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Xencor (XNCR - OUTPERFORM): Attractive Bispecific Candidates Masked by '7195 - XNCR Overlooked and Undervalued Relative to Comps - Reiterate OUTPERFORM

Price: $11.30 **12-Month Price Target: $18**

- **We believe that the novelty, breadth and value of XNCR's Fc-engineering toolkit, particularly their bi-specific candidates, are broadly underappreciated and have been overlooked.** We note that in addition to their attractive lead clinical assets '7195, '5871 and '5574 (MOR208) the company also has 6 internal pre-clinical candidates that exploit their Fc-modification toolkit including 2 bispecific antibodies. Xencor's platform has been validated through 7 ongoing collaborations that may result in a total of $1.31 billion in non-dilutive milestones and additional royalties.

- **We view XNCR as undervalued that at current levels, ~$330M MC – particularly relative to comps such as Macrogenics (MGNX: OUTPERFORM), ~$950M MC and given Micromet's $1.16 billion acquisition by Amgen in early 2012.** Recall that Amgen acquired Micromet in an all cash transaction valuing the company at $1.16 billion in Jan. 2012. The acquisition included blinatumomab, a CD3xCD19 bispecific in Phase II clinical development for ALL and Phase I trials for NHL as well as solitomab a CD3xEpCAM bispecific in Phase I trials for solid tumors. Similarly, Macrogenics has one wholly owned DART bispecific CD32BxCD79B and MGD006 (CD3xIL3), MGD007 (CD3xgpA33) both partnered with Servier.

- **We expect Xencor's first bispecific candidates to be announced in 2014 and to substantially drive the value of the company as they enter the clinic in 2015.** Xencor's Fc-engineered antibody technologies enable the creation of potentially best-in-class, novel, long-half-life bispecifics. Incorporation of Xencor's Fc-domains allows for bispecifics with antibody-like half-lives (6-7 days) and high production yields that are potentially superior to previous generations of bispecific technology. Although promising, early generations of bispecific technology such as the Micromet (Amgen) BiTE have been limited by the requirement for continuous infusion due to their extremely short half-life (3 hours). In addition to half-life extension Xencor's technology may potentially reduce immunogenicity, and result in additional killing via ADCC as well as T-cell engagement.

- **Xencor has disclosed two bispecific candidates with targets CD3xCD38 and CD3xCD123.** CD123, also known as the interleukin-3 α receptor (IL3α), is a cytokine receptor that is broadly up-regulated in B-cell malignancies, especially hairy cell leukemia. CD38, also known as cyclic ADP ribose hydrolase, is expressed on the surface of many immune cells including committed progenitor cells, B lymphocytes in germinal centers, and is implicated in leukemia's myelomas and solid tumors.

- **Importantly, Xencor's technology may facilitate a safer approach to full-size antibodies by allowing for Fc-knock-out variants that maintain structural Fc-domains without inducing FcγR-mediated cross-linking and potential off-target T cell activation.** Additionally, Xencor's bispecific antibodies do not contain potentially immunogenic multi-peptide linkers, exhibit stability and half-life similar to well studied antibodies and have the potential to induce killing both by CD3-mediated T cell activation and FcγR-mediated ADCC.

- **Xencor has also developed a novel technique for generating high yields of bispecific antibodies that facilitate significant flexibility in targeting domains.** Xencor's bispecific technology allows for the production of humanized bispecific antibodies incorporating scFv fragments and Fc modifications, without linkers or other novel antibody formats. Structurally, the company's bispecific technology can produce novel antibodies where one or both heavy/light chain pairs is missing the C_H1 and C_L domains, generating an Fv fragment directly linked to the Fc domain.

- **XmAb7195, Xencor's lead compound, is a Xolair (omalizumab) a bio-superior for the treatment of allergic asthma and other IgE mediated disease, set to enter the clinic in H1:14 with first in humans data by YE:14.** In '7195 XNCR's Fc-modifications impart two novel mechanisms of action to XmAb7195 resulting in superior clearance and reduction of IgE levels compared to Xolair and high-affinity anti-IgE candidates in the clinic.

- **Reiterating our OUTPERFORM rating and an $18 price target.** Our $18 price target is derived from the sum of multiples on sales and royalties from XNCR's proprietary and partnered products each discounted back to YE:14 (Pg 3).

Risks to the attainment of our price target include 1) failure to reach sales expectations for XmAb7195, XmAb5574, XmAb5871 2) failure in the clinic of either XmAb7195, XmAb5574, XmAb5871, 3) changes or discontinuation of Xencor's partnerships for XmAb5574, XmAb5871 or other partnered programs.

Upcoming Milestones

H1:14	Initiation of a Phase Ia trial of XmAb7195 (IgE, immune inhibitor Fc) in healthy subjects
YE:14	Top-line data from the Phase IIa trial of XmAb5871 (CD19, immune inhibitor Fc) in rheumatoid arthritis
YE:14	Top-line data from the Phase Ia trial of XmAb7195 in healthy subjects including IgE reduction
2015	Initiation of a Phase IIb proof-of-concept trial of XmAb5871 (CD19, immune inhibitor Fc) in rheumatoid arthritis
2015	IND filing and first-in-human clinical trials for Xencor's first clinical bispecific candidates
Q1:16	Potential top-line data from the Phase Ib trial of XmAb7195 in mild to moderate asthma
2016	Potential top-line data from the Phase II trial of XmAb5574/MOR208 (CD19, enhanced ADCC Fc) in ALL
2016	Initiation of a Phase IIb proof-of-concept trial of XmAb7195 in poorly controlled asthma
2017	Potential top-line data from the Phase IIb POC trial of XmAb7195 in patients with poorly controlled asthma
2017	Potential top-line data from the Phase IIb trial of XmAb5871 in patients with rheumatoid arthritis
2017	Potential exercise of Amgen's option to license XmAb5871

Investment Thesis

Xencor is a biopharmaceutical protein engineering company focused on developing and commercializing engineered monoclonal antibodies to treat severe and life-threatening diseases with unmet medical needs. The company has developed a substantial antibody toolkit based upon their proprietary Fc-engineering platform. Xencor has systematically and rationally engineered novel Fc-domains that augment the ability of antibodies in several ways including: immune inhibitor Fc domains that target inhibitory and clearance functionality (FcγRIIb target); cytotoxic Fc domains, that increase cytotoxicity/ADCC (targeting FcγRIIIa and FcγRIIa receptors), Xtend Fc domains that extend half-life (targeting FcRn) and allow for the creation of novel bispecifics. We believe this best-in-class platform, which has produced two partnered products in Phase II studies, 6 internal early stage programs and a total of 7 collaborations is the core of Xencor's value.

Importantly Xencor has also created Fc variants that enable heterodimeric Fv domains for the creation of novel bispecific antibodies. We believe that Xencor's bispecific candidates could represent a significant value driver for the company as they enter the clinic potentially in 2015.

Xencor's lead candidate is XmAb7195, an anti-IgE antibody therapy for the treatment of allergic asthma employing Fc-modification to enhance FcγRIIb binding up to 400x. These modifications lead to enhanced liver clearance of IgE and suppressed production through co-engagement with B-cell bound IgE. These new functionalities, in our opinion, make XmAb7195 a best-in-class anti-IgE therapy and highlight potential broad utility of Xencor's technology. The Fc-domain in XmAb7195 is also utilized in their Phase II compound XmAb5871, supporting the safety and tolerability of these Fc-modifications. XmAb7195 is in IND-enabling studies and a Phase I trial is planned for early 2014. Importantly Phase I data, expected around YE:14, will include IgE levels, a marker of activity and potential clinical benefit.

We believe that partnerships with Amgen, Alexion, MorphoSys, Janssen, Merck, Boehringer Ingelheim and CSL have validated Xencor's approach with $65M in revenues to date, potentially $1.31 billion in additional milestones and single to double digit royalties. XmAb5871, optioned to Amgen, is Xencor's Phase II candidate for autoimmune disorders that represents a novel targeted strategy for selectively inhibiting B-cells without depletion. XmAb5871 targets both CD19 and FcγRIIb to uniquely inhibit B-cell activity without depletion, a potentially broadly applicable and valuable approach in autoimmune disorders and oncology. Top-line data from a Phase 2a study is anticipated late 2014. XmAb5574/MOR208, partnered with MorphoSys is Xencor's other CD19 therapy that employs Fc-engineered higher affinity for FcγRIIIa and FcγRIIa receptors to potently deplete CD19 expressing B-cells offering utility in B-cell malignancies where CD20 therapies are not effective.

Valuation Methodology

We arrive at our $18 price target by a sum-of-the-parts analysis. We ascribe $12/share to applying a 6x multiple of our estimated peak revenues of $1.2 billion (2022) for XmAb7195 in severe asthma and IgE mediated diseases, discounted 45% annually. We ascribe $6/share to Xencor's two partnered programs XmAb5871 and XmAb5574 based on royalties (mean 10%) from sales in 2022 of $1 billion and $600 million discounted 45% and 35% annually, respectively. Similarly we also arrive at our $6/share value to Xencor's potential milestones based upon the NPV discounted 45% over an estimated 10 year realization period. We do not value Xencor's early stage pipeline novel bispecifics at this time.

Sum-of-the-Parts Valuation Components

Product	Indication	Est. Addressable Market	Penetration	Annual Cost	Sales	Multiple	Royalty rate	Year	Discount rate	Value per share
XmAb7195	Severe asthma	350,000*	15%	$22K	$1.2B	6x	NA	2022	45%	$12
XmAb5574	ALL	16,000	38%	$100K	$600M	15x	~10%	2022	35%	$3
XmAb5871	RA	460,000	10%	$25K	$1.2B	15x	~10%	2022	45%	$3
Total										$18

**US market only*

Xencor's Novel Bispecific Candidates

Xencor is developing CD3 bispecific antibodies in pre-clinical studies for potential clinical application in liquid tumors. Xencor has disclosed two bispecific candidates targeting CD3/CD38 and CD3/CD123. Both CD38 and CD123 are promising potential bispecific targets and despite competition, provide important validation of Xencor's novel bispecific targeting technology. We believe that these compounds represent early-stage proof-of-concept of Xencor's potentially best-in-class bispecific technologies.

CD38, also known as cyclic ADP ribose hydrolase, is expressed on the surface of many immune cells including committed progenitor cells, B lymphocytes in germinal centers, plasma cells and at very low levels by mature resting cells and lymphocytes. It is expressed at high levels in many myelomas and is used as a prognostic marker in CLL where CD38 expression is correlated with a more aggressive cancer. Three traditional (non-bispecific) anti-CD38 antibodies are currently in development: GenMab (GEN-OMX: not Covered)/J&J (JNJ: not covered) are developing daratumumab in a Phase II trial in multiple myeloma, Sanofi (SNY: not covered) is developing SAR650984 in Phase I trials and MorphoSys (MOR-XETRA: not Covered)/Celgene (CELG: not covered) are jointly developing MOR202 in Phase I trials.

CD123, also known as the interleukin-3 α receptor (IL3α), is a cytokine receptor that is broadly up-regulated in B-cell malignancies, especially hairy cell leukemia. CSL Behring (CSL-AX: not covered) is developing a neutralizing antibody directed against CD123 in Phase I trials that has demonstrated promise in xenograft models of acute myelogenous leukemia (Data presented at ASH 2012). Additionally, a recombinant protein specifically targeting CD123+ cells consisting of diphtheria toxin bound to IL3α demonstrated excellent cytotoxicity against acute myeloid leukemia progenitor cells and spares normal progenitors, but a Phase I trial found it was poorly tolerated.

Fc-Enabled Bispecifics

Xencor has developed a novel technique for generating high yields of bispecific antibodies that facilitate significant flexibility in targeting domains. Xencor's bispecific technology allows for the production of humanized bispecific antibodies incorporating scFv fragments and Fc modifications, without linkers or other novel antibody formats. Structurally, the company's bispecific technology can produce novel antibodies where one or both heavy/light chain pairs is missing the C_H1 and C_L domains (Figures 5, 6), generating an Fv fragment directly linked to the Fc domain.

Bispecific antibodies and fragments function by activating the CD3 receptor on T-cells inducing T-cell activation as though it had been presented with its specific antigen. These molecules re-target the T-cell from the antigen its CD3 receptor is specific for to the antigen bound by the other arm of the bispecific antibody. (Figure 6) In pre-clinical studies in monkeys, Xencor's molecules resulted in bispecific T-cell engagement via two distinct Fv domains while retaining Fc domain mediated half-life extension and potentially allowing for potential further cytotoxic, Xtend or other Fc domain optimization. Xencor's technology also allows for Fc-knock-out variants that keep the FcRn-mediated half-life of the drug without inducing FcγR-mediated cross-linking and potential off-target T cell activation.

Xencor's technology, by incorporating Fc domains allows for a natural antibody-like half-life (6-7 days) superior to previous generations of bispecific technology. Although promising, early generations of bispecific technology such as the Micromet (Amgen) BiTE have been limited by the requirement for continuous infusion due to their extremely short half-life (3 hours). In addition to half-life extension Xencor's technology may potentially reduce immunogenicity, and cause killing via ADCC as well as T-cell engagement. Xencor's technology also allows for Fc-knock-out variants that maintain structural Fc-domains without inducing FcγR-mediated cross-linking and potential off-target T cell activation.

Xencor's bispecific technology facilitates manufacturing at high yields and ease of isolation compared to other approaches. Due to manufacturing difficulties, current bispecific antibodies are either non-humanized or incorporate novel peptide-linked antibody structures. Trion Pharmaceuticals has developed several bispecific rat/mouse chimeric antibodies including the EU-approved catumaxomab (EpCAM/CD3), ertumaxomab (HER2/CD3), Bi20 (CD20/CD3), and two unnamed GD2/CD3 and GD3/CD3 antibodies in early development. Amgen has developed blinatumomab, an anti-CD19 Fv fragment linked to an anti-CD3 Fv fragment by a peptide linker that demonstrated efficacy at extremely low levels in Phase II studies, though short half-life on the order of 3 hours requires constant infusion. MedImmune's novel MEDI-565 consists of two single chain antibodies linked by a flexible peptide linker and is currently in Phase I studies. Xencor's bispecific antibodies do not contain potentially immunogenic multi-peptide linkers, exhibit stability and half-life similar to well studied antibodies and have the potential to induce killing both by CD3-mediated T cell activation and FcγR-mediated ADCC.

Covered Companies Mentioned Table

Macrogenics	MGNX	OUTPERFORM	$70	$33.37

Analyst Certification
I, Christopher N. Marai, Ph.D., Gregory R. Wade, Ph.D., David M. Nierengarten, Ph.D., certify that the views expressed in this report accurately reflect my personal opinion and that I have not and will not, directly or indirectly, receive compensation or other payments in connection with my specific recommendations or views contained in this report.

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The Investment Ratings are based on the expected performance of a stock (based on anticipated total return to price target) relative to the other stocks in the analyst's coverage universe (or the analyst's team coverage).*

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Wedbush Equity Research Disclosures as of March 3, 2014

Company	Disclosure
Xencor MacroGenics	1,3,5,7 1,3,4,5,7

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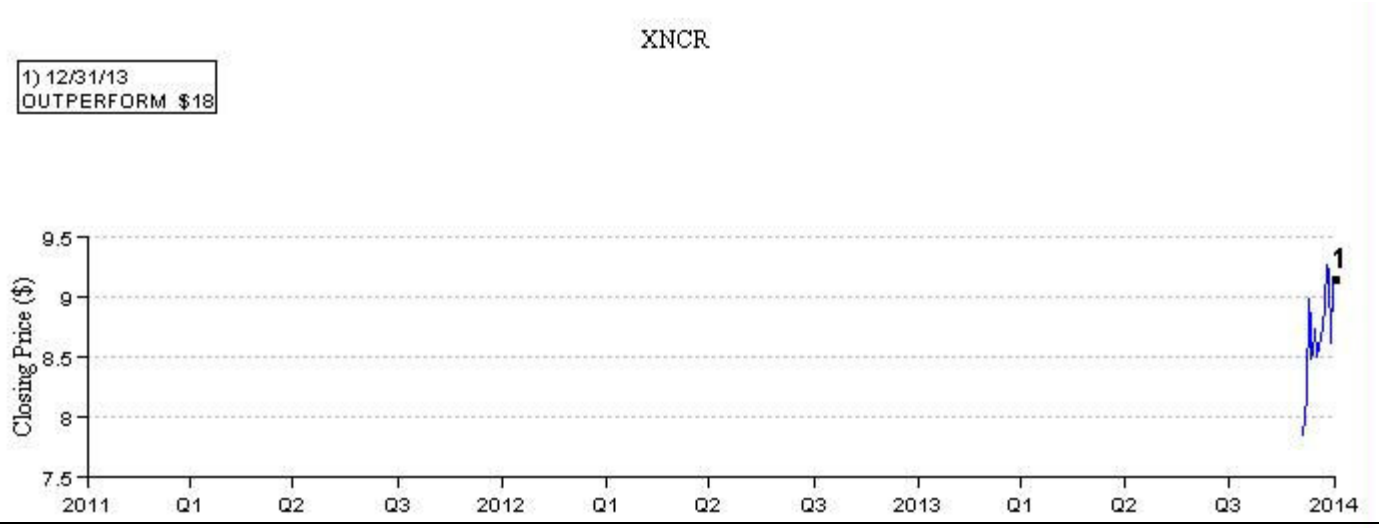

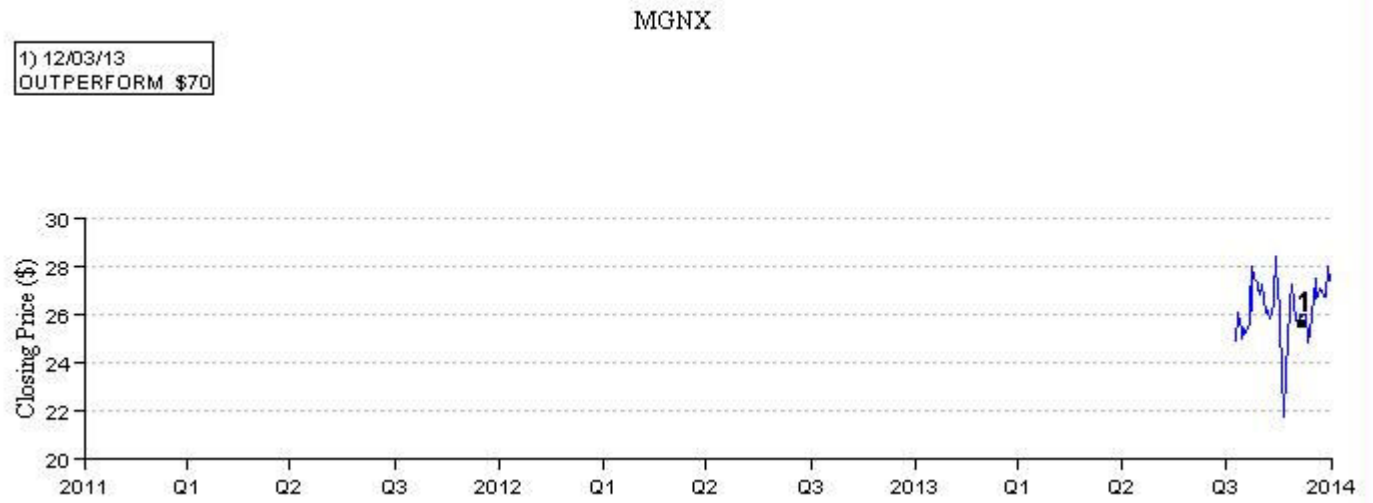

* WS changed its rating system from (Strong Buy/Buy/Hold/Sell) to (Outperform/ Neutral/Underperform) on July 14, 2009.
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