

Biotechnology

# Immune Design

Quick Take: Company Update

**Equity Research** 

June 3, 2015

Price: \$22.91 (06/2/2015)
Price Target: NA

#### **OUTPERFORM (1)**

Boris Peaker, Ph.D., CFA

646.562.1377 boris.peaker@cowen.com

Eric Schmidt, Ph.D.

646.562.1345 eric.schmidt@cowen.com

Joseph Catanzaro, Ph.D.

646.562.1387 joseph.catanzaro@cowen.com

George Chen

646.562.1306 george.chen@cowen.com

**Key Data** 

Symbol NASDAQ: IMDZ

Market Cap (MM) \$458.0

Building A Solid Foundation For Immunotherapy Platform

#### The Cowen Insight

Last night IMDZ hosted a post-ASCO analyst event. Updates for all three of IMDZ's Phase I programs highlighted the potential of the platforms to generate anti-tumor immune responses. LV305, G305 and G100 all appear to be extremely well-tolerated and elicit T-cell and/or antibody responses. We continue to expect IMDZ shares to appreciate as both single-agent and combination data becomes available.

Encouraging Early Data For LV305, Safe & Immune Activating. IMDZ detailed its ongoing Phase I trial of LV305 in NY-ESO-1 expressing tumors. Recall, LV305 is an engineered virus that delivers NY-ESO-1 gene/antigen to dendritic cells. The study has now completed the dose escalation stage with encouraging early signs of immune activation and anti-tumor activity. The study enrolled 12 patients across 4 dosing cohorts. Due to the investigators' research focus on sarcoma, all 12 patients had various subtypes of soft tissue sarcoma (STS). Patients were required to have at least one prior therapy, >5% NY-ESO-1 positivity and low tumor burden (defined by maximum tumor size). The first cohort received three doses of LV305 every 21 days, while all subsequent cohorts received four doses. Completion of treatment schedule was achieved by 11 of the 12 patients; one patient had progressive disease after two doses. There were no DLTs or SAEs, with the majority of reported AEs being low grade fatigue, injection site reactions, and discomfort. At the end of treatment, 8/12 patients exhibited stable disease. Compared to historical data, the incidence of progression at 3 and 6 months was very positive and appeared to double what would be expected with an active agent in the 2nd-line setting. Importantly, NY-ESO-1 specific CD8+ T-cell responses were observed in 6/11 patients and 5/11 exhibited CD4+ T-cells response. Responses were weighted in the highest dosing cohorts, with 4/5 evaluable patients generating a response. As expected, no humoral response was observed following vaccination. Management highlighted the expansion of both NY-ESO-1 specific TCRs and TIL-specific TCRs following vaccination. T-cells against previously unrecognized NY-ESO-1 epitopes were also detected following vaccination. Though only 12 patients, the degree of NY-ESO-1 T-cell responses observed appears to be superior than prior attempts at vaccinating against this tumor antigen (peptide, fowlpox, vaccinia, antibody fusion). We believe these early data are very encouraging for IMDZ's ZVex/LV305 platform. It appears that the vaccine is capable of eliciting an antigen-specifc response. Given the benign safety profile, we believe that it is amenable to various combination strategies. IMDZ has already initiated a Phase I dose-escalation study that combines LV305 with G305 (detailed below) as CMB305. Expansion cohorts (sarcoma, melanoma, ovarian, lung) for CMB305 are expected to open in 3Q15. Additionally, expansion cohorts are currently enrolling (melanoma, ovarian, and lung) and will continue to evaluate LV305 as a single agent. Management also spoke briefly about plans for a Phase II CMB305 + CPI randomized trial in STS, as well as a second indication. This study is expected to begin by YE15.

**Single Agent Activity Of G305 Supports Combination With LV305.** G305 is NY-ESO-1 peptide delivered with IMDZ's GLA adjuvant. IMDZ's plan has always been to

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test the safety of G305 as a single agent and advance it in combination with LV305. Similar to LV305, G305 was evaluated in a Phase I dose-escalation trial. All 12 patients (ovarian, sarcoma, melanoma, bladder) completed vaccination of three doses every 21 days. There were no reports of DLTs or SAEs and like LV305, all AEs were low grade injection site pain, fatigue, and nausea. Stable disease was observed in 8/12 patients. A patient with ovarian cancer in the first cohort exhibited stable disease for >1 year. More importantly, increased antibody responses against NY-ESO-1 were reported in 9/12 patients, as well as NY-ESO-1 CD4+ T-cells in 5/11 evaluable patients. CD8+ T-cell responses, though not expected given G305 mechanism of action, were seen in 2/10 patients. We think IMDZ is taking a very rational and discerning approach with G305 and LV305. In our view these early data clearly demonstrate that G305 can elicit an antibody/CD4+ immune response, while LV305 can prime a CD8+ response. We expect the combo (CMB305) to produce robust immune responses that should translate to clinical activity.

G100: Intratumoral Vaccination With Lots Of Potential. G100 is a GLA-based TLR4 agonist designed to enhance antigen uptake by antigen-presenting cells (APCs) following tumor cell lysis to generate in-situ vaccination. IMDZ detailed early results from a Phase I trial in patients with loco-regional (n=2) and metastatic (n=6) Merkel cell carcinoma (MCC). Those with locally advanced disease received two doses of G100 followed by surgery/radiation. Both of these patients had no evidence of disease following treatment, with one demonstrating a pathological CR prior to surgery/ radiation. This patient remains free of disease for >1 year. Metastatic patients received a single cycle (3 doses) followed by a second cycle with concurrent radiation. In these 6 patients, two achieved a PR. Included in the presentation was a case that showed a striking infiltration of CD8+ T-cells following the first cycle of G100. This patient went on to achieve a PR. All AEs were grade 1/2 and there were no DLTs or SAEs. We are encouraged by these data, especially the anti-tumor activity observed prior to radiation. IMDZ noted that future plans for G100 in MCC are being considered. A Phase I trial in NHL is expected to open in the next 1-2 months. This 30 patient trial will evaluate G100 with radiation and will include a small cohort that will also receive a checkpoint inhibitor. The first data from this trial are expected in 1H16.

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# Valuation Methodology And Risks

### Valuation Methodology

#### **Biotechnology:**

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

#### **Investment Risks**

#### **Biotechnology:**

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

#### **Risks To The Price Target**

There are multiple risks and uncertainties associated with investment in clinical stage biotechnology companies. The key risks are:

**Clinical Trial Risk:** Immune Design will require FDA approval to market its products in the US and EMEA in Europe. Failure to gain such approvals would significantly impact the value of the company.

**Competitive Risk:** There are multiple competing agents in development, for indications in which IMDZ's products are being studied. The success of such agents could significantly affect market share of IMDZ's product should they be approved.

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#### Stocks Mentioned In Important Disclosures

Ticker	Company Name
IMDZ	Immune Design

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Cowen and Company, LLC. New York (646) 562-1000 Boston (617) 946-3700 San Francisco (415) 646-7200 Chicago (312) 577-2240 Cleveland (440) 331-3531 Atlanta (866) 544-7009 London (affiliate) 44-207-071-7500

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Outperform (1): The stock is expected to achieve a total positive return of at least 15% over the next 12 months

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Cowen and Company Rating System until May 25, 2013

Outperform (1): Stock expected to outperform the S&P 500

Neutral (2): Stock expected to perform in line with the S&P 500

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Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period

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Buy - The fundamentals/valuations of the subject company are improving and the investment return is expected to be 5 to 15 percentage points higher than the general market

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Sell – The fundamentals/valuations of the subject company are deteriorating and the investment return is expected to be 5 to 15 percentage points lower than the general market return

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#### **Cowen And Company Rating Definitions**

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Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	450	58.67%	103	22.89%
Hold (b)	302	39.37%	8	2.65%
Sell (c)	15	1.96%	0	0.00%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

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#### Immune Design Rating History as of 06/02/2015

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#### Legend for Price Chart:

I = Initiation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | \$xx = Price Target | NA = Not Available | S=Suspended

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# Points Of Contact

### **Reaching Cowen**

#### **Main U.S. Locations**

#### **New York**

599 Lexington Avenue New York, NY 10022 646.562.1000 800.221.5616

#### Atlanta

3399 Peachtree Road NE Suite 417

Atlanta, GA 30326 866.544.7009

#### **Boston**

Two International Place Boston, MA 02110 617.946.3700 800.343.7068

#### Chicago

181 West Madison Street **Suite 3135** Chicago, IL 60602 312.577.2240

#### Cleveland

20006 Detroit Road Suite 100 Rocky River, OH 44116 440.331.3531

#### San Francisco

555 California Street, 5th Floor San Francisco, CA 94104 415.646.7200 800.858.9316

#### **International Locations**

#### **Cowen International** Limited

## London

1 Snowden Street - 11th Floor London EC2A 2DQ **United Kingdom** 44.20.7071.7500

# Cowen and Company (Asia)

#### Limited

#### **Hong Kong**

Suite 1401 Henley Building No. 5 Queens Road Central Central, Hong Kong 852 3752 2333





