



#### Rating Price (27 May 14, US\$) Target price (US\$) 52-week price range Market cap. (US\$ m) Enterprise value (US\$ m)

OUTPERFORM\* [V]
8.21
14.00<sup>1</sup>
13.90 - 7.55
257.48
210.67

\*Stock ratings are relative to the coverage universe in each analyst's or each team's respective sector.

<sup>1</sup>Target price is for 12 months.

[V] = Stock considered volatile (see Disclosure Appendix).

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## Xencor, Inc (XNCR)

**SMALL & MID CAP RESEARCH** 

# **Key Allergy Program on Track - Phase I Starts On Time**

- XNCR announced the initiation of its Phase I trial for XmAb7195 (antiIgE). This is in-line with its guidance, and initial data from high IgE healthy
  volunteers may be available in early 2015 and could provide biologic proof of
  activity. XNCR also expects initial clinical data from a Phase IIa trial of its
  anti-CD19 arthritis program (XmAb5871) by year-end 2014.
- XmAb7195 is likely a better Xolair: IgE is a well validated target (target for Xolair), which significantly derisks the opportunity from a clinical, regulatory, and commercial perspective. XmAb7195 is significantly more potent than Xolair because it inhibits / down-regulates IgE by three distinct mechanisms. Phase I data are likely to provide strong proof of concept. (IgE levels are a proven surrogate for activity / clinical benefit.)
- MOR208 data in 2014. We also expect XNCR's partner Morphosys to potentially provide clinical data from two ongoing Phase II trials in ALL and NHL. While this space is increasingly competitive, we believe there is room for a safe and effective Fc-engineered CD19 antibody among the new and developmental therapies for B-cell malignancies.
- Model updates. XNCR previously reported Q1:14 results, and we are updating our model to include these results. Our 2014 EPS estimate is now (\$0.72) vs. prior (\$0.65).

#### Financial and valuation metrics

12/13A	12/14E	12/15E	12/16E
-3.85	-0.72	-0.65	-0.62
_	-0.65	-0.64	-0.61
-2.1	-11.5	-12.6	-13.3
-12.3	-71.6	-87.8	-102.9
10.2	5.5	7.0	11.0
-9.8	-22.5	-22.7	-26.3
-0.24	-0.69	-0.43	-0.74
-37.6	-11.9	-18.9	-11.2
-19.2	-8.4	-8.3	-7.2
-69	-47	-124	-100
-234.14	-439.19	-434.59	-501.84
31.36	IC (current, US\$	m)	4.49
2.2	EV/IC (x)	,	36.8
-64.8	Dividend (currer	nt, US\$)	_
-92.5	Dividend yield (9	%)	
	-3.85 -2.1 -12.3 10.2 -9.8 -0.24 -37.6 -19.2 -69 -234.14 31.36 2.2 -64.8	-3.85	-3.85

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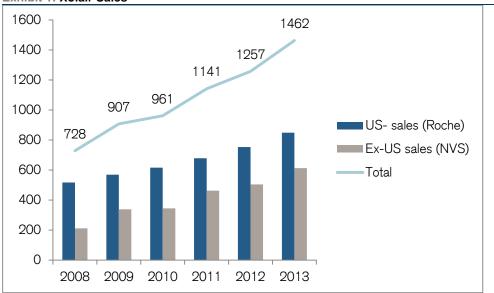


## XmAb7195—A Better Xolair

#### The Good and Bad of Xolair

- Clinically Validated: One culprit in asthma is the over production of an antibody called IgE. Increased IgE levels are associated with worse symptoms, and inhibition of IgE by the antibody Xolair reduces symptoms in moderate to severe asthma patients. For these reasons, IgE is a clinically validated target, with reduced clinical and regulatory risk.
- Commercially Validated: Xolair is marketed by Roche and Novartis, and total worldwide sales were approximately \$1.25B in 2012 and growing at a three-year annualized rate of ~12%. (See Exhibit 1.) The ongoing adoption of Xolair makes IgE a commercially validated target.

**Exhibit 1: Xolair Sales** 

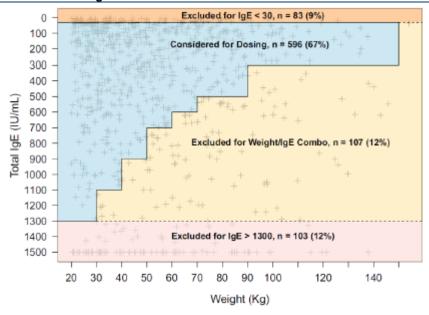


Source: Company data, Credit Suisse estimates

■ Imperfect Drug: Despite the current blockbuster status, Xolair is generally viewed as an imperfect drug. For example, there is a complex dosing table for Xolair that is based on the weight of the patient and their baseline IgE levels. (See Exhibit 2.) Large patients or patients with very high IgE levels cannot be treated with Xolair because the drug has a limited capacity to neutralize its target. Approximately 20% of asthma patients with high IgE or high body mass are ineligible for Xolair because they fall outside the dosing chart. This shortcoming may also reduce the activity of Xolair for patients who are on the margin within the dosing chart. Of the patients treated with Xolair, around 50% do not achieve target IgE reduction. (See Exhibit 3.)

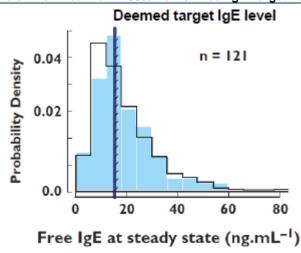


**Exhibit 2: Xolair Dosing Chart** 



Source: Company data, Credit Suisse Research.

Exhibit 3: IgE Levels After Treatment—50% Do Not Meet IgE Target Levels



Source: Company data, Credit Suisse Research.

#### A Better Xolair—XmAb7195 Blocks IgE by Three Mechanisms

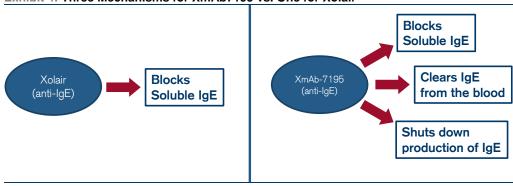
XmAb7195 is designed to have the same IgE binding region as Xolair, but its Fc domain has been modified for enhanced activity. While Xolair simply binds soluble IgE, XmAb7195 also shuts down the production of IgE and facilitates the clearance of IgE from the blood. (See Exhibit 4.) This triple mechanism of action is expected to have a greater impact on IgE levels and therefore asthma symptoms. It is also likely to overcome the dosing problems of Xolair.

The attributes of XmAb7195 have been demonstrated in monkeys who naturally produce high levels of IgE.



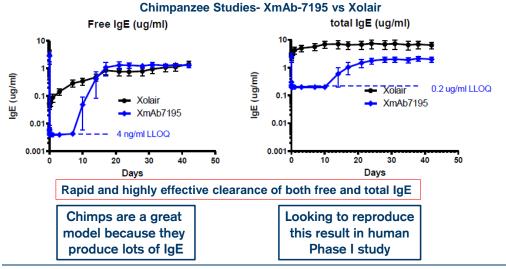
- Xolair Rapidly Reduces Free IgE (Exhibit 5 left panel): Xolair can effectively bind free IgE. The reduction in free IgE is associated with reduced asthma symptoms. XmAb7195 also binds free IgE and effects even greater reduction in free IgE compared to Xolair.
- Xolair Has No Impact on Total IgE (Exhibit 5 right panel): Total IgE includes both antibody-bound and free IgE. Because Xolair does not induce the clearance of IgE, the bound IgE circulates and the free IgE levels return at the rate of antibody clearance. XmAb7195 lowers total IgE because the bound IgE is cleared from the blood. Total IgE levels recover but at a slower rate because of the immune down-regulation.

Exhibit 4: Three Mechanisms for XmAb7195 vs. One for Xolair



Source: Company data, Credit Suisse Research.

Exhibit 5: More Complete Blockade of IgE with XmAb7195



Source: Company data, Credit Suisse Research.

### Immune Down-Regulation (and Target Clearance)

The ability to directly down-regulate the immune system is unique to XNCR's technology and is the source of both its proprietary XmAb7195 program (anti-IgE) and its XmAb5871 program (anti-CD19) optioned to AMGN.

The technology works in two steps.

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 The antibody binds to its target. For XmAb5871, the target is CD19, which is expressed on nearly all B-cells. For XmAb7195, the target is IgE, which is both soluble and expressed on the surface of the cells that produce it.

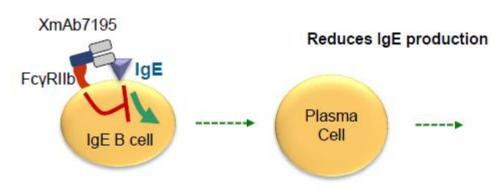
#### **Exhibit 6: Target Binding**



Source: Company data, Credit Suisse Research.

2) Once the antibody is bound to the target (IgE), the modified Fc domain of the antibody binds tightly to the Fc $_{\gamma}$ RIIb receptor on B cells (also known as CD32b). This interaction (binding to both the target and the Fc receptor at the same time) sends an inhibitory signal to the immune cell and turns it off without killing the cells. In the case of XmAb7185, this process sends the signal not to differentiate into IgE-producing cells.

**Exhibit 7: Turning Off IgE Production** 



Source: Company data, Credit Suisse Research.

#### **Immune Down-Regulation**

The mechanism of XmAb7195 contrasts with Xolair, which can block soluble IgE, but does not prevent production of IgE. For this reason, Xolair's activity is limited. XmAb7195 both sequesters soluble IgE and turns off the cells that produce it, providing a double hit to this disease-causing pathway.

This immune down-regulation has potential safety advantages, given that it is:

- Target specific,
- Non-depleting/ cytotoxic, and
- Reversible.

For example, XmAb5871 may have advantages over Rituxan because it does not kill/deplete the B-cells. Once the drug is removed, B-cell activity recovers. This may reduce the risk of infections and long-term immune suppression.



**Exhibit 8: Advantages of Immune Down-Regulating Antibodies** 

Drug	Target	Indication(s)	Stage	Potential advantage
XmAb5871	CD19	Arthritis, lupus	Phase I/II	Non-depleting inhibition of B-cells
XmAb7195	lgE	Asthma	Phase I ready	blocks IgE production and increases IgE clearance
Anti-X/ CD32b	ND	ND	Discovery Lead	ND

ND not disclosed. Source: Company data, Credit Suisse Research.

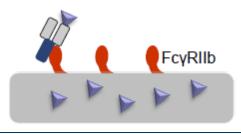
#### **Target Clearance**

The  $Fc_{\nu}RIIb$  receptor is also located on liver sinusoidal endothelial cells. When the antibody binds its soluble target (for example soluble IgE), the enhanced Fc binding to  $Fc_{\nu}RIIb$  facilitates the removal of the target from the blood stream.

This function is particularly useful for drugs that target soluble factors (such as IgE). Binding to the target may inhibit its activity, but if the drug does not remove the target from the blood, then it will only be active when sufficient levels of the antibody are present. By eliminating the target, the antibody can have a longer-lasting effect. This is even more pronounced when the immune down-regulating activity is also employed to inhibit the production of the target.

**Exhibit 9: IgE Clearance Mechanism** 

## Sends IgE to liver sinusoidal enthothelial cells for destruction



Source: Company data, Credit Suisse Research.



**Exhibit 10: XNCR Pipeline** 

Drug	Target	Technology	Indication	Stage	Partner
XmAb5574/MOR208	CD19	High ADCC	CLL, NHL, ALL	Phase II	Morphosys
XmAb5871	CD19	Immune inhibitory	Autoimmune	Phase I/II	AMGN has option
XmAb7195	lgE	Immune inhibitory	Asthma/Allergy	Phase I	Proprietary
BI 836826	CD37	High ADCC	CLL, NHL	Phase I	Boehringer Ingelheim
BI 836858	CD33	High ADCC	AML	Phase I	Boehringer Ingelheim
CSL362	CD123 (IL3R)	High ADCC	AML	Phase I	CSL
Xtend-TNF	TNF	Long half-life	Autoimmune	Preclinical	Proprietary
CD3 X CD38	CD38	Bispecific	Oncology	Preclinical	Proprietary
CD3 X CD123	CD123	Bispecific	Oncology	Preclinical	Proprietary
Xtend-CTLA4	CTLA4	Long half-life	Autoimmune	Preclinical	Proprietary
Anti-X/ CD32b	ND	Immune inhibitory	TBD	Discovery Lead	Proprietary
ND	ND	Long half-life	Hematology	Preclinical	CSL
ND	ND	Long half-life	Autoimmune	Preclinical	Janssen
ND	ND	Stability	Autoimmune	Preclinical	Merck
ND	ND	Long half-life	Undisclosed	Discovery Lead	Alexion

Source: Company data, Credit Suisse estimates

**Exhibit 11: XNCR Newsflow** 

Product/Event	Indication	Catalyst	Expected Date	Price Sensitivity
TBD	N/A	Announce proprietary program to move forward	H1:14	Low
XmAb5871	RA	Phase IIa activity data	H2:14	High
MOR208	ALL, NHL, and CLL	Phase II data in ALL	H2:14	High
MOR208	ALL, NHL, and CLL	First data from open label trial	YE:14	High
XmAb7195	Asthma	Phase la data in patients with asthma and allergic disease (includes high IgE cohort)	YE:14	High
TBD	N/A	IND for proprietary program	2015	Low
XmAb5871	RA	Start Phase Ilb (150-250 pts)	Q1:15	Low
XmAb7195	Asthma	Phase lb start	Q1:15	Low
XmAb7195	Asthma	Start Phase II in poorly	late 15/ early 16	Low
MOR208	ALL, NHL, and CLL	IST to complete enrollment of CLL study	H2:15	High
XmAb5871	RA	Phase Ilb data/ AMGN option	late 16/ early 17	High

Source: Company data, Credit Suisse estimates



Exhibit 12: XNCR Model

	2012A	2013A	Q1:14A	Q2:14E	Q3:14E	Q4:14E	2014E	2015E	2016E	2017E	2018E
Revenues											
US sales of XmAb7195											
Ex-US royalies on XmAb7195											
Royalties on XmAb5871											
Partnering, grants, milestones	9.5	10.2	2.2	0.8	0.8	1.6	5.5	7.0	11.0	26.1	15.0
Total Revenues	9.5	10.2	2.2	0.8	0.8	1.6	5.5	7.0	11.0	26.1	15.0
Expenses											
Cost of goods											
Research and development	12.7	17.0	4.2	5.0	5.6	6.3	21.2	21.7	28.5	31.4	39.3
Sales, general, administrative	3.1	3.7	1.7	1.8	1.8	1.9	7.1	7.9	8.7	9.9	14.3
Total Operating Expenses	15.8	20.7	6.0	6.8	7.4	8.2	28.3	29.6	37.2	41.3	53.6
Operating income (loss)	(6.2)	(10.5)	(3.8)	(5.9)	(6.6)	(6.6)	(22.8)	(22.7)	(26.3)	(15.2)	(38.6)
Total Other Income (Expense)	(2.4)	(49.7)	0.0				0.0				
Pre Tax Income	(8.6)	(60.3)	(3.8)	(5.9)	(6.6)	(6.6)	(22.8)	(22.7)	(26.3)	(15.2)	(38.6)
Income tax											
Net Income	(8.6)	(60.3)	(3.8)	(5.9)	(6.6)	(6.6)	(22.8)	(22.7)	(26.3)	(15.2)	(38.6)
EPS - diluted (proforma)	(\$38.31)	(\$3.85)	(\$0.12)	(\$0.19)	(\$0.21)	(\$0.20)	(\$0.72)	(\$0.65)	(\$0.62)	(\$0.33)	(\$0.77)
Shares outstanding - basic (proforma)	0.22	15.65	31.36	31.67	31.99	32.31	31.83	34.88	42.70	46.21	49.98
Shares outstanding - diluted (proforma)	0.22	15.65	31.36	32.91	33.25	33.60	33.08	36.23	44.16	47.80	51.69

Source: Company data, Credit Suisse estimates



#### Companies Mentioned (Price as of 27-May-2014)

Xencor, Inc (XNCR.OQ, \$8.21, OUTPERFORM[V], TP \$14.0)

#### **Disclosure Appendix**

#### **Important Global Disclosures**

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#### 3-Year Price and Rating History for Xencor, Inc (XNCR.OQ)

XNCR.OQ	Closing Price	Target Price	
Date	(US\$)	(US\$)	Rating
03-Dec-13	8.34		R
03-Jan-14	9.15	14.00	0 *

<sup>\*</sup> Asterisk signifies initiation or assumption of coverage.



The analyst(s) responsible for preparing this research report received Compensation that is based upon various factors including Credit Suisse's total revenues, a portion of which are generated by Credit Suisse's investment banking activities

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**Neutral (N):** The stock's total return is expected to be in line with the relevant benchmark\* over the next 12 months.

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Underperform/Sell*	13%	(46% banking clients)
Restricted	3%	

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Price Target: (12 months) for Xencor, Inc (XNCR.OQ)

Method: Our \$14 target for XNCR is derived using a probability-adjusted DCF, including \$9 for XmAb7195 (40% POS), \$3 for XmAb5871 (25% POS), and \$1 each for MOR208 and the technology licensees. We us a 12% discount rate and model through the products' entire lifecycle.

Risks to our \$14 TP include: 1) unexpected negative result for proprietary or partnered clinical programs, 2) financing risk from expected future equity raises, 3) competition in the CD19 and asthma programs, and 4) significant delay in one or more clinical programs that pushes potential approval timeline(s) out.

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See the Companies Mentioned section for full company names

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