mAbs that agonize their targets only in the presence of Fcγ receptor IIb (FCGR2B; CD32B), which is expressed on immune cells that are enriched in the tumor microenvironment, including B cells, monocytes and NK cells.

Antibody cross-linking mediated by FCGR2B, an inhibitory Fc receptor (FcR), has been shown to enhance mAb agonism of co-stimulatory receptors.

Lyvgen's xLinkAb platform generates mAbs that contain an Fc domain that specifically binds FCGR2B and Fab domains that bind T cell or dendritic cell (DC) co-stimulatory receptors. The company first screens the individual Fc domains for FCGR2B binding and the individual Fab domains for low or no co-stimulatory receptor agonism in the absence of FcR binding, before pairing the two domains in a single mAb that would have agonist activity only upon FCGR2B-mediated cross-linking. The resulting mAbs are then screened for the ability to agonize co-stimulatory receptors in the presence of FCGR2B.

"That gives us an opportunity to activate a target selectively in the presence of FcR binding, which is enriched in the tumor microenvironment," Wang said. "Thus you have activation in the tumor tissues but less so in a normal organ."

Lyvgen's most advanced preclinical compounds are LVGN6051, a mAb against 4-1BB, and LVGN7408, a

### LYVGEN BIOPHARMA CO. LTD.

Shanghai, China

**Technology:** Agonist mAbs that cross-link co-stimulatory receptors to activate T cells and dendritic cells in the tumor microenvironment

**Disease focus:** Cancer

**Clinical status:** Preclinical

**Founded:** 2016 by Jieyi Wang

**University collaborators:** Shanghai Jiao Tong University School of Medicine

**Corporate partners:** Anhui Anke Biotechnology (Group) Co. Ltd.

**Number of employees:** 10

**Funds raised:** \$35 million

**Investors:** 6 Dimensions Capital, Winfair Global, Runling Capital, Morningside Ventures and InnoBio

**CEO:** Jieyi Wang

**Patents:** None issued

mAb against CD40. Wang said unpublished data on both mAbs "showed preclinical efficacy in animal models without toxicity," but he declined to disclose details for those studies.

Lyvgen plans to start Phase I testing of LVGN6051 in 2Q19 and LVGN7408 by YE19. The company will initially develop the products as monotherapies but hopes to test the products in combination with LVGN3616, an anti-PD-1 mAb for which it granted Anhui Anke Biotechnology (Group) Co. Ltd. Chinese rights.

Wang said Lyvgen has not selected lead indications and declined to disclose when it will make that decision.

Bristol-Myers Squibb Co. and Pfizer Inc. both have clinical stage 4-1BB agonists in development. BMS's urelumab (BMS-663513; ONO-4481) is in Phase I/II trials to treat solid tumors and hematologic malignancies and Pfizer's utomilumab (PF-05082566; PF-2566 PF-5082566) is in Phase II testing to treat solid tumors. Clinical studies of both mAbs as monotherapies administered at ≤1 mg/kg have led to

several cases of liver toxicity; higher doses of urelumab resulted in more frequent and more severe toxicity. BMS declined to comment on how it has addressed the observed toxicity; Pfizer did not respond to inquiries.

According to BioCentury's BCIQ database, at least five companies have anti-CD40 antibodies in the clinic for cancer. The most advanced is Apexigen's APX005M, which requires FCGR2B-mediated cross-linking in order to bind CD40. Apexigen and BMS have APX005M in Phase I/II testing for melanoma and non-small cell lung cancer (NSCLC); Apexigen also has the mAb in Phase I/II for pancreatic cancer.

Wang said the Phase II dose of APX005M of 0.3 mg/kg was "suboptimal"; Apexigen declined to comment on the mAb's dosing.

Lyvgen has filed patent applications covering its antibody's sequences. The company raised a \$30 million series B round in July, which Wang said will provide about two years of runway. 

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## COMPANIES AND INSTITUTIONS MENTIONED

**Anhui Anke Biotechnology** (Group) Co. Ltd., Hefei, China

**Apexigen Inc.**, San Carlos, Calif.

**Bristol-Myers Squibb Co.** (NYSE: BMY), New York, N.Y.

**Lyvgen Biopharma Co. Ltd.**, Shanghai, China

**Pfizer Inc.** (NYSE:PFE), New York, N.Y.

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