

# BioCentury

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## Strategy

# More freedom to deal

By **Stephen Hansen**  
Staff Writer

With nondilutive cash at a premium, **Xencor Inc.** is ramping up a partnering campaign built on data that allows the company to expand its XmAb technology into a broader swath of disease areas. The company reached a deal with **CSL Ltd.** last week, expects to announce a deal with **Pfizer Inc.** this week, and aims to disclose another soon.

Before last year, according to President and CEO Bassil Dahiyat, the primary focus of Xencor's XmAb antibody optimization technology was the enhanced antibody-dependent cellular cytotoxicity (ADCC) provided by its engineered Fc domains.

The platform allowed Xencor to sign a number of deals — with **Chugai Pharmaceutical Co. Ltd.**, **Genentech Inc.**, **Johnson & Johnson**, **PDL BioPharma Inc.**, **Roche** and the **MedImmune Inc.** unit of **AstraZeneca plc.** But the biotech worried the technology's value would be diluted if it were licensed to too many partners for too many targets.

Indeed, all the deals were signed by the end of 2005. "We did taper our deal activity a lot," Dahiyat told BioCentury.

The company also wanted to focus on its internal pipeline, which includes XmAb 2513, a humanized mAb against CD30 antigen in Phase I testing to treat Hodgkin's lymphoma and anaplastic large cell lymphoma. Three compounds are in pre-clinical testing.

But Xencor's space opened up last year, when the company

published preclinical data in *Molecular Immunology* showing that XmAb's Fc domain technology was applicable not only to cancer targets through ADCC, but also to autoimmune or inflammatory targets through its ability to inhibit an immune response.

In a mouse model, XmAb 5871 suppressed B cell immune function without depleting or permanently harming the B cells. The anti-CD19 mAb has high affinity to the Fc gamma receptor IIB, which results in an inhibitory signal and regulates the immune system.

According to Dahiyat, the data gave the company confidence that XmAb had value beyond ADCC functionality.

The technology includes a library of engineered Fc domains that have increased potency and tighter binding with any combination of the six human Fc gamma receptors. When the XmAb Fc domain is integrated into an antibody, it can increase the half-life of the protein through its interaction with the neonatal Fc receptor, or increase cytotoxicity compared to

a natural Fc domain through the recruitment and activation of immune cells such as natural killer (NK) cells and macrophages.

Stimulating an immune response is desirable when looking to kill the target cell. However, Dahiyat noted that the mouse data indicated the technology also could be beneficial when the immune system is in overdrive, as in autoimmune disorders.

This is accomplished by reducing the antibody's binding to Fc gamma receptors that induce an immune response, while optimizing its interaction with Fc gamma receptor IIB.

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**Bassil Dahiyat, Xencor**

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The antagonist Fc receptor helps shut down immune responses, Dahiyat said, “and we’ve built an Fc domain that just turns that one on. That gives us a whole new modality.”

With XmAb now applicable to both cancer targets through enhanced ADCC and to autoimmune targets through its immunoregulatory effects, Xencor now thinks it can cut more deals.

“Now that we’ve broadened the palette with the immune inhibitory part of the technology, we feel like we can continue to do deals for high ADCC and for the immunoregulatory aspects of the platform, and still have so much to offer that we are not overly diluting ourselves,” Dahiyat said.

The deal with Pfizer will give the pharma non-exclusive access to the XmAb Fc domain technology for a research period, and includes Xencor’s Xtend antibody half-life prolongation technology and XmAb ADCC-enhancing technology.

Pfizer also received a license to apply the XmAb technology to one program. The biotech will receive an undisclosed upfront payment and is eligible for milestones and royalties.

In last week’s deal, CSL received non-exclusive access to XmAb to enhance ADCC effector function in its antibodies. While the Australian company can broadly apply the technology in the research phase, it is limited to an undisclosed number of commercial licenses to move XmAb-based antibodies into development. Xencor will receive an undisclosed upfront payment and is eligible for development milestones and royalties.

Xencor hopes to announce at least one more deal in the next few weeks.

In addition to having a broader deal space, Dahiyat said, “we are happy to do deals now, when upfront cash is more valuable than ever.” Xencor, which has not disclosed its cash or burn rate, has raised \$146 million in private financing.

While the deals should help the company advance its own pipeline, Dahiyat noted the most realistic exit strategy is to get acquired.

“Would I prefer to find a way to remain independent and keep developing the technology and building programs? I would,” he said. “But in this market, acquisition is more and more what is happening and you’ve got to reflect that reality. Ultimately, the exit strategy here is having enough exciting IP and capability to get acquired. That’s no secret to anybody in this market.”

#### COMPANIES AND INSTITUTIONS MENTIONED

**AstraZeneca plc** (LSE:AZN; NYSE:AZN), London, U.K.

**Chugai Pharmaceutical Co. Ltd.** (Tokyo:4519), Tokyo, Japan

**CSL Ltd.** (ASX:CSL), Melbourne, Australia

**Genentech Inc.** (NYSE:DNA), South San Francisco, Calif.

**Johnson & Johnson** (NYSE:JNJ), New Brunswick, N.J.

**PDL BioPharma Inc.** (NASDAQ:PDLI), Incline Village, Nev.

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

**Roche** (SIX:ROG), Basel, Switzerland

**Xencor Inc.**, Monrovia, Calif.