REMARKABLE IMPACT ON PATIENTS’ LIVES

AbbVie R&D Day
Chicago, IL | June 3, 2016
Forward-Looking Statements and Non-GAAP Financial Information

Some statements in this presentation may be forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995. The words "believe," "expect," "anticipate," "project" and similar expressions, among others, generally identify forward-looking statements. AbbVie cautions that these forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those indicated in the forward-looking statements. Such risks and uncertainties include, but are not limited to, challenges to intellectual property, competition from other products, difficulties inherent in the research and development process, adverse litigation or government action, and changes to laws and regulations applicable to our industry. Additional information about the economic, competitive, governmental, technological and other factors that may affect AbbVie's operations is set forth in Item 1A, "Risk Factors," of AbbVie's 2015 Annual Report on Form 10-K, which has been filed with the Securities and Exchange Commission. AbbVie undertakes no obligation to release publicly any revisions to forward-looking statements as a result of subsequent events or developments, except as required by law.

This presentation contains GAAP and certain non-GAAP financial measures. Non-GAAP financial measures are adjusted for certain non-cash items and for factors that are unusual or unpredictable, and exclude those costs, expenses, and other specified items presented in AbbVie’s reconciliation tables. AbbVie’s management believes non-GAAP financial measures provide useful information to investors regarding AbbVie’s results of operations and assist management, analysts, and investors in evaluating the performance of the business. Non-GAAP financial measures should be considered in addition to, and not as a substitute for, measures of financial performance prepared in accordance with GAAP. Reconciliations of these non-GAAP financial measures to the most comparable GAAP measures are provided in AbbVie’s quarterly earnings releases posted on the company’s website at www.abbvieinvestor.com.

During the course of this meeting, AbbVie will be presenting information about the uses of AbbVie products and AbbVie compounds in clinical development that have not been approved by the U.S. FDA. AbbVie, in no way, intends to recommend or imply that any AbbVie product or compound in development should be used for unapproved uses, or is safe or effective for uses not approved by the FDA.
R&D Day: Opening Remarks

Richard Gonzalez
AbbVie’s R&D Strategy: Re-Statting Standard of Care

Level of Therapeutic Restatement

Early-Stage Pipeline

Late-Stage Pipeline

Current Standard of Care

Meaningful Improvement vs. Standard of Care

Cure or Long-Term, Deep, Durable Disease Control

SOC Re-Statement

Stage of Pipeline Development
Science and Innovation are the Lifeblood of Our Company

AbbVie Mission

Create an innovation-driven, patient-focused, specialty biopharmaceutical company capable of achieving top-tier performance through outstanding execution and a consistent stream of innovative new medicines

Innovative Medicines

Compelling Patient Benefit
Differentiated Clinical Performance
Economic Value

Elevate standard of care and address significant unmet need
### Areas of Focus

<table>
<thead>
<tr>
<th>Core Therapeutic Focus</th>
<th>Developing disease-modifying therapies for Alzheimer's disease, multiple sclerosis and other neurodegenerative conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>Uniquely positioned with growing leadership position in Hematologic Oncology; Rova-T provides strong foundation for Solid Tumors</td>
</tr>
<tr>
<td>Immunology</td>
<td>Leveraging deep scientific expertise to develop next-generation biologics and small molecules that elevate standard of care</td>
</tr>
<tr>
<td>Virology</td>
<td>Highly competitive next-generation HCV combination that addresses remaining unmet medical need</td>
</tr>
<tr>
<td>Neuroscience</td>
<td>Focused investments in areas that fit our core strengths (i.e., Elagolix, cystic fibrosis collaboration, atrasentan, etc.)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>
Tremendous Progress in R&D Since Our Launch as an Independent Biopharmaceutical Company

1. **Heightened our level of R&D spend** to reflect the meaningful opportunities in our pipeline

2. Built upon already strong capabilities with the **addition of new talent** to our R&D organization

3. **Strengthened discovery efforts** through collaborations with leading academic and other institutions

4. **Augmented our pipeline** through concerted focus on strategic licensing, acquisition and partner activity

5. **De-risked key late-stage programs** through numerous positive data readouts
## Robust Pipeline Supports Long-Term Growth

### Near-Term Growth Assets
- Eight key, late-stage de-risked assets
- High probability of regulatory and commercial success
- Differentiated profiles
- On market today or poised to launch over the next 2-3 years

### 50+ Additional Development Programs
- Robust portfolio of promising programs
- Have already established strong proof-of-concept for numerous assets

### Innovative Early-Stage Opportunities
- Early-stage development programs in areas of high unmet need
- Enhanced discovery platforms have high potential for continued asset generation to drive development efforts going forward

### Near-Term Growth Assets Examples
- **Imbruvica**
- **Rova-T**
- **Risankizumab**
- **Venclexta**
- **ABT-494**
- **Next-Gen HCV**
- **Elagolix**
- **Zinbryta**

### 50+ Additional Development Programs Examples
- Anticipate key data readouts from several programs over next 12-24 months to determine next steps
  - Veliparib
  - ABT-414
  - Atrasentan
  - Several DVD-Ig programs
  - Partnered assets (dual PI3K, IL-6 nanobody, etc.)

### Innovative Early-Stage Opportunities Examples
- Entering clinic with novel immuno-oncology and neuroscience assets
- New discovery platforms, including Calico and Stemcentrx, augment existing discovery/early development efforts, have potential to accelerate asset generation
- Early-stage programs to begin driving growth in mid-2020s and beyond
## Near-Term Growth Assets are Significantly De-risked

<table>
<thead>
<tr>
<th>Asset</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Imbruvica</strong></td>
<td>Currently approved for five indications, including recent label update to include 1L CLL; numerous mid- and late-stage studies underway for range of blood cancers</td>
</tr>
<tr>
<td><em>On-market with five approved indications, additional indications expected over next several years</em></td>
<td></td>
</tr>
<tr>
<td><strong>Venclexta</strong></td>
<td>First-in-class BCL-2 inhibitor recently approved for first indication; mid-to-late-stage development ongoing for numerous hematologic malignancies</td>
</tr>
<tr>
<td><em>On-market with initial indication, additional indications expected over next several years</em></td>
<td></td>
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<tr>
<td><strong>Zinbryta</strong></td>
<td>Pivotal data demonstrated significant benefit vs. active comparator; regulatory submissions under review, decisions expected mid-2016</td>
</tr>
<tr>
<td><em>2016 Launch</em></td>
<td></td>
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<tr>
<td><strong>Next-Gen HCV</strong></td>
<td>Mid-stage data indicate combination can deliver cure rates approaching 100% across genotypes; pivotal data expected 2H16</td>
</tr>
<tr>
<td><em>2017 Launch</em></td>
<td></td>
</tr>
<tr>
<td><strong>Rova-T</strong></td>
<td>Compelling Phase 1/2 data in relapsed SCLC; Phase 3 underway; potential in a variety of solid tumors with DLL 3 expression</td>
</tr>
<tr>
<td><em>2018 Launch</em></td>
<td></td>
</tr>
<tr>
<td><strong>Elagolix</strong></td>
<td>Compelling profile illustrated in two registrational trials; on track for regulatory submission in 2017</td>
</tr>
<tr>
<td><em>2018 Launch</em></td>
<td></td>
</tr>
<tr>
<td><strong>ABT-494</strong></td>
<td>Phase 2 RA trials demonstrated potential for best-in-class profile in TNF-IR and MTX-IR; comprehensive Phase 3 program now underway</td>
</tr>
<tr>
<td><em>2019 Launch</em></td>
<td></td>
</tr>
<tr>
<td><strong>Risankizumab</strong></td>
<td>Phase 2 Ps study illustrated potential for best overall profile; Phase 3 currently underway, with potential to advance in several other immune-mediated conditions</td>
</tr>
<tr>
<td><em>2019 Launch</em></td>
<td></td>
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</tbody>
</table>
Magnitude of Near-Term Growth Assets Alone Ensures Substantial Growth Beyond 2020

Humira 2020

De-Risked Late-Stage Assets

$25-30BN*

Imbruvica
Rova-T
Risankizumab
Venclexta
ABT-494
Next-Gen HCV
Elagolix
Zinbryta

*$Represents nominal peak-year revenue opportunity for eight key near-term growth assets
AbbVie: A Unique Investment Opportunity

AbbVie offers top-tier revenue and EPS growth, significant cash flow and strong return of capital to shareholders

- Compelling, de-risked late-stage pipeline poised to fuel long-term growth
- Early-stage pipeline includes programs with the potential to dramatically re-state standard of care
- Strong track record of execution
- Attractive return of capital philosophy, balanced between supporting growth and returning cash to shareholders
- Remain committed to delivering on our long-term objectives
- Double-digit EPS growth on average expected through 2020
Introduction and Overview of R&D Strategy

Michael Severino, M.D.
A Number of Important Considerations Guide Our R&D Strategy

Unmet Medical Need

Clinical Translation

Novel Biology

Core Capabilities

New Technologies
## Our Discovery Efforts Are Focused on Three Main Areas

<table>
<thead>
<tr>
<th>Area</th>
<th>Focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>• Grow our strong position in hematologic malignancies</td>
</tr>
<tr>
<td></td>
<td>• Establish a foundation in solid tumors</td>
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<td></td>
<td>• Leverage our experience in immunology to develop</td>
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<td></td>
<td>next-generation immuno-oncology therapies</td>
</tr>
<tr>
<td>Immunology</td>
<td>• Use core skills in immunology to develop next-generation therapies</td>
</tr>
<tr>
<td></td>
<td>that raise the standard in Rheumatology, Dermatology and Gastroenterology</td>
</tr>
<tr>
<td>Neuroscience</td>
<td>• Capitalize on emerging biology and new technologies to expand into</td>
</tr>
<tr>
<td></td>
<td>Alzheimer's disease and the neurodegenerative components of multiple</td>
</tr>
<tr>
<td></td>
<td>sclerosis</td>
</tr>
</tbody>
</table>
In Addition, We Intend to Pursue Areas That Are a Strong Fit for Our Core Strengths

<table>
<thead>
<tr>
<th>HCV</th>
<th>• Pursue next-generation regimens that address remaining unmet need</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elagolix</td>
<td>• Bring an important new therapeutic option to women with endometriosis and uterine fibroids</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>• Explore whether new insights in biology and medicinal chemistry can lead to a transformational therapy</td>
</tr>
</tbody>
</table>
Recent hires or new to role

**Tom Hudson, M.D.**
VP, Oncology Discovery/Early Development

**Eric Karran, Ph.D.**
VP, Foundational Neuroscience Center

**Rob Scott, M.D.**
CMO and VP, Development

**Shao-Lee Lin, M.D., Ph.D.**
VP, Global Therapeutic Areas and International Development

**Laura Gault, M.D., Ph.D.**
Neuroscience, Clinical Development

**Chris Miller, Ph.D.**
Director, Genetics & Genomics Research

**Anthony Slavin, Ph.D.**
Director, Immunology Biology

**Susie Jun, M.D., Ph.D.**
VP, Oncology Translational Medicine

**Therese Podrebarac, M.D.**
VP, Immunology Development

**Brad Shotwell, Ph.D.**
Senior Group Leader, Hit to Lead Chemistry

**Laura Gasparini, Ph.D.**
Project Director, Neuroscience

**Albert Lai, Ph.D.**
Project Director, Oncology

**Guowei Fang, M.D.**
Head of Discovery, Pharmacylcics

**Patrick John Marroum, Ph.D.**
Director, Biopharmaceutics, Clinical Pharmacology and Pharmacometrics

**Phil Hajduk, Ph.D.**
VP, Research Informatics

**Paul Peloso, M.D.**
Group Medical Director, Elagolix, General Medicine TA

**Maureen Kelly, M.D.**
Group Medical Director, Risankizumab, Immunology TA

**Adam Petrich, M.D.**
Associate Medical Director, Oncology
We Are Increasing our Presence in Hubs of Biotechnology and External Innovation

In addition, AbbVie has an R&D presence around the world

WEST COAST
- Oncology
  - Redwood City, CA
  - South San Francisco, CA
  - Sunnyvale, CA

EAST COAST
- Neuroscience
  - Cambridge, MA
- Immunology
  - Worcester, MA

LAKE COUNTY
### Our Internal Efforts Are Complemented by Our Access to External Innovation

<table>
<thead>
<tr>
<th>Academic Collaborations</th>
<th>Industry Partnerships</th>
<th>Acquisitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harvard</td>
<td>Calico</td>
<td>Stemcentrx</td>
</tr>
<tr>
<td>Yale</td>
<td>argenx</td>
<td>pharmacyclics</td>
</tr>
<tr>
<td>BROAD INSTITUTE</td>
<td>CytomX Therapeutics</td>
<td>immuVen</td>
</tr>
<tr>
<td>MD Anderson Cancer Center</td>
<td>Genentech</td>
<td>Facet Biotech</td>
</tr>
<tr>
<td>THE UNIVERSITY OF CHICAGO</td>
<td>Boehringer Ingelheim</td>
<td></td>
</tr>
<tr>
<td>DEMENTIA Consortium</td>
<td>Infinity Pharmaceuticals</td>
<td></td>
</tr>
<tr>
<td>UCSF</td>
<td>Roche</td>
<td></td>
</tr>
<tr>
<td>FIAT-LUX</td>
<td>Bristol-Myers Squibb</td>
<td></td>
</tr>
<tr>
<td>The Walter and Eliza Hall Institute of Medical Research</td>
<td>Janssen</td>
<td>apogenix</td>
</tr>
<tr>
<td>Seattle Genetics</td>
<td>Galápagos</td>
<td></td>
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<tr>
<td>F-star</td>
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</tbody>
</table>

Not a comprehensive list
Our Calico Collaboration Offers an Additional Opportunity to Explore Novel Biology

Portfolio of ~20 programs targeting fundamental biological mechanisms that underlie neurodegeneration, cancer and other diseases of aging

Adapted from Cell 153, June 6, 2013
Our Strategy Is Supported by Strong Financial Commitment

![R&D Spend ($BN)](chart1)

![R&D Spend as % of Sales](chart2)

Note: Non-GAAP; excluding specified items
AbbVie’s Phase 2 and Phase 3 Success Rates Compare Favorably to Industry Benchmarks

**Late-Stage NME Success Rates**

*Industry Portrait vs AbbVie*

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Phase 2</td>
<td>44% (18)</td>
<td>83% (6)</td>
</tr>
<tr>
<td>Phase 3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Source:** Pharmaceutical Benchmarking Forum/KMR 2015; industry Portrait defined as combined data from all pharma companies participating in PBF/KMR Benchmarking Forum

(xx) Numbers in parenthesis indicate number of phase events (Go/no-go decisions) for ABBV
Pipeline Supports Our Future Growth

<table>
<thead>
<tr>
<th>Select Pipeline Assets</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Registrational/Phase III</th>
<th>Submitted</th>
<th>Recent Approvals</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABBV-2451: Cystic Fibrosis</td>
<td>SC003: Solid Tumors</td>
<td>Venclexta: Multiple Myeloma</td>
<td>Venclexta: CLL (Front-line; Unfit)</td>
<td>Imbruvica: Uveitis (U.S. and EU)</td>
<td>Humira: New Pen Device</td>
</tr>
<tr>
<td>ABT-957: Alzheimer’s</td>
<td>PTK7*: Solid Tumors</td>
<td>Duvelisib: iNHL (R/R)</td>
<td>Imbruvica: Pancreatic Cancer</td>
<td>Duopa: Advanced Parkinson’s</td>
<td></td>
</tr>
<tr>
<td>ABBV-8E12: PSP &amp; AD</td>
<td>EFNA4*: Solid Tumors</td>
<td>Imbruvica: Multiple Myeloma</td>
<td>Imbruvica: DLBCL (TN)</td>
<td>Zinbryta: Multiple Sclerosis (U.S. and EU)</td>
<td></td>
</tr>
<tr>
<td>ABT-555: MS and SCI</td>
<td>ABBV-838: Multiple Myeloma</td>
<td>Imbruvica: AML</td>
<td>Imbruvica: FL (R/R)</td>
<td>Venclexta: HCV (GT1b)</td>
<td></td>
</tr>
<tr>
<td>ABBV-399: Solid Tumors</td>
<td>ABBV-221: Solid Tumors</td>
<td>Imbruvica: FL (TN)</td>
<td>Imbruvica: MCL (TN)</td>
<td>2-DAA Japan: HCV (GT1b)</td>
<td></td>
</tr>
<tr>
<td>ABT-RTA 408: Solid Tumors</td>
<td>ABBV-085: Solid Tumors</td>
<td>Imbruvica: Graft V Host</td>
<td>Elotuzumab: Multiple Myeloma (TN)</td>
<td>Imbruvica: CLL (R/R combo with B/R)</td>
<td></td>
</tr>
<tr>
<td>ABBV-075: Solid Tumors and Hem Onc</td>
<td>ABBV-085: Solid Tumors</td>
<td><strong>AbbVie partnered asset</strong></td>
<td>Veliparib: NSCLC (Squamous)</td>
<td>Empliciti: Multiple Myeloma (Relapsed/Refractory; U.S. EU)</td>
<td></td>
</tr>
<tr>
<td>ABBV-221: Solid Tumors</td>
<td>ABBV-221: Solid Tumors</td>
<td><strong>AbbVie partnered asset</strong></td>
<td>Veliparib: NSCLC (Non-squamous)</td>
<td>Venclexta: CLL (R/R 17P del; US)</td>
<td></td>
</tr>
<tr>
<td>Imbruvica: Solid Tumors</td>
<td>Imbruvica: Solid Tumors</td>
<td><strong>AbbVie partnered asset</strong></td>
<td>Veliparib: Breast Cancer (Neoadjuvant)</td>
<td>ABBV-399: Solid Tumors</td>
<td></td>
</tr>
<tr>
<td><strong>AbbVie partnered asset</strong></td>
<td>ABBV-399: Solid Tumors</td>
<td><strong>AbbVie partnered asset</strong></td>
<td>Veliparib: Breast Cancer (BRCA)</td>
<td>ABBV-075: Solid Tumors and Hem Onc</td>
<td></td>
</tr>
<tr>
<td><strong>AbbVie partnered asset</strong></td>
<td>ABBV-399: Solid Tumors</td>
<td><strong>AbbVie partnered asset</strong></td>
<td>Veliparib: Ovarian Cancer</td>
<td>ABBV-2222: Cystic Fibrosis</td>
<td></td>
</tr>
<tr>
<td><strong>AbbVie partnered asset</strong></td>
<td>ABBV-399: Solid Tumors</td>
<td><strong>AbbVie partnered asset</strong></td>
<td><strong>AbbVie partnered asset</strong></td>
<td>ABBV-2451: Cystic Fibrosis</td>
<td></td>
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<td><strong>AbbVie partnered asset</strong></td>
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</tbody>
</table>

*AbbVie partnered asset*
Our Near-Term Growth Assets Are Significantly De-risked

• **8 products** currently in pivotal development or recently launched

• Potential for **>20 new drug** or new indication approvals by the end of 2020, including **seven approvals** expected to contribute in 2016 and beyond

• Recent data readouts continue to de-risk key assets, increasing our level of confidence in **high likelihood** of clinical, regulatory and commercial success
We’ll See Continued Pipeline Advancement in the Years Ahead

<table>
<thead>
<tr>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>(RESOLUTE-2)</td>
<td></td>
<td>(PCYC-1126)</td>
</tr>
<tr>
<td>P3, 1L CLL (approval)</td>
<td></td>
<td>P3, 1L CLL</td>
</tr>
<tr>
<td>(RELIOS)</td>
<td></td>
<td>(PCYC-1127)</td>
</tr>
<tr>
<td>P3, 1L MDL</td>
<td></td>
<td>P2, 1L MM</td>
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<tr>
<td></td>
<td></td>
<td>(TELENE)</td>
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<tr>
<td>P3, 1L MDL</td>
<td></td>
<td>P3, 1L MDL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(RESONATE-2)</td>
</tr>
<tr>
<td>P1, 1L GBM</td>
<td></td>
<td>P3, 1L (label expansion, +8R)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(HELIOS)</td>
</tr>
<tr>
<td>P1, 1L CLL, 6L (R+, +E, +8R)</td>
<td></td>
<td>P2, 1L CLL &amp; SLL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(CAVALI)</td>
</tr>
<tr>
<td>P1, 1L CLL &amp; NHL</td>
<td></td>
<td>P2, 1L DLBCL *(RCHOP vs RCHOP)</td>
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<tr>
<td></td>
<td></td>
<td>(PHOENIX)</td>
</tr>
<tr>
<td>P1, r/r MM</td>
<td></td>
<td>P2, 1L DLBCL</td>
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<tr>
<td></td>
<td></td>
<td>(Illuminate)</td>
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<tr>
<td>P2, r/r MM</td>
<td></td>
<td>P3, 1L CLL/SLL (+G vs CG)</td>
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<tr>
<td></td>
<td></td>
<td>(PCYC1127)</td>
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<tr>
<td>P1, r/r MM</td>
<td></td>
<td>P3, 1L GBM</td>
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<tr>
<td></td>
<td></td>
<td>(INTELLANCE-2)</td>
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<tr>
<td>P1, 1L GBM</td>
<td></td>
<td>P2, 2L GBM</td>
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<td></td>
<td></td>
<td>(INTELLANCE-J)</td>
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<tr>
<td>P1, 2L GBM</td>
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<td>P1/2, GBM</td>
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<tr>
<td></td>
<td></td>
<td>(VELA)</td>
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<tr>
<td>P1, 1L GBM</td>
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<td>P3, 1L NSCLC SQ</td>
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<td></td>
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<td>(VESTA)</td>
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<td>P1, 1L NSCLC NSQ</td>
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<td>P3, neo-adjuvant TNBC</td>
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<td></td>
<td>(BRIGHTNESS)</td>
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<tr>
<td>P3, 1L BRCA Breast</td>
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<td>P3, 1L GBM</td>
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<td></td>
<td></td>
<td>(BROCADE3)</td>
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<td></td>
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<td>(PCYC-1137)</td>
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<td></td>
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<td>P2/3, Pancreas</td>
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<td></td>
<td></td>
<td>(PCYC-1138)</td>
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<td></td>
<td></td>
<td>P2, r/r MM</td>
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# What We Will Cover Today

## Oncology Overview
- **Stemcentrx**
  - Speaker: Scott Dylla, Ph.D.
- **Imbruvica**
  - Speaker: Danelle James, M.D., M.S.
- **Venclexta, Veliparib and ABT-414**
  - Speaker: Gary Gordon, M.D., Ph.D.
- **Discovery and Early Development**
  - Speaker: Thomas Hudson, M.D.

## Immunology
- **ABT-494 and Risankizumab**
  - Speaker: Shao-Lee Lin, M.D., Ph.D.
- **Highlights from Immunology Discovery**
  - Speaker: Lisa Olson, Ph.D.

## HCV
- **HCV**
  - Speaker: Shao-Lee Lin, M.D., Ph.D.

## Elagolix
- **Elagolix**
  - Speaker: Shao-Lee Lin, M.D., Ph.D.

## Neuroscience
- **Zinbryta and ABT-555**
  - Speaker: Laura Gault, M.D., Ph.D.
- **Alzheimer’s Disease and the Foundational Neuroscience Center**
  - Speaker: Eric Karran, Ph.D.
BUILDING ONCOLOGY LEADERSHIP

- Oncology
- Immunology
- HCV
- Elagolix
- Neuroscience
Oncology Overview

Michael Severino, M.D.
Despite Considerable Progress in Recent Years, Significant Unmet Medical Need Exists in Oncology

**Sources:** American Cancer Society, SEER, Kantar Health.

- Growing patient population, ~21MM by 2030
  - ~ 40% life-time risk of being diagnosed with cancer
- ~30% of all patients diagnosed with cancer die within five years
- ~80% of patients with metastatic tumors die within five years
Our Oncology Efforts Are Guided by Three Strategic Imperatives

1. **Grow** our strong position in hematologic malignancies

2. **Establish** a foundation in solid tumors

3. **Leverage** our strength in immunology to develop next-generation immuno-oncology therapies
Our Oncology Efforts Are Guided by Three Strategic Imperatives

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Imbruvica and Venclexta Provide a Strong Foundation in Hematologic Malignancies

These agents have the potential to transform the treatment of CLL, MCL and Waldenström’s macroglobulinemia

- Monotherapy
- Combination with existing therapies
- Novel/novel combinations

Clinical data show strong signs of activity across a wide range of other hematologic malignancies

- **Imbruvica**
  - NHL
  - Multiple myeloma
  - GVHD

- **Venclexta**
  - NHL
  - Multiple myeloma
  - AML

Our early pipeline provides additional opportunities based on our work in apoptosis and epigenetics
Our Oncology Efforts Are Guided by Three Strategic Imperatives

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3. Leverage our strength in immunology to develop next-generation immuno-oncology therapies
Building a Foundation in Solid Tumors

Our efforts are based on:

**Apoptosis**

1. **Extrinsic Apoptosis Pathway**
   - Death Receptors
   - Mitochondria
   - Apoptosome
   - Apoptosis

2. **Intrinsic Apoptosis Pathway**
   - Pre-apoptotic BCL-2 family members
   - Anti-apoptotic BCL-2 family members
   - Apoptosis

**Epigenetics**

1. **DNA Damage Repair**
   - PARP Inhibitor
   - Cell Survival
   - Cancer Cell Death

2. **Emerging Areas in Cancer Biology**
   - Chromatin fiber
   - Histone binding protein
We Are Also Exploring New Technologies Designed to Extend our Reach

- Target Identification
- Antibody Engineering
- Linker Chemistry
- Toxin Technology
- Clinical Translation

ADCs with Novel Warheads

- We are developing novel warheads that leverage our experience in apoptosis, tumor energetics, and other areas
- Potent anti-tumor activity demonstrated in a range of tumor models
- ADC approach circumvents mechanism-based toxicity of novel warheads in preclinical models
Our Bispecific Platform has the Potential to Create Novel Biology

**Bispecific ADCs**

- Unique properties of bispecific ADCs can be used for multiple approaches:
  - Targeting two epitopes on single cancer target
  - Targeting two distinct antigens on the same tumor cell
  - Targeting two antigens on different cells within the tumor microenvironment

**Bispecific Shows Enhanced Internalization in Cancer Cells**

- Antibody to epitope 1
- Antibody to epitope 2
- Bispecific to epitopes 1 & 2

**Bispecifics Can Direct Cellular Activation**

- Different formats can be constructed to:
  - Direct protein-protein interactions by targeting different proteins on the same cell
  - Activate cells in a specific setting by targeting two targets on different cell types

**‘cis’**

**‘trans’**
Our Oncology Efforts Are Guided by Three Strategic Imperatives

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AbbVie’s Immuno-Oncology Strategy Leverages our Strengths in Immunology and Protein Sciences

**Generation and Regulation of Antitumor Immunity**

**AbbVie Approaches**

- **Emerging Areas:** Suppressive Tumor Microenvironment
e.g., anti-GARP antibodies, CD40 agonists

- **Emerging Biology:** T Cell Agonists & T Cell Activation
e.g., OX40 agonists

- **Disruptive Technologies:**
  T Cell Receptor-based Biologics & Cell-based Therapies
e.g., soluble TCR bispecifics

**Enabling Collaborations**
An Early Immuno-Oncology Program Targets a Central Pathway of the Immune System: CD40

- Tumor microenvironment blunts the immune response
- Activation of CD40 restores cell-mediated immune responses
- However, systemic toxicity has been a challenge for the clinical development of CD40 agonists

AbbVie’s bispecific platform has the potential to deliver tumor-specific immune activation
AbbVie’s Bispecific Platform Can Be Used to Create a Wide Range of Formats, Leading to New Biology
Different Formats Allow for Differing Mechanisms of Action
We Created More than 50 Unique Structures to Engineer a Molecule with the Right Properties

In Vitro Testing of CD40/Tumor Antigen Bispecific Formats
>50 bispecific constructs prepared and screened

<table>
<thead>
<tr>
<th>CD40/tumor antigen Bispecifics</th>
<th>CD40 Binding</th>
<th>Tumor Antigen Binding</th>
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Multiple bispecific formats tested...
...but only the ABBV-428 structure leads to conditional activation

**ABBV-428**: AbbVie’s lead CD40 Bispecific
**Our Lead CD40 Candidate Inhibits Tumor Growth Without Toxicity in Preclinical Models**

**Efficacy**

![Tumor Volume (mm3) vs Days Post Inoculation](image)

- Preclinical Breast Cancer Model
- Conditional activation of CD40 by bispecific leads to efficacy
- No treatment Anti-Tumor
- Anti-CD40
- CD40 Bispecific

**Toxicity**

- Liver Toxicity (ALT)
  - No Treatment: -
  - Anti-CD40: +
  - CD40 Bispecific: -
- Systemic Inflammatory Response
  - No Treatment: -
  - Anti-CD40: +
  - CD40 Bispecific: -

**Program is on track for human studies in 2016**

- Bispecific avoids toxicity of systemic CD40 agents
Our Efforts Have Produced a Strong Oncology Pipeline
# AbbVie's Oncology Pipeline

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** Registration-enabling studies

** Hematologic malignancies
** Solid tumors
** Heme & solid
# AbbVie Oncology Pipeline with Stemcentrx

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- **Hematologic malignancies**
- **Solid tumors**
- **Heme & solid**
- **Stemcentrx**

* Partnered with Pfizer (PF06647263, PF06647020)
** Registration-enabling studies
Stemcentrx

Brian Slingerland
Scott Dylla, Ph.D.
Our Mission

Discover and Develop Cancer Therapies That Cure and Significantly Improve Survival
The Cancer Stem Cell (CSC) Paradigm

1. Only stem cells accumulate compounding mutations
2. Only CSC are capable of fueling continued tumor growth
The Cancer Stem Cell (CSC) Paradigm

1. Only stem cells accumulate compounding mutations
2. Only CSC are capable of fueling continued tumor growth
3. CSC are minimally impacted by current therapeutic regimens

**Traditional Approach**

- Treatment does not target "cancer stem cells"
- Tumor is reduced in size, but eventually relapses driven by "cancer stem cells"

**Stemcentrx**

- Treatment specifically targets "cancer stem cells"
- Tumor progressively exhausts its growth potential
• Founded in 2008 in South San Francisco, CA
• Core research platforms for novel target discovery
  – 706 patient-derived xenograft tumor bank across major cancer subtypes
Focus on Solid Tumor Disease Subtypes

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<tr>
<td>Ovarian</td>
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<td><strong>Total</strong></td>
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- Small Cell Lung Cancer (SCLC)
- NSCLC Adenocarcinoma subtypes (3)
- NSCLC Squamous cell subtypes (2)
- NSCLC Large Cell Neuroendocrine
- Carcinoids (typical, atypical)

- Serous
- Papillary Serous
- Endometroid
- MMMT
- Clear Cell
- Mucinous
- Neuroendocrine

- Triple Negative (non-claudin low)
- Triple Negative (claudin low)
- Luminal B
- Luminal A
- Her2+
PDX Are used to Identify Tumorigenic Subpopulations

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<td><strong>Total</strong></td>
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</table>

CD46+ and CD46- subpopulations are used to identify tumorigenic subpopulations in patient tumors. The table lists the number of tumors for various cancer types, and the graph shows the tumorigenicity based on CD46 expression over time post-transplant.

- **CD46+ 8.0%**
- **Tumorigenic** vs. **Non-Tumorigenic**
Stemcentrx Discovers Drug Targets Expressed on CSC
Stemcentrx Discovers Drug Targets Expressed on CSC

- Small Cell Lung Cancer
- Large Cell NSCLC
- Squamous NSCLC
- Triple-Negative Breast
- Colorectal
- Gastric
- Pancreatic
- Ovarian
- Melanoma

Stroma

Progenitor

Non-Tumorigenic (NTG)
Leveraging CSC Identity to Find Targets
Leveraging CSC Identity to Find Targets
Stemcentrx Targets Have Often Been Overlooked

Dots = 1 of 59 Genes
Color = PDX of interest

Cancer Stem Cells
• Founded in 2008 in South San Francisco, CA

• Core research platforms for novel target discovery
  – 706 patient-derived xenograft tumor bank across major cancer subtypes
  – Proteomic and genetic platforms for cancer stem cell and target identification
  – Bioinformatics software and IT tools for target discovery and validation

• Fully integrated company with 180+ employees
  – 110+ in target/biomarker discovery and validation
  – GMP antibody, chemistry and ADC manufacturing on-site (+ process sciences, QC, QA, regulatory)
  – 5 drugs targeting novel antigens in clinical trials (SCLC, Triple-Negative Breast, Ovarian, NSCLC)
  – Pipeline of CSC-associated targets in NSCLC, pancreatic, colorectal, gastric, melanoma, AML
Stemcentrx Drugs in Human Clinical Trials

1. DLL3-PBD ADC
   Rovalpituzumab Tesirine (Rova-T™)

2. PTK7-Auristatin ADC
   (PF-06647020)

3. EFNA4-Calicheamicin ADC
   (PF-06647263)

4. SC-002 (Undisclosed Target)

5. SC-003 (Undisclosed Target)
**Lung Cancer Statistics**

**Estimated 2013 U.S. cancer deaths**
By selected types of cancer

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Deaths 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>159,480</td>
</tr>
<tr>
<td>Colon</td>
<td>50,830</td>
</tr>
<tr>
<td>Breast</td>
<td>40,030</td>
</tr>
<tr>
<td>Pancreas</td>
<td>38,460</td>
</tr>
<tr>
<td>Prostate</td>
<td>29,720</td>
</tr>
<tr>
<td>Leukemia</td>
<td>23,720</td>
</tr>
<tr>
<td>Brain/nervous system</td>
<td>14,080</td>
</tr>
</tbody>
</table>

Source: American Cancer Society, National Cancer Institute
Graphic: Chicago Tribune

**American Cancer Society**

<table>
<thead>
<tr>
<th></th>
<th>Newly Diagnosed – US, EU, Japan</th>
<th>Newly Diagnosed – Worldwide</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Lung Cancer</td>
<td>540,000</td>
<td>1,825,000</td>
</tr>
<tr>
<td>SCLC</td>
<td>81,000</td>
<td>274,000</td>
</tr>
</tbody>
</table>

**5-Year Survival**

<table>
<thead>
<tr>
<th></th>
<th>All Lung Cancer</th>
<th>SCLC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Carcinoid 5%
Large Cell NEC 10%
SCLC 15%
NSCLC-Squamous 30%
NSCLC-Adenocarcinoma 40%
Small Cell Lung Cancer

1st Line SCLC: Carbo/Cisplatin + Etoposide
~70% Response Rate
92% G3+ Toxicities

Duration of Response
~3 months

2nd Line SCLC: Topotecan
7-17% Response Rate
89% G3+ Toxicities

3rd Line SCLC
No Approved Drug

Rova-T Phase 1 Trial = 74 SCLC Patients
ASCL1 and Notch Inhibition Promote Neuroendocrine Cell Fates

- **Normal Lung Stem Cell**
- **Common Progenitor Cell**
  - ASCL1
  - Notch
- **Committed Progenitor Cells**
- **Mature Epithelial Cell**
- **Mature Neuroendocrine Cell**

References:
- Morimoto (2012) *Development* **139**:4365
RB1 Mutations in the Lung Induce Neuroendocrine Tumors

Delta-Like Protein 3 (DLL3) Is Overexpressed in High Grade Pulmonary Neuroendocrine Tumor-Initiating Cells
DLL3 Is a Dominant Inhibitor of Notch Signaling

- Normally expressed during development and localized to Golgi intracellular compartment
- Interacts with and inhibits Notch1 localization to the cell surface
- Mediates DLL1 intracellular retention in concert with LFNG, inhibiting Notch activation in trans


DLL3 Elevations May Drive Neuroendocrine Tumorigenesis

- Precancerous Lung Stem Cell
  - p53/−
- p53/− RB1/− Cancer Stem Cell
  - ASCL1
  - DLL3
  - Notch
- Committed Progenitor Cells
- Mature Epithelial Cell
- Tumor Progenitor Cell
- Mature Neuroendocrine Tumor Cell

Graph:
- Pearson $r^2 = 0.66$
- $P < 0.0001$
- SCLC
- LCNEC
Notch Receptor Mutations May Contribute to Tumorigenesis in a Subset of SCLC

DLL3 Elevations May Drive Neuroendocrine Tumorigenesis

Precancerous Lung Stem Cell

\[ p53^{-/-} \]

Cancer Stem Cell

\[ p53^{-/-} RB1^{-/-} \]

Tumor Progenitor Cell

Mature Neuroendocrine Tumor Cell

DLL3 Elevations ~80%

Notch signalling/ neuroendocrine differentiation

- NOTCH 25%
- DLK1
- HES1/HEY1
- ASCL1

Neuroendocrine markers (CHGA, SYP)
DLL3 Is on the Surface of SCLC Tumor Cells

DLL3 Is Normally Retained in the Golgi

DLL3 Reaches the Cell Surface When Overexpressed in SCLC

\( \Rightarrow \) = DLL3
Rovalpituzumab Tesirine (Rova-T™; SC16LD6.5)

Drug-to-Antibody Ratio (DAR) = 2
Rova-T Leverages Surface DLL3 to Deliver PBD Toxin

\[ \text{ DLL3 } = \text{ DLL3} \]

Rova-T (SC16LD6.5)
Rova-T Leverages Surface DLL3 to Deliver PBD Toxin

\[ \text{DLL3} \]

Rova-T (SC16LD6.5)
PBD Dimer Toxin Mediates Tumor Cell Killing

\[ \text{DLL3} \]

\[ \text{Rova-T (SC16LD6.5)} \]
Stemcentrx ADCs Eliminate Large Solid PDX Tumors

n = 5 mice/group
Rova-T Is Efficacious in DLL3+ SCLC PDX Tumors
Rova-TEliminatesTumor-Initiating Cells; Chemo Does Not
Rova-T vs. SOC in SCLC & LCNEC PDX Tumors

<table>
<thead>
<tr>
<th></th>
<th>Cisplatin/Etoposide (5 mpk x 1, 8 mpk Qdx3)</th>
<th>Single Agent Rova-T (1 mpk q4d x 3)</th>
<th>DLL3 Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%TGI</td>
<td>TTP (days)</td>
<td>%TGI</td>
</tr>
<tr>
<td>LU102</td>
<td>97%</td>
<td>28</td>
<td>100%</td>
</tr>
<tr>
<td>LU95</td>
<td>56%</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td>LU117</td>
<td>98%</td>
<td>21</td>
<td>100%</td>
</tr>
<tr>
<td>LU149</td>
<td>90%</td>
<td>18</td>
<td>100%</td>
</tr>
<tr>
<td>LU129</td>
<td>87%</td>
<td>52</td>
<td>100%</td>
</tr>
<tr>
<td>LU111</td>
<td>84%</td>
<td>22</td>
<td>100%</td>
</tr>
<tr>
<td>LU37</td>
<td>60%</td>
<td>4</td>
<td>100%</td>
</tr>
<tr>
<td>LU64</td>
<td>78%</td>
<td>12</td>
<td>100%</td>
</tr>
<tr>
<td>LU124</td>
<td>83%</td>
<td>19</td>
<td>88%</td>
</tr>
<tr>
<td>LU73</td>
<td>85%</td>
<td>28</td>
<td>75%</td>
</tr>
<tr>
<td>LU80</td>
<td>75%</td>
<td>15</td>
<td>75%</td>
</tr>
<tr>
<td>LU86</td>
<td>26%</td>
<td>0</td>
<td>95%</td>
</tr>
<tr>
<td>LU100</td>
<td>100%</td>
<td>63</td>
<td>0%</td>
</tr>
<tr>
<td>Avg</td>
<td>78%</td>
<td>22</td>
<td>87%</td>
</tr>
</tbody>
</table>

Number of XY Pairs: 13

<table>
<thead>
<tr>
<th>Number of XY Pairs</th>
<th>Pearson r</th>
<th>95% confidence interval</th>
<th>P value (two-tailed)</th>
<th>P value summary</th>
<th>Is the correlation significant? (alpha=0.05)</th>
<th>R square</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>0.7296</td>
<td>0.2985 to 0.9134</td>
<td>0.0046</td>
<td>**</td>
<td>Yes</td>
<td>0.5323</td>
</tr>
</tbody>
</table>

Number of XY Pairs: 13

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<thead>
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<th>R square</th>
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<tbody>
<tr>
<td>13</td>
<td>0.7296</td>
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<td>0.0046</td>
<td>**</td>
<td>Yes</td>
<td>0.5323</td>
</tr>
</tbody>
</table>
Rova-T: Best Response Data in Evaluable SCLC Patients
0.2 mg/kg q3w and 0.3 mg/kg q6w cohorts (n=53)

% Change in Tumor Diameter (RECIST)

Expression   % of SCLC
High         71%
Intermediate 11%
Low          18%
Unknown

Presented at ESMO/ECC’15 - Vienna
Rova-T: Best Response Data in Evaluable DLL3hi Patients
0.2 mg/kg q3w and 0.3 mg/kg q6w cohorts (n=27)

• 44% ORR (CR/PR)
• 78% CBR (CR/PR/SD)

DLL3+ = H-score ≥ 180 on scale of 300

% Change in Tumor Diameter
(RECIST)

Presented at ESMO/ECC’15 - Vienna

^3 Pts whose target lesions were noted as SD or better by RECIST had clinical progression
Efficacy in the 3\textsuperscript{rd} Line Setting, Where No Standard of Care Exists

- \textbf{2\textsuperscript{nd} Line}: 44% ORR, 81% CBR (Topotecan = 7-17%)
- \textbf{3\textsuperscript{rd} Line}: 45% ORR, 73% CBR (No Approved Drug)

\textit{Presented at ESMO/ECC'15 - Vienna}

\textbf{DDL3+} = H-score $\geq 180$ on scale of 300
3rd Line Case Study #1: 54 Year Old Male

Dose #1
0.3 mpk

Dose #2
0.3 mpk

Dose #3
0.3 mpk

PR
-37%

PR
-49%

PR
-51%,
PET Scan
SUV Negative

PR
-54%

Residual Tumor
Resected
(Adrenalectomy)
Residual Metastatic Tumor Mass After Rova-T

“Upon pathology review, there are only isolated clusters of viable tumor with an estimated >95% treatment effect.”
3rd Line Case Study #1: 54 Year Old Male

- **Dose #1**: 0.3 mpk
- **Dose #2**: 0.3 mpk
- **Dose #3**: 0.3 mpk

**Residual Tumor Resected** (Adrenalectomy)

- **Day 556** (3/3/16)

**PR -37%**

**PR -49%**

**PR -51%, PET Scan SUV Negative**

**PR -54%**

**Starting Tumor Diameter (RECIST)**

0 60 120 180 240 300 360 420 480 540 600

0 40 60 80 100

**Not for Promotional Use**
3rd Line Case Study #2: 60 Year Old Female

Doses #1 & 2
0.2 mg/kg

Dose #3
0.1 mg/kg

PET/CT Scans
(No abnormal SUV)

SD
+13%

Day 665
(4/18/16)
Rova-T Pivotal Study in 3rd Line SCLC

<table>
<thead>
<tr>
<th>Historical (n = 120) Simos’14</th>
<th>Rova-T DLL3^Hi (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>18%</td>
</tr>
<tr>
<td>CBR</td>
<td>51%</td>
</tr>
<tr>
<td>mOS (Mo)</td>
<td>4.7</td>
</tr>
<tr>
<td>1 Year OS</td>
<td>12%</td>
</tr>
</tbody>
</table>

1st Line SCLC: Carbo/Cisplatin + Etoposide
~70% Response Rate
91% G3+ Toxicities

Duration of Response
~ 3 months

2nd Line SCLC: Topotecan
17% Response Rate
89% G3+ Toxicities

3rd Line SCLC
No Approved Drug

TRINITY

AbbVie
TRINITY: A Phase II Clinical Trial in Small Cell Lung Cancer

The study of Rovalpituzumab Tesirine as a third-line or later treatment in patients who have relapsed or refractory small cell lung cancer (SCLC).
28 Sites in the U.S. and Europe Currently Enrolling TRINITY
1\textsuperscript{st} Line SCLC Strategy

1\textsuperscript{st} Line SCLC: Carbo/Cisplatin + Etoposide
~70\% Response Rate
91\% G3+ Toxicities

Duration of Response
~ 3 months

2\textsuperscript{nd} Line SCLC: Topotecan
17\% Response Rate
89\% G3+ Toxicities

TRINITY
3\textsuperscript{rd} Line SCLC
No Approved Drug
Additive Activities of ADCs and Checkpoint Inhibitors

<table>
<thead>
<tr>
<th></th>
<th>Nivo (2L+) (n = 80)</th>
<th>Nivo+Ipi (2L+) (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>13%</td>
<td>31%</td>
</tr>
<tr>
<td>CBR</td>
<td>29%</td>
<td>53%</td>
</tr>
<tr>
<td>mOS (Mo)</td>
<td>*3.6</td>
<td>*7.8</td>
</tr>
</tbody>
</table>

*Data to be updated Saturday morning (ASCO’16)
Other Indications for Rova-T
DLL3 Is Expressed in Extrapulmonary Neuroendocrine Tumors

Metastatic Melanoma
NE Prostate
NE Pancreatic

NE Colorectal
Medullary Thyroid
Glioblastoma

Abstract 11611, Poster Board: #308 – Tumor Biology, Hall A, 1-4 PM, Jun 6th
Rova-T Clinical Development

2016

- 3rd Line DLL3+ SCLC Single-Arm Pivotal (TRINITY)
- All SCLC DLL3 +/-
- 1st Line SCLC Phase I
- Basket Study (8 arms) Phase I
- Checkpoint Inhibitor Combo Phase I
- Japan Phase I

2017

- Pre-pivotal 1L
- Indication Expansion
- 1L Rx Selection
- Confirmatory
- CA in JP

2018

- Purpose
  - AA in US; CA in EU
  - QT; DLL3 agnostic
  - Pre-pivotal 1L
  - Indication Expansion
  - 1L Rx Selection
  - Confirmatory
  - CA in JP
Clinical Drug #2: αPTK7-Auristatin
(PF-06647020)
Non-Small Cell Lung, Breast and Ovarian Cancer
Preclinical Efficacy with PTK7-ADC

- **TNBC BR22**
  - Tumor Volume (mm$^3$)
  - Days Post-Randomization

- **NSCLC LU176**
  - Tumor Volume (mm$^3$)
  - Days Post-Randomization

- **Ovarian OV55**
  - Tumor Volume (mm$^3$)
  - Days from Randomization

- PTK7-ADC, 3 mpk
- PTK7-ADC, 1 mpk
- Standard of care
- Vehicle
A Phase I Study of PF-06647020, an Antibody-Drug Conjugate Targeting Protein Kinase 7 (PTK7), in Patients with Advanced Solid Tumors

Tolcher AW¹, Calvo E², Doger B², Maitland ML³, Gibson B⁴, Xuan D⁴, Joh T⁴, Jackson-Fisher A⁵, Damelin M⁵, Barton J⁴, Xin X⁴, Sachdev JC⁶

¹South Texas Accelerated Research Therapeutics, ²South Texas Accelerated Research Therapeutics Madrid, ³University of Chicago Medicine, ⁴Pfizer Biotechnology Clinical Development, La Jolla, CA, ⁵Pfizer Oncology Research Unit, ⁶TGen – Virginia G. Piper Cancer Center at Scottsdale Healthcare
PF-06647020 Is Efficacious as a Single Agent in Humans

Data cut-off as of July 31, 2015

Tumor Size Change Data
(Number of Subjects = 18)

Breast cancer ≥ 2.1 mg/kg
Ovarian cancer ≥ 2.1 mg/kg

Tolcher AW et al. ESMO’15 - Vienna
Confirmed Complete Response in Ovarian Cancer Patient

- 52 yo woman with advanced ovarian cancer (serous papillary carcinoma) previously treated with multiple lines of chemotherapies including carboplatin/taxol, cisplatin/gemcitabine, carboplatin/pegylated liposomal doxorubicin, and nab paclitaxel (the last immediate therapy) → Progressive Disease
- Patient received PF-06647020 at 2.1 mg/kg IV, q3w
- The CR was confirmed, and she has been in the study for 6 months

Tolcher AW et al. ESMO’15 - Vienna
Confirmed Partial Response in a Patient with TNBC

- 49 yo woman with advanced TNBC previously treated with multiple lines of chemotherapies and investigational agents (the last immediate therapy) → Stable Disease
- Patient received PF-06647020 at 2.1 mg/kg IV, q3w
- The PR was confirmed, and treatment duration was 6 months

Tolcher AW et al. ESMO’15 - Vienna
<table>
<thead>
<tr>
<th></th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Any AEs</td>
<td>5 (25.0)</td>
<td>6 (30.0)</td>
<td>4 (20.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>15 (75.0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4 (20.0)</td>
<td>2 (10.0)</td>
<td>1 (5.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>Headache</td>
<td>0 (0.0)</td>
<td>6 (30.0)</td>
<td>1 (5.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (25.0)</td>
<td>2 (10.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>2 (10.0)</td>
<td>3 (15.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (5.0)</td>
<td>4 (20.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>Chills</td>
<td>3 (15.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (10.0)</td>
<td>1 (5.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>0 (0.0)</td>
<td>1 (5.0)</td>
<td>2 (10.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>2 (10.0)</td>
<td>1 (5.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Rash maculo-pap</td>
<td>2 (10.0)</td>
<td>1 (5.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Hypomagnesaemia</td>
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<td>0 (0.0)</td>
<td>0 (0.0)</td>
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<td>2 (10.0)</td>
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<tr>
<td>Myalgia</td>
<td>1 (5.0)</td>
<td>1 (5.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>2 (10.0)</td>
</tr>
</tbody>
</table>

Data cut-off as of July 31, 2015

Tolcher AW et al.
ESMO'15 - Vienna
Clinical Drug #3: αEFNA4-Calicheamicin (PF-06647263)

Triple-Negative Breast and Ovarian Cancer
90% of TNBC PDX Express and Respond to EFNA4-ADC

PDX-Breast 5
(High Expresser)

<table>
<thead>
<tr>
<th>Tumor (Subtype)</th>
<th>% TGI (0.3 mpk)</th>
<th>TTP (0.3 mpk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR5 (Basal)</td>
<td>100%</td>
<td>172+</td>
</tr>
<tr>
<td>BR31 (Basal)</td>
<td>100%</td>
<td>147</td>
</tr>
<tr>
<td>BR56 (Basal)</td>
<td>98%</td>
<td>63</td>
</tr>
<tr>
<td>BR13 (Bas/Lum)</td>
<td>99%</td>
<td>97</td>
</tr>
<tr>
<td>BR22 (Bas/Lum)</td>
<td>90%</td>
<td>43</td>
</tr>
<tr>
<td>BR25 (Claudin low)</td>
<td>27%</td>
<td>--</td>
</tr>
<tr>
<td>BR64 (Claudin low)</td>
<td>0%</td>
<td>--</td>
</tr>
<tr>
<td>BR17 (Her2+)</td>
<td>0%</td>
<td>--</td>
</tr>
</tbody>
</table>

~90% TNBC

Dosing

Vehicle
IgG Control ADC

1.5 mpk Doxorubicin

n = 5 mice/group

Tumor (Subtype)

Tumor Volume (mm^3)

Days from Randomization

EFNA4-ADC
PF-06647263 Is Efficacious as a Single Agent

Hong DS et al. ASCO 2015 poster
### PF-06647263 Adverse Event Profile

#### Treatment-Emergent AEs (≥ 20%) Q3W

<table>
<thead>
<tr>
<th></th>
<th>All Causality n=17 (%)</th>
<th>Treatment-Related n=17 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Gr</td>
<td>Gr 3*</td>
</tr>
<tr>
<td>Fatigue</td>
<td>13 (77)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>12 (71)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (65)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>8 (47)</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>8 (47)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>7 (41)</td>
<td>0</td>
</tr>
<tr>
<td>Skin hyperpigmentation</td>
<td>7 (41)</td>
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<tr>
<td>Mucosal inflammation</td>
<td>6 (35)</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Vomiting</td>
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<td>1 (6)</td>
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<tr>
<td>Back pain</td>
<td>5 (29)</td>
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<tr>
<td>Constipation</td>
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<tr>
<td>Diarrhea</td>
<td>5 (29)</td>
<td>1 (6)</td>
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<tr>
<td>Dry mouth</td>
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<tr>
<td>Oedema Peripheral</td>
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<tr>
<td>Pyrexia</td>
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<td>Stomatitis</td>
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<td>1 (6)</td>
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<tr>
<td>Headache</td>
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<tr>
<td>Hypomagnesemia</td>
<td>4 (24)</td>
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</tr>
<tr>
<td>Rash</td>
<td>4 (24)</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

* No Gr 4-5

Other ≥Gr 3 AEs [Treatment-Related]:
- Gr 3 (all n=1): [anaemia, blood bilirubin increased, platelet count decreased, AST increased]
- Gr 4: None
- Gr 5 (n=1): death cause undetermined

#### Treatment-Emergent AEs (≥ 20%) QW

<table>
<thead>
<tr>
<th></th>
<th>All Causality n=13 (%)</th>
<th>Treatment-Related n=13 (%)</th>
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<tr>
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<td>All Gr</td>
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<tr>
<td>Nausea</td>
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<tr>
<td>Decreased appetite</td>
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<td>1 (7)</td>
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<td>Mucosal inflammation</td>
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<tr>
<td>Constipation</td>
<td>3 (23)</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (23)</td>
<td>0</td>
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</tbody>
</table>

* No Gr 4-5

Other ≥Gr 3 AEs [Treatment-Related]:
- Gr 3 (all n=1): [pyrexia, pain in extremity, hypotension, [dehydration, asthenia]]
## Stemcentrx Coverage of Major Cancers

<table>
<thead>
<tr>
<th>Target</th>
<th>SCLC</th>
<th>TNBC</th>
<th>OV</th>
<th>MEL</th>
<th>NSCLC</th>
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<tbody>
<tr>
<td>DLL3</td>
<td>Stemcentrx</td>
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<tr>
<td>SC-003</td>
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<td></td>
<td>Stemcentrx</td>
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<tr>
<td>Target</td>
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<td>TNBC</td>
<td>OV</td>
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<td>IND # 9</td>
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<tr>
<td>IND #10</td>
<td></td>
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</table>
Our Vision: Provide Disease-Specific CSC-Targeted Therapies

Patient #1
Target 1
Target 1 ADC

Patient #2
Target 2
Target 2 ADC
Summary

- 3 of 3 first clinical drugs showing single-agent efficacy at tolerated doses
- All 3 targeting antigens (DLL3, PTK7, EFNA4) never before pursued clinically
- Discovery platform unveiling additional novel targets (ADC, CAR-T/NK/TCR, SM)
- 2016 Milestones
  - TRINITY pivotal study initiated
    - Continue to ensure rapid enrollment
  - Initiate 1st line SCLC induction studies for regimen selection
  - Initiate 1st line SCLC maintenance confirmatory study by 4Q’16/1Q’17
  - Initiate neuroendocrine basket study
  - Initiate checkpoint inhibitor combo studies
A new approach to treating cancer
Imbruvica

Danelle James, M.D., M.S.
Despite Efficacy of Current Standard of Care, Unmet Need Remains in CLL and NHL

- **B-cell NHL**
- **New Cases and Deaths, U.S., 2016**
  - Incidence: 72,580
  - Deaths: 20,150

Cancer Facts and Figures 2016

From Target Validation to Front-line Indication: 
*Rapid Development of the First Inhibitor of Bruton Tyrosine Kinase (BTK), Ibrutinib*

1952
Colonel Bruton described a genetic disorder, agammaglobulinemia

1993
BTK gene was cloned and characterized

2009
First human treated with ibrutinib

2005
First synthesis of ibrutinib (PCI-32765)

2005
NDA submitted for two R/R B-cell malignancy indications: MCL & CLL
Three Breakthrough Therapy Designations Received

2010

2013
Approved for MCL patients who received at least 1 prior therapy

2013
CLL & MCL top-line data published in NEJM

2014
Approved for CLL patients who received at least 1 prior therapy

2014
Approved for CLL patients with deletion 17p

2014
RESONATE™ Data published in NEJM

2015
Approved for WM patients

2015
sNDA Treatment Naïve submitted
Oct 2015

2016
FDA Approval in SLL
May 2016

Mar 2016
FDA approval for front-line. Extremely rapid development of First-in-Class BTK Inhibitor

Dec 2015
RESONATE-2 Data published in NEJM

Jan 2015
Treon paper on Waldenström’s published in NEJM

2014
Approved for CLL patients with deletion 17p

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BTK gene was cloned and characterized

1952
Colonel Bruton described a genetic disorder, agammaglobulinemia
# Imbruvica (ibrutinib) Has the Potential to Broadly Transform the Management of Treatment-Naïve CLL/SLL

<table>
<thead>
<tr>
<th>Study</th>
<th>Age ≥ 65</th>
<th>Age &lt; 70</th>
<th>Age ≥ 65 or comorbidities</th>
<th>Watch &amp; Wait</th>
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</thead>
<tbody>
<tr>
<td><strong>Patient Population</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Regimen</strong></td>
<td><strong>Ibr vs Chl</strong></td>
<td><strong>Ibr-Ritux vs FCR</strong></td>
<td><strong>Ibr or Ibr-Ritux vs BR</strong></td>
<td><strong>Ibr vs placebo</strong></td>
</tr>
<tr>
<td><strong>RESONATE-2™ PCYC-1115</strong></td>
<td><strong>UK CLL NCRN &amp; ECOG 1912</strong></td>
<td><strong>Alliance 041202</strong></td>
<td><strong>iLLUMINATE PCYC-1130</strong></td>
<td><strong>CLL 12</strong></td>
</tr>
</tbody>
</table>

NEJM: Imbruvica Front-Line CLL Data (RESONATE-2)

- 91% reduction in risk of progression or death with Imbruvica
- 84% reduction in the risk of death compared to chlorambucil
  - With a median of 28.1 months of follow up and crossover of 41% of chlorambucil patients a statistically significant 54% reduction in risk of death for Imbruvica arm

→ NCCN category 1 for key front-line patient segments in addition to all previously treated segments
→ Full FDA approval for CLL/SLL (all lines of therapy and all genetic subgroups)
→ EMEA review ongoing for first-line indication, positive opinion from CHMP received April 2016

USPI Imbruvica May 2016

NEJM Burger 2016
Studying Imbruvica in a Comprehensive Development Program in Treatment-Naïve CLL/SLL

<table>
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<td><strong>Ibr or Ibr-Ritux vs BR</strong></td>
<td><strong>Ibr-obinutuz vs Chl-obinutuz</strong></td>
<td><strong>Ibr vs placebo</strong></td>
</tr>
</tbody>
</table>

We anticipate data from studies to read out from 2017 - 2019

Rationale: Imbruvica + Venclexta Combination

Strong expression of BCL-2 observed throughout Imbruvica treatment

Leukemia cells from patients treated with Imbruvica are highly sensitive to apoptosis with Venclexta

Serial samples of CLL cells obtained before and 2, 4, or 12 weeks after the start of Imbruvica showed no reduction in BCL-2 protein, and sensitivity to Venclexta


*Rawston EHA 2015
Clinical Evaluation of the Combination of Imbruvica and Venclexta

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Phase</th>
<th>Disease</th>
<th>Treatment Comparison</th>
<th>Patients</th>
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</thead>
<tbody>
<tr>
<td>CLL13 –OBVIOUS Study</td>
<td>Phase 3</td>
<td>TN CLL</td>
<td>Ibr + Ve + Obinutuz vs. Ve + Obinutuz vs. Ve + Ritux vs. FCR/BR</td>
<td>n = 920</td>
</tr>
<tr>
<td>CLL13b</td>
<td>Phase 2</td>
<td>TN del 17p CLL</td>
<td>Ibr + Ve + Obinutuz</td>
<td>n = 60</td>
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<tr>
<td>CLARITY Study</td>
<td>Phase 2</td>
<td>R/R CLL</td>
<td>Ibr + Ve</td>
<td>n = 100</td>
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<tr>
<td>PCYC-1142</td>
<td>Phase 2</td>
<td>TN CLL patients &lt;70yrs</td>
<td>Ibr + Ve</td>
<td>n = 150</td>
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<tr>
<td>OAsIs Study</td>
<td>Phase 1</td>
<td>R/R MCL</td>
<td>Ibr + Obinutuz + Ve</td>
<td>n = 33</td>
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<tr>
<td>AIM Study</td>
<td>Phase 2</td>
<td>TN &amp; R/R MCL</td>
<td>Ibr + Ve</td>
<td>n = 24</td>
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</tbody>
</table>

The Combination of Imbruvica and Venclexta Rapidly Achieves CR in Patients with R/R MCL: Preliminary Results of the Phase 2 AIM Study

**Objective:** to Determine Complete Response Rate

**Patients**
- Median age: 72 y (53-77); median prior Tx: 2 (1-7); high MIPI score: 63%

**Safety**
- Full Venclexta dose (400 mg) reached in all 4 pts who entered ramp-up with no TLS
- Most common AEs (all Gr 1-2): nausea (n=4), diarrhea (2), oral candidiasis (2)

**Efficacy**
- Response after 4-week ibr induction (n=5 evaluable): 2 PR, 2 SD, 1 PD
- Response after 4 mo (n=3 evaluable): 2 CR, 1 PR
  - CR: normalization of PET ± endoscopy, and complete clearance of previous marrow involvement, including flow cytometry at >10^-4 sensitivity

Early experience with Imbruvica + Venclexta shows no unexpected safety signals with promising efficacy

*ASCO abstract 7519, Tam 2016*
# Imbruvica Has Broad Potential Beyond CLL and MCL

<table>
<thead>
<tr>
<th>Molecule &amp; Program / Indication</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<tr>
<td>**Imbruvica (PCI-32765): Bruton’s tyrosine kinase (BTK) inhibitor for Oncology *</td>
<td><img src="image1" alt="Phase 2" /></td>
<td><img src="image2" alt="Phase 3" /></td>
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<tr>
<td>Chronic lymphocytic leukemia</td>
<td><img src="image1" alt="Phase 2" /></td>
<td><img src="image2" alt="Phase 3" /></td>
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<td>Small Lymphocytic Lymphoma</td>
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<td>Mantle cell lymphoma</td>
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<td>Diffuse large B-cell lymphoma</td>
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<td><img src="image2" alt="Phase 3" /></td>
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<tr>
<td>Multiple myeloma</td>
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<tr>
<td><strong>Follicular lymphoma</strong></td>
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<td>Marginal zone</td>
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<td>Waldenström’s macroglobulinemia</td>
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<td>Acute myeloid leukemia</td>
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<tr>
<td><strong>Solid Tumor</strong></td>
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<td><img src="image2" alt="Phase 3" /></td>
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<tr>
<td>PD1/PDL1 combinations in solid tumor and NHL</td>
<td><img src="image1" alt="Phase 2" /></td>
<td><img src="image2" alt="Phase 3" /></td>
<td><img src="image3" alt="Approved" /></td>
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<tr>
<td><strong>Chronic GVHD</strong></td>
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<td><img src="image2" alt="Phase 3" /></td>
<td><img src="image3" alt="Approved" /></td>
</tr>
</tbody>
</table>

*Janssen Biotech: global partnership*
Imbruvica Is Clinically Active in non-Germinal Center B-cell Subtype DLBCL and Can Be Combined with R-CHOP

**Single Agent Imbruvica**

- **ABC DLBCL**
  - CR: 41% (12/29)
  - PR: 5% (1/20)
- **GCB DLBCL**

Overall response and depth of response was significantly better with single-agent ibrutinib in patients with ABC subtype compared to GCB subtype.

*de Vos et al. 2013.*

**Imbruvica + R-CHOP in Treatment-Naïve DLBCL Patients**

- **Efficacy Evaluable Patients (N=22)**
  - **ORR 100%**
    - (91% CR, 9% PR)
  - **4 non-GCB pts**
    - (all CR)
  - **14 GCB pts**
    - (86% CR, 14% PR)

*Younes et al. ASH 2013.*

**Ongoing Phase 3 study, PHOENIX, evaluating Imbruvica in combination with R-CHOP for the first-line treatment of Non-GCB DLBCL in >800 patients**

High Activity of Imbruvica + rituximab for the First-line Treatment of Follicular Lymphoma

Maximum Tumor Reduction

- ORR 82% in all treated patients (49 of 60)
- Median duration of Imbruvica treatment: 12.55 months

Abbreviations: CR, complete response; PR, partial response; SD, stable disease; SPD, sum of the products of the greatest perpendicular diameters

*Response recorded in database is SD; unresolved query

Ongoing pivotal studies in indolent lymphoma to read out 2016–2018
Imbruvica Significantly Enhances the Activity of Chemoimmunotherapy – the Objective of Several Phase 3 Studies

- **HELIOS** the first of three Phase 3 studies in the Imbruvica program Imbruvica-BR
  - Combination data added to USPI and approval of SLL May 2016
- **SELENE**, a fully enrolled Phase 3 study, evaluating Imbruvica+BR vs placebo-BR in previously treated FL and MZL
- **SHINE**, a fully enrolled Phase 3 study, assessing Imbruvica+BR vs placebo-BR as first-line therapy for MCL

**HELIOS CLL/SLL - PFS**

- **Ibrutinib + BR**
  - Median PFS: NR
  - Median follow-up: 17.02 months
- **Placebo + BR**
  - Median PFS: 13.3 mos

**HR: 0.203 (95% CI, 0.15 – 0.28) P < 0.0001**

Median follow-up: 17.02 months

Fraser et al, iwCLL, 2015.
Ongoing Investigation in Solid Tumors

Three ongoing – enrolling company-sponsored clinical trials evaluating Imbruvica in multiple different solid tumors

- Two evaluating Imbruvica in combination with standard of care (chemotherapy or targeted agents)
  - One randomized and one basket study
- One basket study evaluating Imbruvica in combination with checkpoint inhibitor

**Human Pancreatic Adenocarcinoma**

- Prominent phospho-BTK in CD20⁺, CD11b⁺ and CD64⁺ (FcγR1) cells infiltrating human PDAC, but NOT spleen

**Human Spleen**


**Imbruvica Prolongs Survival in Preclinical Models**

- *P = 0.002* for control vs ibritinib
- *P = 0.04* for Gemcitabine vs Gemcitabine + ibritinib

*Daniel Massó-Vallés et al. Cancer Res 2015;75:1675-1681*
Imbruvica, Targeting both B and T Cells Combats the Multifactorial Pathology of cGVHD Leading to Responses in High-Risk Patients

Imbruvica Inhibition:

- Self-reactive B-Cells
- Tfh Cells
- Th17 Cells
- Th2 Cells
- Overproduction of Self-reactive T and B-cells from Donor-Driven Bone Marrow

Self-reactive Antibody Complexes

Deposit Within Healthy Tissues & Blood Vessels

Cytokines

cGVHD immune Pathology

Kill Healthy Cells & Tissues

Clinical Data of Imbruvica in high-risk cGVHD

Best Response per NIH criteria (n=22)

- CR: 55%
- PR: 50%
- NR: 5%

Miklos et al. European Society for Blood and Marrow Transplantation 2016

cGVHD is a common complication of stem cell transplant with substantial morbidity – where there are no approved therapies representing a significant unmet medical need
# Imbruvica: Upcoming Milestones

<table>
<thead>
<tr>
<th>Year</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
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</thead>
<tbody>
<tr>
<td><strong>CLL/SLL</strong></td>
<td>✔️ <em>RESONATE-2</em> 1L CLL (approval) ✔️ <em>HELIOS</em> R/R CLL/SLL (label expansion &amp; SLL approval) +BR</td>
<td></td>
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<tr>
<td><strong>Solid Tumor</strong></td>
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<td><strong>NHL</strong></td>
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<td><strong>MM</strong></td>
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<tr>
<td><strong>cGVHD</strong></td>
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</tbody>
</table>

* Approximate dates. Timing for some studies will be based on event rates and interim analysis triggers.

R= Rituxan; G= Gazyva; BR= bendamustine/Rituxan; CG= chlorambucil/Gazyva; GI= Gazyva/Imbruvica; RCHOP= Rituxan, cyclophosphamide, doxorubicin, vincristine, prednisone; Vel= velcade; Dex= dexamethasone; pom= pomalidomide
Venclexta (venetoclax)

Gary Gordon, M.D., Ph.D.
AbbVie Has Pioneered the Field of BCL-2 Inhibition

Venclexta Mechanism of Action

- Ability to evade apoptosis (programmed cell death) is a hallmark of cancer
- Increased production of BCL-2 proteins is a key mechanism for preventing the apoptotic process from occurring
- Venclexta binds selectively to BCL-2 proteins initiating a cascade of events leading to rapid cell death
Venclexta Is a BCL-2 Selective Inhibitor

**Restoration of apoptosis through BCL-2 Inhibition**

**Cancer Cell Survival**
- **BCL-2**
- **Pro-apoptotic protein**

**Cancer Cell Death**
- **Venclexta**
- **Pro-apoptotic protein**

**BCL-2 overexpression allows cancer cells to evade apoptosis by sequestering pro-apoptotic proteins.**

**Venclexta binds selectively to BCL-2, freeing pro-apoptotic proteins that initiate programmed cell death (apoptosis).**
Venclexta Has Significant Potential Across a Range of Hematologic Malignancies With High Unmet Need

<table>
<thead>
<tr>
<th>Combination (study name)</th>
<th>Indication</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Rituxan (MURANO)</td>
<td>r/r CLL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Gazyva (CLL14) monotherapy</td>
<td>CLL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Rituxan +BR +Gazyva</td>
<td>r/r CLL &amp; SLL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Gazyva/Imbruvica (CLL13)</td>
<td>r/r CLL &amp; CLL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Rituxan/MURANO</td>
<td>r/r CLL after BCRi</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>NHL</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>+R-CHOP vs R-CHOP (CAVALLI) +BR</td>
<td>1L DLBCL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Gazyva/polatuzumab</td>
<td>r/r CLL &amp; r/r NHL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+bortezomib/dex monotherapy</td>
<td>r/r MM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+bortezomib/dex (a)</td>
<td>r/r MM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AML</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+dec / +aza (a) monotherapy</td>
<td>AML</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+dec / +aza +Ara-C</td>
<td>AML</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(a) Starting H2:2016.
* Data to be presented at ASCO.

Supported by three breakthrough therapy designations
Venclexta Has Significant Potential Across a Range of Hematologic Malignancies With High Unmet Need

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<td>+Gazyva (CLL14)</td>
<td>CLL</td>
</tr>
<tr>
<td>monotherapy</td>
<td></td>
</tr>
<tr>
<td>+Rituxan</td>
<td>r/r CLL</td>
</tr>
<tr>
<td>+BR</td>
<td></td>
</tr>
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<td>+Gazyva</td>
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</tr>
<tr>
<td>+Gazyva/Imbruvica (CLL13)</td>
<td></td>
</tr>
<tr>
<td>(a)</td>
<td>1L CLL</td>
</tr>
<tr>
<td><strong>NHL</strong></td>
<td></td>
</tr>
<tr>
<td>+R-CHOP vs R-CHOP (CAVALLI)</td>
<td>1L DLBCL</td>
</tr>
<tr>
<td>+BR</td>
<td>r/r NHL</td>
</tr>
<tr>
<td>monotherapy</td>
<td>r/r CLL &amp; r/r NHL</td>
</tr>
<tr>
<td>+Gazyva/polatuzumab</td>
<td>DLBCL &amp; FL</td>
</tr>
<tr>
<td><strong>MM</strong></td>
<td></td>
</tr>
<tr>
<td>monotherapy</td>
<td>r/r MM</td>
</tr>
<tr>
<td>+bortezomib/dex</td>
<td>r/r MM</td>
</tr>
<tr>
<td>+bortezomib/dex (a)</td>
<td>r/r MM</td>
</tr>
<tr>
<td><strong>AML</strong></td>
<td></td>
</tr>
<tr>
<td>+dec / +aza (a)</td>
<td>AML</td>
</tr>
<tr>
<td>monotherapy</td>
<td>AML</td>
</tr>
<tr>
<td>+dec / +aza</td>
<td>AML</td>
</tr>
<tr>
<td>+Ara-C</td>
<td>AML</td>
</tr>
</tbody>
</table>

(a) Starting H2:2016.

**Supported by three breakthrough therapy designations**
• FDA approved for r/r 17p deletion CLL
• Active in broader CLL population
• Next anticipated indication: combination with rituximab
• Minimal residual disease (MRD) negativity – no detectable CLL cells in the patients’ bone marrow

« Next step: Phase 3 in 1L CLL »

~ RESPONSE RATES IN RELAPSED CLL ~

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Objective response rate (ORR)</th>
<th>Complete responses (CR)</th>
<th>Partial responses (PR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venclexta 17pdel (a)</td>
<td>80%</td>
<td>7%</td>
<td>73%</td>
</tr>
<tr>
<td>Venclexta (b)</td>
<td>79%</td>
<td>20%</td>
<td>59%</td>
</tr>
<tr>
<td>Venclexta + Rituxan (c)</td>
<td>86%</td>
<td>47%</td>
<td>39%</td>
</tr>
</tbody>
</table>

MRD = 3% 
(bone marrow & peripheral blood)

Venclexta 17pdel IIT population, N=49

Davids et al. ASCO 2016 (Abstracts # 7527, 7528).

Update June 6, 8:00-11:30 (Hall A).

(a) Venclexta package insert. (b) Roberts et al, NEJM 2016. (c) Ma et al. ASH 2015.
Venclexta Monotherapy in CLL Patients Who Progress on BCRi Regimens is Highly Effective

**BCRi – inhibitor of B-cell receptor signaling pathway.**

- Progression can be rapid when B receptor pathway inhibitors fail
- Treatment options are limited and prognosis is poor
- Alternatives are required to meet this unmet need

**RESPONSES AT 24 WEEKS ON VENCLEXTA AFTER BCRi**

<table>
<thead>
<tr>
<th></th>
<th>Objective response rate (ORR)</th>
<th>Complete responses (CR)</th>
<th>Partial responses (PR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imbruvica progression (N=38)</td>
<td>61%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Zydelig / CD20 progression (N=10)</td>
<td>50%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Stable disease: 26% and 40% in Imbruvica and Zydelig cohorts, respectively.**

Jones et al. ASCO 2016 (Abstract #7519).  
Update June 6, 1:15-2:45 (E354b).

**Next step: Phase 2 readout in 2017**
Venclexta Has Significant Potential Across a Range of Hematologic Malignancies with High Unmet Need

<table>
<thead>
<tr>
<th>Combination (study name)</th>
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<tbody>
<tr>
<td><strong>CLL</strong></td>
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<td>+Rituxan monotherapy</td>
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</tr>
<tr>
<td>+Rituxan</td>
<td>r/r CLL after BCRi</td>
</tr>
<tr>
<td>+BR</td>
<td>r/r CLL &amp; SLL</td>
</tr>
<tr>
<td>+Gazyva</td>
<td>r/r CLL &amp; CLL</td>
</tr>
<tr>
<td>+Gazyva/imbruvica (CLL13)</td>
<td>1L CLL</td>
</tr>
</tbody>
</table>

| **NHL**                  |            |
| +Rituxan vs BR (CONTRALTO) | r/r FL     |
| +R-CHOP vs R-CHOP (CAVALLI) | 1L DLBCL  |
| +BR                      | r/r NHL    |
| monotherapy              | r/r CLL & r/r NHL |
| +Gazyva/polatuzumab      | DLBCL & FL |

| **MM**                   |            |
| monotherapy              | r/r MM     |
| +bortezomib/dex          | r/r MM     |
| +bortezomib/dex (a)      | r/r MM     |

| **AML**                  |            |
| +dec / +aza (a)          | AML        |
| monotherapy              | AML        |
| +dec / +aza              | AML        |
| +Ara-C                   | AML        |

(a) Starting H2:2016.

Supported by three breakthrough therapy designations
Non-Hodgkin Lymphoma

U.S. Epidemiology

- Incidence: 72,580
- Treated Population:
  - 1L: 69,775
  - 2L: 41,230
  - 3L+: 25,461

- 20,150 deaths annually

Disease

- Median age at diagnosis: 66
- Multiple subtypes: aggressive (DLBCL, MCL) and indolent (FL, CLL/SLL)
- DLBCL 50% cure; FL median PFS 70 months

Standard of Care

- R-CHOP, BR
- Rituxan
- Imbruvica (MCL)

Unmet Needs

- Curative treatment (FL)
- More efficacious therapies for relapsed/refractory aggressive disease (DLBCL)

Sources: American Cancer Society, SEER, Kantar Health.
Venclexta Monotherapy Has Demonstrated Clear Activity in R/R NHL

**OBJECTIVE RESPONSES**

- **Objective response rate (ORR)**
- **Complete responses (CR)**
- **Partial responses (PR)**

<table>
<thead>
<tr>
<th>Disease</th>
<th>N (patients)</th>
<th>ORR (%)</th>
<th>CR (%)</th>
<th>PR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZL</td>
<td>N=3</td>
<td>67%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WM</td>
<td>N=4</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLBCL</td>
<td>N=41</td>
<td>22%</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>FL</td>
<td>N=29</td>
<td>38%</td>
<td>14%</td>
<td>24%</td>
</tr>
<tr>
<td>MCL</td>
<td>N=28</td>
<td>75%</td>
<td>21%</td>
<td>54%</td>
</tr>
<tr>
<td>All patients</td>
<td>N=106</td>
<td>44%</td>
<td>13%</td>
<td>31%</td>
</tr>
</tbody>
</table>

Gerecitano et al. ASH 2015.

« **Next step: Phase 2 readouts (1L DLBCL, CAVALLI* and r/r FL, CONTRALTO) in 2017 »

* Zelenz et al. ASCO 2016 (Abstract #7566). **Update June 6, 8:00-11:30 (Hall A).
Multiple Myeloma

U.S. Epidemiology

Incidence: 30,330
treated population: 18,444
3L+: 13,611
2L: 9,791
1L: 18,444
- 12,650 deaths annually -

Disease
- Median age at diagnosis: 69
- Five-year survival: 48%

Standard of Care
- Velcade/Revlimid/Dex
- Pomalyst, Kyprolis
- New agents: Empliciti, Darzalex, Ninlaro

Unmet Needs
- Curative treatment
- Therapies for relapse/refractory patients

Sources: American Cancer Society, SEER, Kantar Health.
Venclexta Plus Bortezomib-dexamethasone Is Active in MM

Strong mechanistic rationale for combination of Venclexta with the proteasome inhibitor bortezomib, which is a cornerstone therapy in multiple myeloma

- Overall response rates in r/r MM are superior to historical Velcade data and encouraging compared to novel regimens
- Deep responses (VGPR or CR) in half of these patients
- >80% response rates in patients who received one to three prior lines of therapy


« Next step: Phase 3 trial start (r/r MM) in H2:16 »

CR=complete response; sCR=stringent complete response; VGPR=very good partial response; PR=partial response; bortez/dex=bortezomib, dexamethasone.

* Bortezomib naïve, sensitive, 1-3 prior treatments (ENDEAVOR trial. Dimepoulos et al. Lancet Oncol 2016)
Acute Myeloid Leukemia

**U.S. Epidemiology**

- **Incidence**: 19,950
- **Treated Population**
  - **1L**: 15,591
  - **2L**: 5,251
  - **3L+**: 1,945

- **Median age at diagnosis**: 67
- **Five-year survival**: 27% (<5% in pts 65+ yrs.)
- **No improvements in treatment in 25 yrs.**

**Disease**

- Standard of Care
  - Younger patients, high-dose intensive chemo (cytarabine/anthracycline)
  - Patients with co-morbidities (low-dose cytarabine, hypomethylators)
  - Stem-cell transplant

**Unmet Needs**

- Stem-cell transplant only curative therapy
- Improved options for patients unable to tolerate intensive therapy
- Improved survival for relapsed/refractory setting

Sources: American Cancer Society, SEER, Kantar Health.
Venclexta Has Demonstrated Significant Activity in AML and Is Supported by FDA Breakthrough Therapy Designation

**OBJECTIVE RESPONSES**

Historical benchmarks (CR+CRi)
- azacitidine = 28%
- decitabine = 26%


Historical benchmark (CR+CRi) LoDAC = 11%
Kantarjian et al. JCO 2012.

CR = complete remission. CRi = complete remission with incomplete blood count recovery.

Pollyea et al. ASCO 2016 (Abstract #7009). Lin et al. ASCO 2016 (Abstract #7007). *Update June 4, 3:00-6:00 (Arie Crown Theatre) and June 6, 11:30-12:45 (E354b).*

### OBJECTIVE RESPONSES

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage of patients responding (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venclexta + decitabine or azacitidine</td>
<td>5% (N=34)</td>
</tr>
<tr>
<td>Venclexta + LoDAC</td>
<td>44% (N=18)</td>
</tr>
</tbody>
</table>

**Next step: Phase 3 trial start in H2:2016**
## Venclexta: Upcoming Milestones

<table>
<thead>
<tr>
<th>Year</th>
<th>CLL</th>
<th>NHL</th>
<th>MM</th>
<th>AML</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td><img src="image1" alt="Three CLL readouts" /></td>
<td><img src="image2" alt="P1, r/r CLL &amp; r/r NHL" /></td>
<td><img src="image3" alt="P1, r/r MM (+bortez/dex)" /></td>
<td><img src="image4" alt="P1, AML (+dec, +aza)" /></td>
</tr>
<tr>
<td>2017</td>
<td><img src="image5" alt="P3, r/r CLL (+R)" /> (MURANO)</td>
<td><img src="image6" alt="P2, r/r CLL after BRCI" /></td>
<td><img src="image7" alt="P1, r/r MM" /></td>
<td><img src="image8" alt="P1, AML (+Ara-C)" /></td>
</tr>
<tr>
<td>2018</td>
<td><img src="image9" alt="P1, r/r CLL &amp; SLL (+ BR)" /></td>
<td><img src="image10" alt="P2, r/r FL (+R vs BR) (CONTRALTO)" /></td>
<td><img src="image11" alt="P1, r/r MM (+BR)" /></td>
<td><img src="image12" alt="P3, AML" /></td>
</tr>
<tr>
<td>2019</td>
<td><img src="image13" alt="P3, r/r CLL (+G)" /> (CLL14)</td>
<td><img src="image14" alt="P1, r/r CLL &amp; SLL (+ BR)" /></td>
<td><img src="image15" alt="P1, AML (+dec, +aza)" /></td>
<td><img src="image16" alt="P3, AML" /></td>
</tr>
<tr>
<td>2020</td>
<td><img src="image17" alt="P3, r/r CLL (+G)" /> (CLL13)</td>
<td><img src="image18" alt="P2, r/r CLL after BRCI" /></td>
<td><img src="image19" alt="P1, r/r CLL &amp; SLL (+ BR)" /></td>
<td><img src="image20" alt="P3, AML" /></td>
</tr>
</tbody>
</table>

* Approximate dates. Timing for some studies will be based on event rates and interim analysis triggers.

R=Rituxan; G=Gazyva; BR=bendamustine/Rituxan; GI=Gazyva/Ibruvica; RCHOP=Rituxan, cyclophosphamide, doxorubicin, vincristine, prednisone; Bortez=bortezomib; Dex=dexamethasone; Dec=decitabine; Aza=azacitidine; Ara-C=cytarabine.
Veliparib and ABT-414
Veliparib Activity in Phase 2 Trials Provides Evidence for: 1) Monotherapy Efficacy; and 2) Synergy with Chemotherapy

Veliparib inhibits PARPs 1 and 2 which are critical nuclear enzymes for DNA damage repair.

1. Veliparib has demonstrated single-agent activity in BRCA-deficient tumors

<table>
<thead>
<tr>
<th>Population (study)</th>
<th>N</th>
<th>ORR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent ovarian cancer (GOG 0280)</td>
<td>50</td>
<td>26</td>
</tr>
<tr>
<td>Recurrent ovarian cancer (CTEP 8282)</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>Recurrent ovarian cancer (VeliBRCA)</td>
<td>32</td>
<td>65 (a)</td>
</tr>
</tbody>
</table>

(a) RECIST or GCIG CA125 criteria.

2. Overall survival benefit in a pre-specified population of smokers in a randomized trial (n = 95)

Current Smoker Subset
OS: 12.5 vs 5.4 mos
HR: 0.41 (0.25-0.68)
Veliparib Has Built a Foundational Strategy Across BRCA and non-BRCA Tumors in Combination with Standard Chemotherapy

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Pivotal Phase 3 Trials Underway</th>
<th>Follow-on Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic Defects + DNA-Damaging Chemotherapy</td>
<td>1-3L BRCA Breast (BROCADE3)</td>
<td>Tumors with HRD phenotype e.g., Fanconi anemia related, prostate, pancreas</td>
</tr>
<tr>
<td>Inherited defects in BRCA1/2, impair DNA repair</td>
<td>1L Ovarian (VELIA)</td>
<td></td>
</tr>
<tr>
<td>DNA-Damaging Chemotherapy (non-BRCA)</td>
<td>1L NSCL SQ (VELA)</td>
<td>Indications where platinums or topoisomerase inhibitors are used as standard therapies</td>
</tr>
<tr>
<td>Reliance on PARP-mediated DNA repair (NER/TLS)</td>
<td>1L NSCLC NonSQ (VESTA)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TNBC Neo-adjuvant (BRIGHTNESS)</td>
<td></td>
</tr>
</tbody>
</table>

« Readouts anticipated between 2017–2019 »
**ABT-414 Is an Antibody-Drug Conjugate (ADC) Which Targets Epidermal Growth Factor Receptor (EGFR)**

**Glioblastoma (GBM) kills more than 95% of those diagnosed**

- Most common primary brain tumor in adults (peak age 55–65 yr)
- Grows rapidly and infiltrates tissue
- Chemotherapy has marginal benefit
  - Median survival of ~14 months
  - 5-year survival rate of <5%
- Worldwide incidence ~28,000

- ABT-414 targets unique epitope exposed upon EGFR activation
- Activation occurs when either EGFR is amplified or has vIII mutation
- Selective binding to tumors confirmed in first-in-human and imaging studies
- No typical EGFR inhibitor skin rash

**Zirconium ImmunoPET in a patient with GBM**

1. ABT-414 in blood
2. ABT-414 binds EGFR selectively expressed on tumor cell
3. ABT-414 enters cell
4. Toxin releases from ABT-414
5. Toxin kills cell

4h, 72h, 120h
ABT-414 Has Encouraging Efficacy in Refractory GBM

Best percent change from baseline in tumor size (target lesion) – monotherapy and combination with TMZ in recurrent GBM and EGFR amplified positive –

11 patients had change in tumor sized between 100–850%.
AbbVie Has Launched an Aggressive Program in GBM for ABT-414

- Since the first patient with GBM was treated with ABT-414 (2013), ABT-414 has advanced to international, randomized trials
- ABT-414 is now being studied in over 30 countries in both recurrent and front-line settings
- Collaborations with recognized, academic cooperative groups (EORTC, RTOG)
- Biomarker work will refine the population most likely to benefit (e.g., EGFR amp+)

### Table: GBM Indication (study name) and Anticipated Readouts

<table>
<thead>
<tr>
<th>Combination</th>
<th>Indication (study name)</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
<th>Anticipated readouts</th>
</tr>
</thead>
<tbody>
<tr>
<td>+temozolomide</td>
<td>1L GBM (INTELLANCE-1)</td>
<td></td>
<td></td>
<td></td>
<td>2019</td>
</tr>
<tr>
<td>+temozolomide</td>
<td>2L GBM (INTELLANCE-2)</td>
<td></td>
<td></td>
<td></td>
<td>2017</td>
</tr>
<tr>
<td>monotherapy</td>
<td>GBM (INTELLANCE-Japan) (a)</td>
<td></td>
<td></td>
<td></td>
<td>2018</td>
</tr>
<tr>
<td>+temozolomide</td>
<td>GBM</td>
<td></td>
<td></td>
<td></td>
<td>2016</td>
</tr>
</tbody>
</table>

(a) Phase I/II.

We Expect Our Oncology Pipeline To Show Significant Advancement Over the Next Two to Three Years

<table>
<thead>
<tr>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Imbruvica</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ (RESONATE-2) 1L CLL (approval)</td>
<td></td>
<td>□ (PHOENIX) P3, 1L DLBCL *</td>
<td>□ (PCYC-1126e) P3, 1L CLL *</td>
<td>□ (ALLIANCE-CTEP) P1, 1L GBM</td>
</tr>
<tr>
<td>□ (HELIOS) r/r CLL/SLL (label expansion; +BR)</td>
<td></td>
<td>□ (MURANO) P3, r/r CLL (+R)</td>
<td>□ (PCYC-1137) P2/3, Pancreas *</td>
<td>□ (CLL13) P3, 1L CLL (+G)</td>
</tr>
<tr>
<td>□ (DAWN) P2, r/r FL</td>
<td>□ (CONTRALTO) P2, r/r CLL (+R vs BR)</td>
<td>□ (PCYC-1138) P2, r/r MM *</td>
<td>□ (CLL13) P3, 1L CLL (+G)</td>
<td></td>
</tr>
<tr>
<td>□ (PCYC-1121) P2, MZL</td>
<td>□ (CAVALLI) P2, 1L DLBCL (+RCHOP vs RCHOP)</td>
<td>□ (PCYC-1127) P3, 1L &amp; r/r WM *</td>
<td>□ (CLL13) P3, 1L GBM</td>
<td></td>
</tr>
<tr>
<td>□ SHINE P3, 1L MCL *</td>
<td>□ (PCYC-1129) pGVHD</td>
<td>□ (SELENE) P3, r/r FL/MZL *</td>
<td>□ (CLL13) P1, 1L + GBM</td>
<td></td>
</tr>
<tr>
<td>□ (SELENE) P3, r/r FL/MZL *</td>
<td></td>
<td></td>
<td>□ (INTELLANCE-1) P3, 1L GBM</td>
<td></td>
</tr>
</tbody>
</table>

| Venclexta | | | | |
| □ 17p del CLL (approval) | □ (VELA) P3, 1L NSCLC SQ | □ (VELA) P3, 1L Ovarian |
| □ P1, r/r CLL & SLL (+R, +G, +BR) | □ (VESTA) P3, 1L NSCLC SQ | |
| □ P1, r/r CLL & NHL | □ (BRIGHTNESS) P3, neo-adjuvant TNBC | |
| □ P1, r/r MM (+bortez/dex) | □ (BROCADE3) P3, 1-3L BRCA Breast | |

| veliparib | | | | |
| □ (INTELLANCE-2) P2, 2L GBM | | □ (INTELLANCE-I) P1/2, GBM | | |

| ABT-414 | | | | |
| □ P1, 1L GBM | □ (INTELLANCE-I) P3, 1L GBM | | |

R=Rituxan; G=Gazyva; BR=bendamustine/Rituxan; CG=chlorambucil/Gazyva; GI=Gazyva/Imbruvica; RCHOP=Rituxan, cyclophosphamide, doxorubicin, vincristine, prednisone; Bortez=bortezomib; Dex=dexamethasone; Dec=decitabine; Aza=azacitidine; Ara-C=cytarabine.

* Interim data
Innovative Medicines in Oncology
Better and Safer Therapies for Cancer Patients

Thomas Hudson, M.D.
Background

“In the U.S., one in two men and one in three women will get cancer in their lifetime; one out of four Americans will die from cancer.”
- American Cancer Society

In his State of the Union Address, President Obama invited Vice President Joe Biden to champion and spearhead a national effort – a “moonshot” in the fight against cancer.

“I know that we can help solidify a genuine global commitment to end cancer as we know it today — and inspire a new generation of scientists to pursue new discoveries and the bounds of human endeavor.”
- U.S. Vice President Joe Biden
Experience in Genomics and Cancer Research

Human Genome Project

1990
1995
2000
2003
2004
2005
2007
2013

Global Alliance for Genomics & Health

International Cancer Genome Consortium

International HapMap Project

nature: the human genome

OICR: Ontario Institute for Cancer Research
The International Cancer Genome Consortium
A Moonshot Launched in 2007 by the Global Cancer Research Community

Thomas Hudson, M.D.
Chair, ICGC Executive and International Scientific Steering Committees
Cancer Is a Disease of the Genome

- Every tumor is different
- Every cancer patient is different
Goals of the International Cancer Genome Consortium (ICGC)

- Collect ~500 tumor/normal pairs from each of 50 different major cancer types
- Comprehensive genome analysis of 25,000 cancer genomes, transcriptomes and methylomes
- Make the data available to the research community and public

...GATTATCCAGGTAT...
...GATTATGCAGGTAT...
...GATTATGCAGGTAT...
In 2007 – ICGC Was a Moonshot!

- The study of cancer genomes offered the potential to identify hundreds of new targets for better diagnoses and drug development
- No cancer genome had been sequenced
- Sequencing 25,000 cancer genomes was deemed an ambitious goal!
- Next generation technologies were on the horizon
- The spectrum of cancers across the world varies greatly

- The founders of ICGC realized the importance of coordination, standardization and need for uniform quality measures to enable the merging of datasets and increasing power to detect new cancer biomarkers and targets
88 ICGC Projects as of April 2016

UNITED STATES
- Bladder cancer (Invasive urothelial bladder cancer)
- Blood cancer (Acute lymphoblastic leukemia/Acute myeloid leukemia/lymphoid neoplasm diffuse large B-cell lymphoma)
- Bone cancer (Osteosarcoma)
- Brain cancer (Glioblastoma multiforme/ Lower grade glioma)
- Breast cancer (Ductal & lobular)
- Cervical cancer (Squamous)
- Colorectal cancer (Adenocarcinoma)
- Endometrial cancer (Uterine corpus endometrial carcinoma)
- Gastric cancer (Adenocarcinoma)
- Head and neck cancer (Squamous cell carcinoma/ Thyroid carcinoma)
- Liver cancer (Hepatocellular carcinoma)
- Lung cancer (Adenocarcinoma/ Squamous cell carcinoma)
- Ovarian cancer (Serous cystadenocarcinoma)
- Pancreatic cancer (Adenocarcinoma)
- Pediatric solid tumor (Neuroblastoma)
- Prostate cancer (Adenocarcinoma)
- Renal cancer (Clear cell carcinoma/ Clear cell sarcoma/ Kidney chromophobe/Papillary carcinoma/Rhabdoid tumor)
- Skin cancer (Cutaneous melanoma)
- Soft tissue cancer (Liposarcoma and multiple subtypes)

CANADA
- Pancreatic cancer (Ductal adenocarcinoma)
- Pediatric brain tumors (Medulloblastoma)
- Prostate cancer (Adenocarcinoma)

EU / UNITED KINGDOM
- Bone cancer (Osteosarcoma/ Chondrosarcoma/ rare subtypes)
- Breast cancer (Triple negative/lobular/ other)
- Chronic Myeloid Leukemia (Myelodysplatic syndromes, myeloproliferative neoplasms and other chronic myeloid malignancies)
- Esophageal cancer (Adenocarcinoma)
- Gastric cancer (Adenocarcinoma)
- Hepatobiliary cancer (Mainly biliary and gallbladder)
- Liver cancer (Hepatocellular carcinoma)
- Lung cancer (Multiple subtypes)
- Prostate cancer (Early onset)

UNITED KINGDOM
- Pancreatic cancer (Ductal adenocarcinoma)
- Pediatric brain tumors (Medulloblastoma and Pediatric pilocytic astrocytoma)
- Prostate cancer (Early onset)

GERMANY
- Breast cancer (Malignant lymphoma, Acute lymphoblastic leukemia/ Chronic myeloid leukemia)
- Lung cancer (Multiple subtypes)
- Prostate cancer (Triple negative)

ITALY
- Esophageal cancer (Squamous carcinoma)
- Gastric cancer (Intestinal and diffuse-type)
- Rare pancreatic tumors (Endocrine, neuroendocrine tumors)

CHINA
- Bladder cancer (Urothelial carcinoma)
- Blood cancer (Acute myeloid leukemia and Chronic myelogenic leukemia)
- Brain cancer (Glioblastoma multiforme)
- Breast cancer (Triple negative)
- Colorectal cancer (Adenocarcinoma, non-GI)
- Esophageal cancer (Squamous carcinoma)
- Gastric cancer (Intestinal and diffuse-type)

SAUDI ARABIA
- Thyroid cancer (Papillary carcinoma)

JAPAN
- Biliary tract cancer (Multiple histological subtypes)
- Gastric cancer (Adenocarcinoma and Multiple histological subtypes)
- Liver cancer (Hepatocellular carcinoma/ Virus-associated)

SOUTH KOREA
- Blood cancer (Acute myeloid leukemia)
- Breast cancer (Lung, osteosarcoma, Soft tissue sarcoma, Stomach, Leukemia)
- Colorectal cancer
- Gastric cancer
- Liver cancer (Hepatocellular carcinoma)

AUSTRALIA
- Ovarian cancer (Serous cystadenocarcinoma)
- Pancreatic cancer (Ductal adenocarcinoma/ Endocrine neoplasms)
- Prostate cancer
- Skin cancer
- Melanoma

MEXICO
- Blood cancer (Diffuse large B-cell lymphoma)
- Breast cancer (Ductal carcinoma)
- Colorectal cancer
- Head and neck cancer (Squamous cell carcinoma of oral cavity/ oropharyngeal/ sinonasal cavity/ hypopharynx/larynx)
- Pediatric solid tumors

SPAIN
- Bone cancer (Chronic lymphocytic leukemia with mutated and unmutated IGH)
- Breast cancer (Ovarian carcinoma)
- Chronic Myeloid Leukemia (Myelodysplastic syndromes, myeloproliferative neoplasms and other chronic myeloid malignancies)
- Esophageal cancer (Adenocarcinoma)
- Gastric cancer (Adenocarcinoma)

FRANCE
- Bone cancer (Chronic lymphocytic leukemia)
- Breast cancer (Subtype defined by an amplification of the HER2 gene)
- Chronic lymphocytic leukemia (B-cell)
- Chronic myeloid leukemia
- Colorectal cancer
- Endometrial cancer
- Hepatocellular carcinoma
- Hepatobiliary cancer
- Liver cancer (Hepatocellular carcinoma)

BRAZIL
- Skin cancer (Melanoma)

INDIA
- Oral cancer (Stomach/Colon)

SINGAPORE
- Bilary tract cancer (Cholangiocarcinoma)
- Blood cancer (Acute myeloid leukemia)
- Lung cancer (Small cell carcinoma)
- Renal cancer (Clear cell renal cell carcinoma)

Grey = Collaboration
Growth of ICGC datasets

ICGC Data Portal Cumulative Donor Count for Member Projects

- Cancer pathways
- New biomarkers
- New targeted drugs
- New diagnostic tools
- Precision medicine

Number of Donors

- Release 8
- Release 9
- Release 10
- Release 11
- Release 12
- Release 13
- Release 14
- Release 15
- Release 16
- Release 17
- Release 18

Release 18
55 ICGC projects

ICGC projects Growth of ICGC datasets
Downstream Impact of ICGC
ICGC Led to a Flood of Discoveries

International network of cancer genome projects

The International Cancer Genome Consortium*

The International Cancer Genome Consortium (ICGC) was launched to coordinate large-scale cancer genome studies in tumours from 50 different cancer types and/or subtypes that are of clinical and societal importance across the globe. Systematic studies of more than 25,000 cancer genomes at the genomic, epigenomic and transcriptomic levels will reveal the repertoire of oncogenic mutations, uncover traces of the mutagenic influences, define clinically relevant subtypes for prognosis and therapeutic management, and enable the development of new cancer therapies.

Seminal publications reporting new cancer genes and pathways in Nature, Nature Genetics, Science, Cell, etc.
Cancer Genomes Have Become Informative Biomarkers of Drug Response

- **Oncogenes**
  - Oncogene inhibition
  - Pathway inhibition
- **DNA Instability**
  - DNA damage
  - Inhibition of DNA repair
- **Neo-antigens**
  - Immuno-modulation
  - CAR T cells
  - Cancer vaccines

Cancer genomes as predictive biomarkers
The Ontario Institute for Cancer Research
A Translational Research Institute Launched by the Government of Ontario

Thomas Hudson, M.D.
President and Scientific Director, OICR
The **Ontario Institute for Cancer Research (OICR)** is a translational research institute headquartered in downtown Toronto’s Discovery District, with an Ontario-wide mandate and global reach.

**Ontario investments since 2006:** $750 M

**Other sources (federal, charities, private sector):** $540 M
Mission: Partner with the Ontario oncology community to accelerate the development and implementation of clinically important knowledge, products, services and policies to improve cancer prevention, detection, diagnosis and treatment and enable patients in Ontario and worldwide to live longer and better lives.

Translational Research Priorities

1. THERAPEUTIC INNOVATION
   Find new ways to treat difficult cancers.

2. CLINICAL IMPACT
   Optimize cancer patient management and treatment decisions.

3. POPULATION HEALTH
   Drive improvements in cancer prevention and care delivery.

Research areas build on Ontario strengths: Small molecules, biologics, stem cells, imaging, genomics, informatics and bio-computing, pathology, clinical trials and health outcomes.
The OICR Story So Far

OICR FUNDING CREATING NEW JOBS

Funds Leveraged by FACIT Companies

(IN MILLIONS OF DOLLARS)

#1 of 103
for research excellence and impact in Canada
These are size-independent indicators from SCImago institutions rankings 2014

425
colon cancer deaths/year potentially averted due to improved participation in colon cancer screening

1,700
investigators, clinician scientists, research staff and trainees supported by OICR research across Ontario

32
outstanding scientists/clinician researchers have been attracted to Ontario

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## OICR Pipeline

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>Discovery</td>
<td>Biomarkers to avoid over-treatment of early disease</td>
</tr>
<tr>
<td></td>
<td>Early Translation</td>
<td>Biomarkers for customizing treatment of invasive breast cancer so that patients receive safe and effective therapy</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>Early Translation</td>
<td>Better imaging technique for minimizing over-treatment of early disease</td>
</tr>
<tr>
<td></td>
<td>Late Translation</td>
<td>Biomarkers to personalize treatment for intermediate disease so that patients receive safe and effective therapy</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>Late Translation</td>
<td>Molecular or radiomic biomarkers predictive of patient outcome, treatment response and drug sensitivity</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Adoption</td>
<td>New drug for disease subtype resistant to current therapy</td>
</tr>
<tr>
<td>Leukemia</td>
<td>Adoption</td>
<td>Stem cell biomarkers to personalize therapy and develop new drugs</td>
</tr>
<tr>
<td>Multiple cancers</td>
<td>Discovery</td>
<td>Novel therapeutic approaches</td>
</tr>
<tr>
<td></td>
<td>Immunotherapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Radiopharmaceuticals</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Therapeutic ultrasound</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nanoparticles for drug delivery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Software, databases for personalized medicine</td>
<td></td>
</tr>
</tbody>
</table>

### Legend

- April 2015 — April 2017
Dr. John Bell

OICR Program Director, Immuno- and Bio-therapies (ORBiT)

Senior Scientist, Cancer Therapeutics, Ottawa Hospital Research Institute

Professor, Departments of Medicine and Biochemistry, Microbiology and Immunology, University of Ottawa

Innovative concept of associating tumour vaccine (MAGE-A3) and oncolytic virus (Maraba)
OICR Catalyzed the Development of a Novel Experimental Approach

Prime: Boost
Dr. Brian Lichty
2009-12

Maraba Virus
Dr. David Stojdl
2009-12

POC
- Assay development
- Manufacturing
- Toxicology (NHP)
- Regulatory (CTA)
- Clinical operations

Phase 1/2 Trial
2015-16

Constant interactions between translation teams and basic/science discovery teams

2012-2014
Looking Forward to New Opportunities at AbbVie

Build on experience with ICGC, OICR and moonshots

• Inspire individuals and groups to think BIG!
• Stimulate creative thinking and risk taking
• Intensify the interactions between discovery teams and clinician researchers to accelerate translation and make new discoveries
• Capitalize on new technologies and new biology

What will be my priorities?

• Continue to grow the existing AbbVie Pipeline
• Build critical mass in immuno-oncology
  – Unlock the potential of different types of immune cells
  – Explore interactions between cancer genome signatures and immune response

Bring long-term benefits to individuals and society
IMMUNOLOGY

Oncology

Immunology

HCV

Elagolix

Neuroscience
Immunology

Shao-Lee Lin, M.D., Ph.D.
Development

Lisa Olson, Ph.D.
Discovery
AbbVie Immunology: A Promise that Extends into the Future

Currently being used to treat more than **975,000 patients** in **13 indications** worldwide.

**PIPELINE**

- **20 new molecules** being evaluated across **14 disease states**.
- **195 active immunology studies** in **more than 50 countries**.
Focused on Redefining the Standard of Care in our Core Areas

**Rheumatology**
Achieve deep response and remission

**Dermatology**
Achieve full clearance with durable response
Oral agent

**Gastroenterology**
Improve remission rates and achieve mucosal healing
ABT-494 and Risankizumab: Poised to Make a Remarkable Impact

**Rheumatology**
- JAK Phase 3 in RA
- ABT-494 has potential for best efficacy, particularly in the most difficult to treat RA patients

**Dermatology**
- IL-23 Phase 2 in PsA
- Risankizumab has potential for best efficacy and most convenient dosing in psoriasis

**Gastroenterology**
- IL-23 Phase 3 in Crohn’s
- ABT-494 and risankizumab both have potential in IBD

**Gastroenterology**
- JAK Phase 2 in Crohn’s

IL-23 Phase 3 in PsA

IL-23 Phase 2 in PsA

JAK Phase 3 in RA

JAK Phase 2 in PsA

JAK Phase 2 in Crohn’s

IL-23 Phase 2 in Crohn’s

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**Rheumatology**
- JAK Phase 3 in RA

**Dermatology**
- IL-23 Phase 2 in PsA

**Gastroenterology**
- IL-23 Phase 3 in Crohn’s
- ABT-494 and risankizumab both have potential in IBD
Leveraging our Strength in Immunology for ABT-494
JAK-1 Selectivity Offers Potential for Higher Efficacy, While Limiting Pan-JAK Side Effects

JAK1 inhibition blocks signaling driving rheumatoid arthritis disease process

JAK2 inhibition leads to anemia

JAK3 inhibition affects cells that monitor for tumors and infections

<table>
<thead>
<tr>
<th>Molecule</th>
<th>JAK1 Potency</th>
<th>JAK1/JAK2 Selectivity</th>
<th>JAK1/JAK3 Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABT-494</td>
<td>8.5 nM IC50</td>
<td>74 X</td>
<td>19 X</td>
</tr>
</tbody>
</table>
Potential for Best-in-Class Efficacy Among JAK1 Selective Agents

Efficacy of ABT-494 relative to other JAK1 inhibitors based on model-based meta analysis

Difference from Placebo in Percentage of Subjects Achieving ACR Response

*Meta analysis across all clinical trials in RA to date for these agents

**Figure Details**
- **ACR20, ACR50, ACR70** categories represent different levels of ACR (American College of Rheumatology) response.
- **ABT-494** dosages: 2 mg QD, 6 mg BID, 12 mg BID, 15 mg QD, 30 mg QD.
- **Baricitinib** dosages: 2 mg QD.
- **Filgotinib** dosages: 100 mg QD, 200 mg/Day.

**Dose Equivalents**
- 15 mg QD = 6 mg BID
- 30 mg QD = 12 mg BID
Results from the Most Challenging Population, TNF-inadequate Responders, Are Especially Encouraging

- **ABT-494 12 mg BID** (BALANCE I; Phase 2)
- **ABT-494 12 mg BID** (BALANCE I; Phase 2)
- **Baricitinib 4 mg QD** (BEACON; Phase 3)
- **Baricitinib 2 mg QD** (BEACON; Phase 3)

(Data from cross-study comparison)
ABT-494 RA Phase 3 Program is Expected to Deliver a Strong and Comprehensive Label

<table>
<thead>
<tr>
<th>Type of Therapy</th>
<th>MTX-naïve</th>
<th>MTX-IR</th>
<th>csDMARD-IR</th>
<th>MTX-IR</th>
<th>Biologic-IR</th>
<th>Biologic-IR</th>
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<tbody>
<tr>
<td>Background</td>
<td>Mono</td>
<td>Combo</td>
<td>Combo</td>
<td>Mono</td>
<td>Combo</td>
<td>Combo</td>
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<tr>
<td>Active Comparator</td>
<td>MTX</td>
<td>Adalimumab</td>
<td>Placebo</td>
<td>MTX</td>
<td>Placebo</td>
<td>Abatacept</td>
</tr>
<tr>
<td>Duration of Period 1</td>
<td>48 weeks</td>
<td>48 weeks</td>
<td>12 weeks</td>
<td>14 weeks</td>
<td>24 weeks</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

Supports use earlier in therapy

Supports use after first biologic failure

Rapid Phase 2-to-Phase 3 transition for RA. Three months from ‘go’ decision to first subject dosed in Phase 3.
Maximizing the Potential of ABT-494

<table>
<thead>
<tr>
<th></th>
<th>Tofacitinib</th>
<th>Filgotinib</th>
<th>Baricitinib</th>
<th>ABT-494</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheum</td>
<td></td>
<td></td>
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<tr>
<td>RA</td>
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<tr>
<td>PsA</td>
<td>●</td>
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<tr>
<td>AS</td>
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<td></td>
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<td>●</td>
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<tr>
<td>Derm</td>
<td></td>
<td>●</td>
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<td>●</td>
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<tr>
<td>Atopic Dermatitis</td>
<td>●</td>
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<tr>
<td>Gastro</td>
<td></td>
<td>●</td>
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<td>●</td>
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<tr>
<td>CD</td>
<td>●</td>
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<tr>
<td>UC</td>
<td>●</td>
<td>●</td>
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<td>●</td>
</tr>
</tbody>
</table>

= Ongoing program  = Planned study
Leveraging our Strength in Immunology for Risankizumab

ultimma-1

immhance

ultimma-2

Risankizumab licensed from Boehringer Ingelheim
IL-23 Is Implicated in the Inflammatory Cascade Across Multiple Autoimmune Diseases

Risankizumab recognizes an epitope on IL-23p19

- Inhibits binding of IL-23 to its receptor
- Binding is highly specific for the p19 subunit
- No direct impact on T\textsubscript{H}1 pathway

Singh S et al. mAbs 2015;7:778
Patel M et al. Dermatol Ther 2012;2:16
Sofen H et al. J Allergy Clin Immunol 2014;133:1032
Muranski P & Restifo NP. Blood 2013;121:2402
Risankizumab Has Potential to Be a Transformational New Therapy in Psoriasis

- Expected PASI90 efficacy above anti-IL-12/23, IL-17s and other IL-23s after 12 weeks
- Dosing has potential to be the most patient friendly at once every 3 months
- Potential for durability above IL-12/23 and IL-17s at one year

### Comparison of PASI 90 Scores at 12 wks*

- Humira
- Stelara
- Cosentyx
- Ixekizumab
- Tildrakizumab
- Gusekumab
- Risankizumab

### Comparison of PASI 100 Scores at 12 wks*

- Humira
- Stelara
- Cosentyx
- Ixekizumab
- Tildrakizumab
- Gusekumab
- Risankizumab

PASI90 and PASI100 data from multiple studies, including: Humira (CHAMPION), Stelara (ave PHOENIX 1+2), Cosentyx (ave ERASURE/FIXTURE, 300 mg), Ixekizumab (UNCOVER2/3), Tildrakizumab (ClinicalTrials.gov), Gusekumab (NEJM 2015), BI655066 (EADV2015).

* Tildrakizumab data at 16wks
Risankizumab Has Demonstrated Encouraging Phase 2 Data in Crohn’s Disease

Clinical Remission (CDAI<150, placebo adjusted, Bio-IR)

- **Adalimumab**: week 12, 19%
- **Vedolizumab**: week 10, 15%
- **Ustekinumab**: week 8, 14%
- **anti-IL6**: Week 12, 16%
- **Risankizumab**: week 12, 22%
- **Filgotinib**: week 10, 8%
- **Medi2070**: week 8, 12%

Data from multiple studies, including: Adalimumab: EXTEND, data on file; Vedolizumab: GEMINI 3; Ustekinumab: UNITI-1; anti-IL6: ANDANTE; Risankizumab: DDW 2016; Filgotinib: ECCO 2016; Medi2010: ECCO 2015
Risankizumab Phase 3 Psoriasis Program Includes Two Head-to-Head Studies Versus Stelara

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Trial Description</th>
<th>N</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>ultimma-1</td>
<td>Phase 3 head-to-head, placebo-controlled study of the efficacy and safety of Risankizumab compared with ustekinumab for moderate-to-severe psoriasis</td>
<td>500</td>
<td>sPGA0/1 @ wk 16, PASI 90 @ wk 16</td>
</tr>
<tr>
<td>ultimma-2</td>
<td>Phase 3 head-to-head, placebo-controlled study of the efficacy and safety of Risankizumab compared with ustekinumab for moderate-to-severe psoriasis</td>
<td>500</td>
<td>sPGA0/1 @ wk 16, PASI 90 @ wk 16</td>
</tr>
<tr>
<td>immhance</td>
<td>Phase 3 placebo-controlled, withdrawal and retreatment study of the efficacy and safety of Risankizumab for moderate-to-severe psoriasis</td>
<td>500</td>
<td>sPGA 0/1 @ wk 16, PASI 90 @ wk 16</td>
</tr>
<tr>
<td>immvent</td>
<td>Phase 3 Risankizumab Compared to Active Comparator (adalimumab) in patients with moderate-to-severe chronic plaque psoriasis</td>
<td>600</td>
<td>sPGA0/1 @ wk 16, PASI 90 @ wk 16</td>
</tr>
<tr>
<td>LIMMitless</td>
<td>Open-label extension enrolling subjects from all of the Phase 3 efficacy studies</td>
<td>Phase 3 completers</td>
<td></td>
</tr>
</tbody>
</table>
Maximizing the Potential of Risankizumab

<table>
<thead>
<tr>
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• = Ongoing program  ■ = Planned study
AbbVie’s Pipeline Anticipated to Provide Sustained Growth for the Franchise

### Anticipated News Flow

<table>
<thead>
<tr>
<th></th>
<th>2Q 2016</th>
<th>3Q 2016</th>
<th>4Q 2016</th>
<th>2017</th>
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</table>
Our Early Programs Bring New Approaches to Redefining the Standard of Care in our Core Disease Areas

**Rheumatology**
- JAK Phase 3 in RA
- JAK-BTK Combo
- IL-23 Phase 2 in PsA
- IL-23 Phase 3 in PsA
- Anti-TNF Steroid ADC
- Our goal is to achieve deep remission.

**Dermatology**
- IL-23 Phase 2 in PsA
- IL-23 Phase 3 in Psoriasis
- RORγT
- Developing an oral agent with high efficacy.

**Gastroenterology**
- JAK Phase 2 in Crohn’s
- IL-23 Phase 2 in Crohn’s
- Anti-TNF Steroid ADC
- Unmet need in remission and mucosal healing.
Targeting Complete Remission in RA and IBD

Anti-TNF Steroid ADC Project

Targeted Release of Novel Steroid

Blue = LysoTracker
Red = Anti-TNF
Targeting Complete Remission in RA and IBD

Anti-TNF Steroid ADC Project

Resolution of Disease with a Single Dose in Mouse Arthritis Model

Anti-TNF ADC Demonstrates Comparable Efficacy to High Dose Steroid Without Side Effects

Remarkable efficacy with just a single dose of anti-TNF Steroid ADC

Lack of unwanted steroid side effects
Hypothesis: Combining inhibitors of JAK1 and BTK will confer additive efficacy in autoimmune disease.

Combination Therapy Is a Well-accepted Practice in Rheumatology

JAK1 / BTK Inhibitor Combination for RA

Paw swelling in rat collagen-induced arthritis model

% inhibition paw swelling

Combo efficacy

JAK

BTK

JAK BTK
Oral Small Molecule for Moderate-to-Severe Psoriasis
RORγt Inverse Agonists Target the Clinically Validated IL17/IL23 Pathway

RORγt essential for production of IL-17

Activated T cell

T_H17 cell

RORγt inverse agonist

Differentiation

Effector function

Th-17 lymphocyte

RORγt inhibition significantly decreased inflammation and reduced the frequency of IL17-producing cells
AbbVie’s Pipeline Is Positioned for Continued Leadership in Immunology

### Anticipated News Flow

#### 2Q 2016
- **RHEUM**
  - ABT-122 TNF/IL-17 PsA Phase 2
- **DERM**
  - ALX-0061 IL-6 RA Phase 2
- **GASTRO**
  - ABT-308 IL-13 EoE Phase 2

#### 3Q 2016
- **RHEUM**
  - ABT-981 IL-1α/β Hand OA Phase 2
  - Risankizumab IL-23 PsA Phase 2
- **DERM**
  - ABT-494 JAK AD Phase 2
- **GASTRO**
  - ABT-494 JAK CD Phase 2

#### 4Q 2016
- **RHEUM**
  - ABT-981 IL-1α/β Knee OA Phase 2
  - ABBV-599 JAK-BTK Phase 1
  - ABT-494 JAK RA Phase 3
- **DERM**
  - ABBV-553 RORγT Phase 1
- **GASTRO**
  - Risankizumab IL-23 CD Phase 2
  - ABBV-323 CD40 Phase 2

#### 2017
- **RHEUM**
  - ABBV-599 JAK-BTK Phase 1
  - Anti-TNF-Steroid ADC Phase I
  - ABT-494 JAK Ra Phase 3
- **DERM**
  - ABBV-553 RORγT Phase 1
- **GASTRO**
  - ABBV-323 CD40 Phase 2
  - ABBV-323 CD40 Phase 2

#### 2018
- **RHEUM**
  - ABT-494 JAK RA Phase 3
  - Anti-TNF-Steroid ADC Phase I
  - Risankizumab IL-23 PsA Phase 2
- **DERM**
  - Risankizumab IL-23 PsA Phase 3
- **GASTRO**
  - ABT-494 JAK UC Phase 2
  - Risankizumab IL-23 UC Phase 2
HCV and Elagolix

Shao-Lee Lin, M.D., Ph.D.
Advancing the Next Generation of HCV Cure

**Current therapies**
- >1 million patients cured
- Cure rates >95% for many genotypes

**Unmet Need:**
- >100 million patients remain*
- Pan-genotypic
- Resistance associated variants
- Difficult to treat populations
- Shorter treatment durations

**AbbVie’s Next Gen:**
*Once-daily oral combo*

- ABT-530
  NS5A inhibitor
- +
  ABT-493
  NS3/4a protease inhibitor

* WHO assessment (many are undiagnosed)
Next Gen Has Potent Activity Against Common Resistance-Associated Variants In-Vitro

Source: AbbVie data on file
High Cure Rates Are Achieved in Patients with Baseline Resistance: Phase 2 Data from MAGELLAN-1 study

<table>
<thead>
<tr>
<th></th>
<th>ABT-493 300mg + ABT-530 120mg + Ribavirin 800mg</th>
<th>ABT-493 300mg + ABT-530 120mg</th>
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<tr>
<td>SVR&lt;sub&gt;12&lt;/sub&gt;, n (%)</td>
<td>90.1 (20/22)</td>
<td>86.3% (19/22)</td>
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<tr>
<td>Breakthrough</td>
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<td>Relapse</td>
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<tr>
<td>Other</td>
<td>1*</td>
<td>2**</td>
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<tr>
<td>mITT SVR&lt;sub&gt;12&lt;/sub&gt;, n (%)</td>
<td>95.2% (20/21)</td>
<td>95% (19/20)</td>
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</table>

* 1 LTFU, ** 1 death from CA after UD RNA at PTW 8 and 1 LTFU

Baseline Resistance-Associated Variants

- 82% patients with RAVs at NS3 and/or NS5A
- 32% with both NS3 and NS5A RAVs detected
- 24% with double- or triple-NS5A RAVs
# High Cure Rates Across All Patient Populations in Phase 2

<table>
<thead>
<tr>
<th>GT/ F stage</th>
<th>Treatment History</th>
<th>Duration (weeks)</th>
<th>SVR\textsubscript{12} (non-virologic failures excluded)</th>
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<tbody>
<tr>
<td>1/ F0-F3</td>
<td>Treatment naïve and experienced</td>
<td>8</td>
<td>100%</td>
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<tr>
<td></td>
<td>Treatment naïve and experienced</td>
<td>12</td>
<td>100%</td>
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<tr>
<td></td>
<td>DAA experienced</td>
<td>12</td>
<td>95%</td>
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<tr>
<td>1/ F4</td>
<td>Treatment naïve and experienced</td>
<td>12</td>
<td>96%</td>
</tr>
<tr>
<td>2/ F0-F3</td>
<td>Treatment naïve and experienced</td>
<td>12</td>
<td>100%</td>
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<td>12</td>
<td>97\textsuperscript{a}</td>
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<tr>
<td></td>
<td>Treatment naïve</td>
<td>8</td>
<td>100%</td>
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<tr>
<td></td>
<td>Experienced</td>
<td>12</td>
<td>92%</td>
</tr>
<tr>
<td>3/ F4</td>
<td>Treatment naïve</td>
<td>12</td>
<td>100\textsuperscript{b}</td>
</tr>
<tr>
<td>4-6/ F0-F3</td>
<td>Treatment naïve and experienced</td>
<td>12</td>
<td>100%</td>
</tr>
</tbody>
</table>

\textsuperscript{a} SVR\textsubscript{12} in TN patients was 100%.

\textsuperscript{b} Screening of GT3 cirrhotic PR-exp. was stopped prematurely (FDA recommendation); only 4 GT3 cirrhotic PR-experienced (not included in the table) were randomized and their duration was extended to 16 weeks, 1 out of these 4 patients relapse.

DAA = Direct Acting Antivirals
## High Cure Rates Across All Patient Populations in Phase 2

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<td>12</td>
<td>100%</td>
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</table>

8wk regimen being tested in Phase 3

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a. SVR12 in TN patients was 100%; b. Screening of GT3 cirrhotic PR-exp. was stopped prematurely (FDA recommendation); only 4 GT3 cirrhotic PR-experienced (not included in the table) were randomized and their duration was extended to 16 weeks, 1 out of these 4 patients relapse.

DAA = Direct Acting Antivirals
The Next Gen Phase 3 Program Is Designed to Address Residual Unmet Medical Need

ENDURANCE
- DAA naïve
- Non-cirrhotic
- Pan-genotypic
- HIV co-infection
- Tx as short as 8wks

MAGELLAN
- DAA experienced
- Cirrhotic and Non-cirrhotic

EXPEDITION
- Special populations
  - GT1, GT2, GT4-6
  - Cirrhotic
  - Renal impairment

SURVEYOR
- Difficult to treat
  - GT3 cirrhotic
  - 8wks in GT2, GT4-6

Next Gen commercialization expected in 2017
Elagolix Profile

Attributes and Mechanism of Action

- Orally active
- Gonadotropin releasing hormone (GnRH) antagonist
- Dose dependent suppression of estrogen and progesterone
- Rapid onset of action and readily reversible when therapy stopped
- Potential for management of hormonally-mediated conditions, such as endometriosis and uterine fibroids

Female HPG Axis

[Diagram showing the Female HPG Axis with Hypothalamus, GnRH, Anterior pituitary, LH, FSH, Ovaries, Estrogen, and Progesterone, with a GnRH antagonist indicated.]
## Endometriosis

### Abnormal growth of endometrial tissue
- Tissue that lines the uterus grows outside of the uterus
- Tissue is responsive to estrogen

### Epidemiology
- Endometriosis affects an estimated 176 million women worldwide.\(^1\)

### Symptoms:
- Menstrual pain (Dysmenorrhea)
- Chronic non-menstrual pelvic pain
- Infertility

---

\(^1\) The World Endometriosis Research Foundation: Facts about Endometriosis.
Elagolix Has the Potential to Improve the Limited Treatment Options for Endometriosis-Associated Pain (EAP)

- **Elagolix**
  - **Efficacy on EAP**
  - **Invasiveness**

**Analgesics**
- OCPs: low efficacy
- Depo-Provera: side effects

**GnRH agonists**
- Complete hormonal suppression

**Laparoscopic Surgery**
- Invasive
- High recurrence
- Adhesions

**Unmet Need**
- Oral agent
- Rapid reversibility
- Significant pain reduction
- Laparoscopy not required to initiate treatment
- Long-term efficacy
Elagolix Endometriosis Phase 3 Pivotal Studies
Change from Baseline in Dysmenorrhea (DYS)

Violet Petal
Responder Rates

Solstice
Responder Rates

*P vs. PBO: <0.001
Elagolix Endometriosis Phase 3 Pivotal Studies
Change from Baseline in Non-Menstrual Pelvic Pain (NMPP)

### Violet Petal

**Responder Rates**

<table>
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<tr>
<th></th>
<th>Month 3</th>
<th>Month 6</th>
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<tbody>
<tr>
<td>PBO (n=373)</td>
<td>36.5</td>
<td>34.9</td>
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<tr>
<td>E150 QD (n=248)</td>
<td>50.4</td>
<td>54.5</td>
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<tr>
<td>E200 BID (n=244)</td>
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<td><strong>62.1</strong></td>
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*P vs. PBO: <0.001; **P vs. PBO: <0.01; ***P vs. PBO: 0.003

### Solstice

**Responder Rates**

<table>
<thead>
<tr>
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<th>Month 3</th>
<th>Month 6</th>
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<tbody>
<tr>
<td>PBO (n=353)</td>
<td>36.5</td>
<td>40.6</td>
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<tr>
<td>E150 QD (n=221)</td>
<td>49.8</td>
<td>51.6</td>
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<tr>
<td>E200 BID (n=225)</td>
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<td><strong>62.2</strong></td>
</tr>
</tbody>
</table>

*P vs. PBO: <0.001; **P vs. PBO: <0.01; ***P vs. PBO: 0.003
Elagolix Endometriosis Phase 3 Pivotal Studies
Mean Percent Change from Baseline in Bone Mineral Density

Violet Petal

- Limited BMD decrease at Elagolix 150 mg QD
- Higher BMD decrease at 200 mg BID
  - Options for bone protection are under evaluation, including hormonal add-back therapy
- Lupron 3.75 mg IM dosed monthly, is approved for 6 months when used without hormonal add-back therapy

Solstice

Lupron

- Lupron approved for 6mo use

*p vs. PBO: <0.001
**p vs. PBO: 0.002

BMD measured in Lumbar Spine
Elagolix for the Management of Uterine Fibroids

### Uterine Fibroids

**Benign uterine tumors**
- One or multiple tumors
- Tumors are estrogen and progesterone responsive
- Resolve after menopause

**Epidemiology**
- Estimated that the lifetime incidence in pre-menopausal women is 50–80%

**Symptoms:**
- **Heavy menstrual bleeding, often with anemia**
- Bulk symptoms (e.g., pelvic pressure, urinary frequency, etc.)
- Early pregnancy loss and infertility
Elagolix Has the Potential to Provide a Continuously Effective Treatment for Heavy Menstrual Bleeding (HMB) Associated with Uterine Fibroids (UF)

- **Elagolix**
  - Has the potential to provide a continuously effective treatment for HMB associated with UF.

- **OCPs, Progestins**
  - Short-term use
  - Limited Efficacy

- **GnRH agonists**
  - Pre-op short term use
  - No approved add-back

- **Hysterectomy**
  - Fertility loss
  - Surgical risk
  - Myomectomy
  - High recurrence

**Unmet Need**
- Long-term efficacy without surgery
Elagolix Demonstrated Marked Efficacy in Uterine Fibroids in Ph2b Add-back Therapy Is Effective in Preventing Loss of Bone Density

**Heavy Menstrual Bleeding**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% Responders (HMB)</th>
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<tbody>
<tr>
<td>PBO (n=64)</td>
<td>26.6</td>
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<tr>
<td>E300 BID (n=62)</td>
<td>91.9 *</td>
</tr>
<tr>
<td>E300 BID + LDA (n=62)</td>
<td>85.5 *</td>
</tr>
<tr>
<td>E300 BID + add-back (n=62)</td>
<td>79 *</td>
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</table>

**Bone Mineral Density**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Change from Baseline in Spinal BMD</th>
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<tbody>
<tr>
<td>Placebo</td>
<td>0.78</td>
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<tr>
<td>E Alone</td>
<td>-3.59 *</td>
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<tr>
<td>E + add-back</td>
<td>-0.12 **</td>
</tr>
</tbody>
</table>

*E = Elagolix 300 mg BID
Add-back = standard dose Activella (E2 1.0 mg/NETA 0.5 mg) QD

*P vs. PBO: <0.001; **P vs. PBO: 0.148
Elagolix on Track to Be the First Approval for Endometriosis Since Lupron in 1990

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12mo data
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Regulatory submission
Regulatory approval
Zinbryta and ABT-555

Laura Gault, M.D., Ph.D.
Development

Eric Karran, Ph.D.
Discovery
AbbVie Neuroscience: Providing Novel and Effective Treatments for Neurodegenerative Disorders

**Parkinson’s Disease**
- Symptomatic Treatments
- Disease Modification
- Less invasive, efficacious symptomatic treatments
- Halt disease progression

**Multiple Sclerosis**
- Immunomodulation, Neuroprotection, Neuroregeneration
- Higher efficacy and manageable safety
- Improve function

**Alzheimer’s Disease**
- Disease Modification
- Maintain function
- Identify appropriate time to initiate treatment
**Abbvie Neuroscience Pipeline**

*Marketed Products and Select Clinical Development Programs*

### Parkinson’s Disease

**Duodopa/Duopa:** Levodopa-Carbidopa Intestinal Gel
- Marketed worldwide
- Improves function

### Multiple Sclerosis

**Zinbryta:** Anti-CD25 mAb
- Partnered with Biogen
- Demonstrated reduction in relapse and disability progression

**ABT-555:** RGMa mAb
- Phase 1
- Extensive preclinical evidence of neuroprotection and regeneration
- Based on biology pioneered at AbbVie*

### Alzheimer’s Disease

**ABBV-8E12:** Anti-tau mAb
- Phase 1
- Targets tau pathology
- Initial antibody development in Holtzman lab at Washington University

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* Demicheva et al., 2015, Cell Reports 10:1-12
MS Is an Unpredictable, Progressive, Immune-mediated Disease

MS progression over time

1. Inflammation
2. Demyelination
3. Axonal loss
4. Atrophy

Time since onset of disease

Inflammation in the CNS
Regeneration
Neurodegeneration

MS = Multiple Sclerosis  CNS = Central Nervous System
AbbVie is committed to meeting all the needs of patients with MS:

- Zinbryta will provide a novel immunomodulatory treatment option for patients
- ABT-555 under evaluation for neuroprotective and neuroregenerative effects
People with MS Need Additional Innovative Therapies

- Age of onset in the 30s, with unpredictable severity and progression
- Relapses often occur on initial therapies, prompting switch to another medication
- Drug efficacy/safety profiles inform the right choice for each patient
- New treatments with novel mechanisms of action are needed to provide additional individualized treatment options
Zinbryta (daclizumab)
Novel Mechanism to Address Unmet Needs in Multiple Sclerosis

• Humanized IgG1 mAb that binds specifically to the α-subunit of the interleukin-2 receptor (CD25, IL-2Rα)

• Novel biology – selectively blocks high affinity IL-2 receptor signaling:
  – Specifically inhibits activated effector T cells
  – Expands immunoregulatory CD56brightNK cells
  – Decreases regulatory T (Treg) cells
  – Immunomodulatory effects without broad immune cell depletion

Zinbryta Demonstrated Efficacy in Two Pivotal Trials

**SELECT STUDY**

- **Placebo** (n=196): 0.46
- **Zinbryta 150mg** (n=201): 0.21
- **Zinbryta 300mg** (n=203): 0.23

**Decade Reductions**:
- **Placebo**: 54% reduction, *P* < 0.0001
- **Zinbryta 150mg**: 50% reduction, *P* = 0.0002

Zinbryta 150 mg demonstrated a 54% reduction in annualized relapse rate v placebo over 52 weeks

12 week confirmed disability progression

13% (placebo) v 6% (Zinbryta), *p* = 0.02

**DECIDE STUDY**

- **IFN Beta-1a** (n=922): 0.395
- **Zinbryta 150mg** (n=919): 0.216

**Decade Reductions**:
- **IFN Beta-1a**: 45% reduction, *p* < 0.0001
- **Zinbryta 150mg**: 45% reduction

Zinbryta 150 mg demonstrated a 45% reduction in annualized relapse rate v IFN beta-1a at 2-3 years

12 week confirmed disability progression

14% (IFN beta-1a) v 12% (Zinbryta), *p* = 0.16

Gold et al., *Lancet* 2013 (SELECT); Kappos et al., NEJM, 2015 (DECIDE)
Benefit/Risk of Zinbryta Consistent with Other High Efficacy Agents

- Overall exposure in clinical trials is approximately 4,100 patient years
  - 2,133 MS patients treated with Zinbryta, for up to six years

- Warnings include: Hepatic injury, immune mediated disorders, acute hypersensitivity, infections, depression and suicide

- The most common adverse reactions (incidence ≥5% and ≥2% higher incidence than comparator) were: Nasopharyngitis, upper respiratory tract infection, influenza, dermatitis/rash, oropharyngeal pain, bronchitis, eczema, lymphadenopathy, depression, pharyngitis, and increased alanine aminotransferase (ALT)

- Zinbryta risks and side effects are generally manageable, including a REMS program with monthly monitoring
Zinbryta: A New Efficacious Treatment Option for People with Relapsing Forms of Multiple Sclerosis

Increased efficacy (v IFN beta-1a) with a unique mechanism of action and convenient administration

- Novel mechanism of action that inhibits activated T-cells, while major immune cell subsets (T, B, NK) remained within normal ranges
- Zinbryta has shown superior, sustained efficacy versus IFN beta-1a (a standard first line therapy)
- Zinbryta risks and side effects are generally manageable, including a REMS program with monthly monitoring
- Monthly, self-administered subcutaneous dosing
A Fundamental Abnormality in MS and Spinal Cord Injury is Increased RGMa; Neutralizing RGMa Is a Way to Allow Nerves to Regenerate

RGMa expression in MS promotes degeneration and inhibits axon regrowth and remyelination

ABT-555 blocks the effects of RGMa enabling axonal regeneration and remyelination
Anti-RGMA mAbs Demonstrated Neuroprotective and Neuroregenerative Effects in Preclinical Models of Neuroinflammatory Injury

**Targeted Optic Nerve Model**

- Inflammatory cytokines injected into optic nerve
- Rats treated systemically with anti-RGMA antibody showed increased growth of nerve fibers into inflammatory lesion

**Targeted Spinal EAE Model**

- Injection of inflammatory cytokines into rat spinal cord
- Anti-RGMA antibody administered after injury at weekly intervals improved recovery
Anti-RGMa mAbs Demonstrated Neuroprotective and Neuroregenerative Effects in Preclinical Models related to MS

- Preclinical experiment in rats that recapitulates aspects of optic neuritis
- Treatment with anti-RGMa antibody preserved approximately 80% of axons compared to only 10% in control antibody treatment group
- Anti-RGMa antibody treatment prevents degeneration of the retinal fiber layer measured by optical coherence tomography (OCT)

### Injury Model

**Normal retina**

**Control Ab**

**Anti-RGMa Ab**

---

**Multiple Sclerosis**

2016

2017

2018

First patient dosed

Initial evidence of biologic activity

Initial evidence of biologic activity

**Spinal Cord Injury**

Patient first dosed
Alzheimer’s Disease Is an Emerging Global Crisis

- **115 million** AD patients by 2050
- Cost of care in the US was **$225 billion** in 2015; will be **$1.1 trillion** by 2050
- **Therapeutic options** for AD are **limited**; progress lags well behind successes in oncology, inflammation, metabolic diseases and cardiology
Alzheimer’s Disease

Amyloid plaques - **do not correlate** with death of neurons or clinical symptoms

Tau tangles - **do correlate** with death of neurons and clinical symptoms
Alzheimer’s Disease

Biochemical phase

Cellular phase

Clinical phase
Recent Advances in Alzheimer’s Research Are Promising

Recent Advances in Alzheimer’s Research Are Promising

Growing understanding of the underlying pathobiology

Primarily Aβ approaches

Increased target diversity

http://memory.ucsf.edu/research/studies/eoad
Recent Advances in Alzheimer’s Research Are Promising

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Primarily Aβ approaches

Increased target diversity

Trials frequently omit biomarkers of target engagement & efficacy

Availability of biomarkers

Amyloid imaging broadly available, tau imaging emerging, CSF biomarkers

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Primarily Aβ approaches

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Availability of biomarkers

Amyloid imaging broadly available, tau imaging emerging, CSF biomarkers

Novel clinical trial designs

Mild to moderate patients

MCI/presymptomatic patients
Foundational Neuroscience Center

• To **gain** a fundamental understanding of disease processes and targets.

• To **execute** the highest caliber science internally and with world-class academic researchers and biotechs.

• To **populate** the AbbVie Neuroscience portfolio with innovative drug targets.

• Three focus areas:
  – **Tau pathobiology** spreading through the brain
  – **Neuroinflammation**: Microglial biology informed by new genetic findings
  – **Autophagy**: Why can’t brain cells clear abnormal, toxic protein aggregates?
Amyloid/Aβ-based Therapeutics – AbbVie’s Perspective
Amyloid/Aβ-based Therapeutics – AbbVie’s Perspective

All causal mutations increase the probability of amyloid depositing in the brain. This is consistent with amyloid triggering the disease process, rather than driving it.

Amyloid/Aβ-based Therapeutics – AbbVie’s Perspective

Tau Protein Supports the Intracellular “Skeleton” of Neurons

Normal

Alzheimer’s Disease

Tau Protein Supports the Intracellular “Skeleton” of Neurons

Normal

Alzheimer’s Disease

The Potential for Tau Therapeutics

- Tau pathology correlates spatially with symptomatology
- Amyloid does not

The Potential for Tau Therapeutics

Braak stages  
I-II  
III-IV  
V-VI  

Braak & Braak  
Acta Neu  
82:239-259  
(1991)

Therapeutic intervention

Braak Stage

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MMSE Score

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MCI  
Mild  
Moderate  
Severe  

Wischik et al  
Em  
Drugs &  
Targets For AD  
1:210-232  
(2010)
ABBV-8E12 Proposed to Prevent Spread of Tau Pathology by Disrupting Transcellular Propagation of Misfolded Tau

Misfolded tau “seeds” released into synapses and taken up by 2° neurons. Serve as templates that seed further aggregation in downstream neuron. Process repeated. Tau pathology is spread along neuronal pathways and networks.

ABBV 8E12 antibody prevents misfolded seeds from being taken up by downstream neurons – pathology is ameliorated.
ABBV-8E12 History and Preclinical Data

In-licensed from C2N in March 2015

Anti-tau antibody inhibits tau seeding in vitro


Anti-tau antibody reduces tau aggregates in vivo (P301S) tau transgenic mouse

Progressive Supranuclear Palsy

Alzheimer’s Disease

First patient dosed 2015

Initial evidence of biologic activity 2016

Additional evidence of biologic activity 2017

First opportunity to demonstrate clinical efficacy 2018

First patient dosed 2015

Initial evidence of biologic activity 2016

Additional evidence of biologic activity 2017

First opportunity to demonstrate clinical efficacy 2018
Summary

• The inauguration of the Foundational Neuroscience Center in Cambridge exemplifies AbbVie’s commitment to finding effective disease-modifying therapies for Alzheimer’s disease.

• The FNC will grow over the next two years and deliver new therapeutic targets to the neuroscience portfolio.

• Neuroscience is developing a suite of anti-tau antibodies to augment our first clinical candidate ABBV 8E12.