The Future of Immuno-Oncology: Perspectives from Academia and Industry

September 19, 2014
Defined Health is pleased to present:

**CANCER PROGRESS by Defined Health**

26th Annual Cancer Progress Conference  
March 17 – 18, 2015  
New York City  
www.cancerprogressbyDH.com

**THERAPEUTIC INSIGHT by Defined Health**

Therapeutic Insight by Defined Health  
BIO-Europe Spring  
March 9 – 11, 2015  
Paris  

Defined Health will also be participating in the following industry events:

- **BioPharm America™ 2014** | September 22 - 24, 2014 | Boston, MA
- **The Pharmaceutical Strategy Conference** | September 29 – October 1 | New York, NY
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- **Cancer Progress by Defined Health** | March 2015 | New York City
- **Therapeutic Insight by Defined Health at BIO-Europe Spring®** | March 9 - 11, 2015 | Paris, France
Our Distinguished Panelists

- Axel Hoos, Vice President of Oncology Research and Development at GSK
- Drew Pardoll, Abeloff Professorship of Oncology and Director of Cancer Immunology at Johns Hopkins University
- Moderated by Jeffrey M. Bockman, PhD, Vice President, Defined Health
Because Cancers Under-Cut a Key Defense of the Host, Tumor Immunology Has Been a Longstanding Focus of Research

The Commercial Market for Immuno-Oncology Products is Projected to Grow Significantly – Though How Quickly and by How Much is Not Clear

- Roughly 30% of the nearly $43B in worldwide sales coming from the top 10 antibodies in oncology in 2020 will come from anti-PD1 and anti-CTLA4.¹
- A recent Citi report forecasts that in ten years, immunotherapy drugs of various sorts will be treating 60% of cancers and earning US$35 billion per year.²

¹Evaluate Pharma; ²Nature 497, 544 (30 May 2013); Defined Heath
The Field Has a Diversity of Platforms Currently in Mid-to-Late Stage Clinical Development

Comparison of Late-Stage Immuno-Oncology Products in Development (Phase II through Registration)

### Products by Category

<table>
<thead>
<tr>
<th>Category</th>
<th># of Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer vaccine</td>
<td>86</td>
</tr>
<tr>
<td>Antibody</td>
<td>10</td>
</tr>
<tr>
<td>Cytokine</td>
<td>9</td>
</tr>
<tr>
<td>Cell-therapy</td>
<td>9</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
</tr>
<tr>
<td>Gene therapy</td>
<td>6</td>
</tr>
<tr>
<td>Oncolytic virus</td>
<td>4</td>
</tr>
<tr>
<td>Small molecule</td>
<td>3</td>
</tr>
</tbody>
</table>

Adis R&D Insight

Defined Health Oncology Webinar, Sept 19, 2014

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Major Oncology Players Have Staked Out Their Positions, Primarily in Checkpoint and Costimulatory Antibodies and Adoptive Cell Therapies

- Categories of major immunotherapeutic intervention include methods to increase the frequency of tumor antigen-specific effector T cells in the circulation, strategies to block or uncouple a range of immune suppressive mechanisms within the tumor microenvironment, and tactics to induce de novo immune inflammation within the tumor microenvironment.

Citi, 14 February 2014, *Immunotherapy - The Beginning of the End for Cancer*
Principles for Combining Different Types of Immunotherapies With Each Other and Standard of Care

- The range of combinations are quite daunting and, as noted by KOLs, very difficult to gauge from preclinical data; therefore, to **increase optionality and reduce risk**, players must make multiple bets across the diverse range of platforms and approaches.

![Diagram](Journal for ImmunoTherapy of Cancer 2013, 1:16)
Principles of Combination with “Targeted” Therapies

- There are also many opportunities for franchise plays in combining immunotherapies with targeted therapies and other modalities.


Defined Health Oncology Webinar, Sept 19, 2014
The Potential of Immunotherapy, in Combination, and on Top of Standard of Care Regimens, to Shift Survival Towards Chronic Disease, or Even Cure

- Really for the first time, oncologists are talking about potentials for significant advances in survival, and even cures, using immunotherapies. 

_Clin Cancer Res 2013;19:5300-5309; Citi, 14 February 2014, Immunotherapy - The Beginning of the End for Cancer_
Seven of the Top 14 Deals Were Oncology – Five of These Were Immuno-Oncology...Plus Yesterday’s (9/18) Deal

<table>
<thead>
<tr>
<th>Buyer</th>
<th>Seller</th>
<th>Size (US $ M)</th>
<th>Upfront (US $M)</th>
<th>Subject</th>
<th>Stage</th>
<th>Primary Rx Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>Collectis</td>
<td>$2,855</td>
<td>$80</td>
<td>Allogenic CAR-T Immunotherapies with 15 Pfizer and 4 Collectis targets</td>
<td>Discovery</td>
<td>Cancer</td>
</tr>
<tr>
<td>Celgene</td>
<td>Giuliani/ Nogra</td>
<td>$2,575</td>
<td>$710</td>
<td>GED-0301 oral oligonucleotide vs SMAD-7 for Crohn’s disease and other gastrointestinal indications</td>
<td>Phase II complete</td>
<td>Al/Inflam</td>
</tr>
<tr>
<td>Merck</td>
<td>Ablynx</td>
<td>$2,341</td>
<td>$27</td>
<td>Nanobody technology to discover nanobody-based immunotherapies</td>
<td>Discovery</td>
<td>Cancer</td>
</tr>
<tr>
<td>Merck</td>
<td>Bayer</td>
<td>$2,100</td>
<td>$1,000</td>
<td>Adempas, BAY102 and other soluble guanylate cyclase (sGC) modulators for cardiovascular diseases</td>
<td>Approved</td>
<td>CV</td>
</tr>
<tr>
<td>Viking Therapeutics</td>
<td>Ligand</td>
<td>$1,564</td>
<td>$29M in Viking equity upon IPO</td>
<td>FBPase, SARM, TR-Beta, EPOR, DGAT-1 programs for type 2 diabetes, cancer cachexia, dyslipidemia, obesity</td>
<td>Phase II</td>
<td>Endo/Meta</td>
</tr>
<tr>
<td>BMS</td>
<td>CytomX</td>
<td>$1,242</td>
<td>$50</td>
<td>Proodies against up to 4 immuno-oncology targets including CTLA-4</td>
<td>Discovery</td>
<td>Cancer</td>
</tr>
<tr>
<td>Biogen Idec</td>
<td>Etisai</td>
<td>$1,100</td>
<td>$100</td>
<td>E2609 BACE Inhibitor and BANZ401 anti-AB ab for Alzheimers + option for 2 additional BIB Alz ab</td>
<td>Phase II</td>
<td>Neurology</td>
</tr>
<tr>
<td>Novartis</td>
<td>Ophthotech</td>
<td>$1,030</td>
<td>$200</td>
<td>Fovista anti-PDGF for wet AMD worldwide ex-US</td>
<td>Phase III</td>
<td>Ophthalmic</td>
</tr>
<tr>
<td>Servier</td>
<td>Collectis</td>
<td>$850</td>
<td>$10</td>
<td>Option to UCART19 for leukemia + 5 CAR-Ts to undisclosed solid tumor targets</td>
<td>Preclinical</td>
<td>Cancer</td>
</tr>
<tr>
<td>Merck KGaA / EMD Serona</td>
<td>Mersana</td>
<td>$792</td>
<td>CON</td>
<td>Fleximer technology to develop ADCs for multiple undisclosed targets</td>
<td>Not applicable (Technology)</td>
<td>Cancer</td>
</tr>
<tr>
<td>BMS</td>
<td>Five Prime</td>
<td>$650</td>
<td>$20M + $21M equity</td>
<td>Discovery of targets in 2 undisc. immune checkpoint pathways to develop immune-oncology therapies</td>
<td>Discovery</td>
<td>Cancer</td>
</tr>
<tr>
<td>Regeneron</td>
<td>Avalanche</td>
<td>$640</td>
<td>$2M + $3M preferred stock</td>
<td>8 gene therapies for ophthalmologic diseases</td>
<td>Phase II</td>
<td>Ophthalmic</td>
</tr>
<tr>
<td>Roche</td>
<td>Oryzon</td>
<td>$521</td>
<td>CON</td>
<td>ORY-1001 small molecule inhibitor of LSD1 epigenetic modulator for AML + option to additional programs</td>
<td>Phase II</td>
<td>Cancer</td>
</tr>
<tr>
<td>Takeda</td>
<td>MacroGenics</td>
<td>$502</td>
<td>$15</td>
<td>MGD010 bi-specific DART vs. CD32B and CD798</td>
<td>Preclinical</td>
<td>Al/Inflam</td>
</tr>
</tbody>
</table>

| Boehringer Ingelheim   | CureVac               | $556M         | $45M            | CV9202 is a combination of mRNA molecules coding for six antigens overexpressed in lung cancer, designed to induce an immune response against the tumor. | Phase I       | Cancer          |
As With Other Areas of Oncology, Combination Therapies Pose Additional Hurdles for Demonstrating Value – the Pharmaco-Economics of Pricing

- The challenges of developing and pricing immunotherapies are substantive.
- Such challenges are underscored by the scientific and clinical difficulty of showing synergy and acceptable tolerability.
- This may explain in part the number of clinical trial collaborations rather than strict licensing deals that are occurring.

*Nature* 497, 544 (30 May 2013); Peter Bach, Center for Health Policy & Outcomes, MSKCC, [http://www.mskcc.org/research/health-policy-outcomes](http://www.mskcc.org/research/health-policy-outcomes)
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Featured Keynotes:
Peter Bach, MD, Memorial Sloan-Kettering Cancer Center
Clifford A. Hudis, MD, Memorial Sloan Kettering Cancer Center, 2013-2014 President, ASCO
Michael Kolodziej, MD, Aetna
Lee Newcomer, MD, MHA, United Healthcare
Lynda Chin, MD, MD Anderson Cancer Center
Our Featured Panelists

Peter C. Adamson, MD, The Children’s Hospital of Philadelphia
Rafael Amado, MD, GlaxoSmithKline
Jeff Bockman, PhD, Defined Health
Renier J. Brentjens, MD, PhD, Memorial Sloan Kettering Cancer Center
Meredith K. Chuk, MD, FDA
Robert Cohen, MD, Calico Life Sciences
Barbara A. Conley, MD, National Institute of Health
Heather Cooper-Ortner, Dr. Susan Love Research Foundation
Lou DeGennaro, PhD, Leukemia & Lymphoma Society
Thomas O. Daniel, MD, Celgene Corporation
Kathleen A. Denis, PhD, The Rockefeller University
Kapil Dhingra, MD, KAPital Consulting LLC
James H. Doroshow, MD, National Cancer Institute
Thomas J. Farrell, Bellicum Pharmaceuticals
Stanley R. Frankel, MD, Amgen
Richard Brian Gaynor, MD, Eli Lilly and Company
Brad Gray, NanoStrings Technologies
William Grossman, MD, PhD, AbbVie
Ivan Horak, MD, Symphogen A/S
Axel Hoos, MD, PhD, GlaxoSmithKline
Johanna Joyce, PhD, Memorial Sloan Kettering Cancer Center
Thomas J. Kipps, MD, PhD, Moores UCSD Cancer Center
Michael Kolodziej, MD, Aetna
Amy Krie, MD, Avera Cancer Institute
Manfred Lehner, MD, Takeda Pharmaceuticals International
Christoph Lengauer, MD, PhD, Blueprint Medicines
Ross Levine, MD, Memorial Sloan Kettering Cancer Center
Hy Levitsky, MD, Roche Pharmaceuticals
Brian Leyland-Jones, MD, Avera Cancer Institute
Nils Lonberg, PhD, Bristol-Myers Squibb
Patricia LoRusso, D.O., Smilow Cancer Center, Yale University
Susan Love, MD, Dr. Susan Love Research Foundation
Frantiska Michor, PhD, Harvard School of Public Health
Ronnie Morris, MD, Champions Oncology
Larry Norton, MD, Memorial Sloan Kettering Cancer Center
Mike Rice, MS, MBA, Defined Health
Dr. Harlan Robins, PhD, Adaptive Biotechnologies
Carlos Rodriguez-Galindo, MD, Harvard Medical School
Noemi Rosa, MD, PhD, GlaxoSmithKline
Neal Rosen, MD, PhD, Memorial Sloan Kettering Cancer Center
Raphaël F. Rousseau, MD, PhD, Genentech Inc.
Eric Rowinsky, MD, Stemline Therapeutics
Rob Ruijtenbeek, PamGene BV
Prof. Dolores J. Schendel, PhD, Medigene
Jeffrey Settleman, PhD, Genetech
Angela Shen, MD, MBA, Novartis Pharmaceuticals Corp.
Ellen V. Sigal, PhD, Friends of Cancer Research
Mark J. Simon, Torreya Partners LLC
Eric Slosberg, PhD, Novartis Oncology
Malcolm A. Smith, MD, PhD, National Cancer Institute
John J. Sninsky, PhD, Quest Diagnostics
David Solit, MD, Memorial Sloan Kettering Cancer Center
Chris H. Takimoto, MD, PhD, Janssen Research & Development
Marc Theoret, MD, FDA
Alain Thibault, MD, arGEN-X N.V.
Jedd Wolchok, MD, PhD, Memorial Sloan-Kettering Cancer Center
Cassian Yee MD, MD Anderson Cancer Center
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