Takeda Research Investment, Inc.

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Takeda is a research-based global pharmaceutical company. As the largest pharmaceutical company in Japan and one of the global leaders of the industry, Takeda focuses on therapeutic areas including diabetes, cardiovascular disease, oncology, gastroenterology and neurology.

228 years old
- Founded in 1781 and incorporated in 1925

- Net Sales (FY’08) : ¥1,375 billion ($13.748 billion)*
  - Net Income (FY’08) : ¥355 billion ($3.555 billion)*

- #15 in Global Rx Sales (as of 12/2008)
- Approximately 15,000 Employees Worldwide (as of 2008)

* Exchange rate of ¥ 100= $1
Takeda’s Growth in North America

- Joint research partnership with Abbott (1977)
- Commercial JV (TAP) with Abbott (1985)
- Independent development organization, Takeda Research & Development Center (1994)
- Dissolution of the TAP JV, integrating TAP into TPNA/TGRD (2008)
- Takeda Canada, Inc. established (March 2009)
- Takeda Pharmaceuticals North America (TPNA) (1998)
- Acquire Millennium Pharmaceuticals (2008)
- Takeda Global Research & Development Center (TGRD) (2004)
- Takeda Pharmaceuticals Mexico, S.A. de C.V. established (Sept 2009)
Commitment to Partnerships

Past and present partners include:
Takeda Research Investment, Inc.

www.tri-takeda.com

- Operations started April 2002
  - 100% US subsidiary of Takeda
- Palo Alto, CA – “Biotech Bay”

- Broad + deep global networks to maximize deal flow
  - E.g. A M Pappas Life Sciences Fund III LP
Organization Chart and TRI

CEO

BD

Corporate Planning

MPI

CSO

CAO

IO

Global Develop

CMC

Pharm. Res.

PRD

CMC

Financial

Legal

GA

CC

3 Companies in NA

11 Companies in EU

5 Companies in Asia

IP

TRI

Takeda Research Investment, Inc.
Investment Budget

- Committed Capital: $100 million
- Investment Size: $0.5 - $3 million (co-invest)
- Under Management: $30mm
- Budget: PRD research budget
- Annual budget: project by project
- Limitation: <15% shares
### Venture Investment

<table>
<thead>
<tr>
<th>Investment Stage:</th>
<th>Seed → Mid-Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Criteria:</td>
<td>Innovative target, product, technology concepts; Strong management; Globally solid IP position</td>
</tr>
<tr>
<td>Sector Preference:</td>
<td>All major disease areas; industry and academia</td>
</tr>
<tr>
<td>Geographic Preference:</td>
<td>USA; Canada; Europe</td>
</tr>
</tbody>
</table>
Mission

- A strategic “intelligence hub” - enrich Takeda drug discovery and development capabilities
  - Venture Investment
  - Research Alliances and Collaborations
  - Pre-IND Product Licensing
- As a strategic investor, TRI focuses on extracting **strategic benefits** from portfolio companies, **not financial returns** as a primary goal
<table>
<thead>
<tr>
<th>Company</th>
<th>Investment Type</th>
<th>% Strategic</th>
<th>% Financial</th>
<th>Purpose</th>
<th>Started</th>
<th># Deals</th>
<th>$</th>
</tr>
</thead>
<tbody>
<tr>
<td>J&amp;J Dev. Corp</td>
<td>70</td>
<td>30</td>
<td></td>
<td>Evergreen: Access technologies to accelerate internal process</td>
<td>1973</td>
<td>194</td>
<td>$5MM / round</td>
</tr>
<tr>
<td>GSK / SR-One</td>
<td>10</td>
<td>90</td>
<td></td>
<td>$500mm: Enabling technologies, drug candidates. Long term capital gains</td>
<td>1985</td>
<td>106</td>
<td>$0.5-5MM / round</td>
</tr>
<tr>
<td>Novartis Venture Fund</td>
<td>10</td>
<td>90</td>
<td></td>
<td>Evergreen - $650mm: Company spin-offs; New businesses; long term capital</td>
<td>1996</td>
<td>135</td>
<td>$0.5-5MM / round</td>
</tr>
<tr>
<td>Merck Capital Ventures</td>
<td>70</td>
<td>30</td>
<td></td>
<td>Evergreen: Access technologies to accelerate internal process</td>
<td>2000</td>
<td>9</td>
<td>$3MM / round $8MM total</td>
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<tr>
<td>Novo Nordisk Biotech Fund</td>
<td>90</td>
<td>10</td>
<td></td>
<td>Evergreen: Access technologies to accelerate internal process</td>
<td>2000</td>
<td>15</td>
<td>~$2MM / round</td>
</tr>
<tr>
<td>TRI</td>
<td>100</td>
<td>0</td>
<td></td>
<td>$100mm: Therapeutic and drug discovery technologies</td>
<td>2004</td>
<td>10</td>
<td>$3MM / round</td>
</tr>
<tr>
<td>Lilly Bioventures</td>
<td>10</td>
<td>90</td>
<td></td>
<td>Evergreen - $175mm: Enabling technologies for drug discovery, drug products</td>
<td>2001</td>
<td>26</td>
<td>$3MM / round $5-6MM total</td>
</tr>
<tr>
<td>GenenFUND</td>
<td>90</td>
<td>10</td>
<td></td>
<td>Evergreen: Access technologies to accelerate internal process</td>
<td>2002</td>
<td>29</td>
<td>$0.5-2MM</td>
</tr>
<tr>
<td>MedImmune (Astra Zeneca) Ventures</td>
<td>50</td>
<td>50</td>
<td></td>
<td>$300mm: Therapeutic pipeline; Enabling technologies for drug discovery; drug products</td>
<td>2002</td>
<td>31</td>
<td>$7MM / round $30MM total</td>
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<tr>
<td>Roche Venture Fund</td>
<td>10</td>
<td>90</td>
<td></td>
<td>Evergreen - $450mm: Enabling technologies, drug candidates. Long term capital gains</td>
<td>2002</td>
<td>31</td>
<td>$1-3MM / round</td>
</tr>
<tr>
<td>Amgen Ventures</td>
<td>70</td>
<td>30</td>
<td></td>
<td>$100mm: Enabling technologies, drug candidates. Long term capital gains</td>
<td>2004</td>
<td>16</td>
<td>$1-3MM / round</td>
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<tr>
<td>Biogen-Idec New Ventures</td>
<td>50</td>
<td>50</td>
<td></td>
<td>$100mm: Enabling technologies, drug candidates. Long term capital gains</td>
<td>2004</td>
<td>7</td>
<td>$1-5MM / round</td>
</tr>
<tr>
<td>Pfizer Venture Investments</td>
<td>70</td>
<td>30</td>
<td></td>
<td>$200mm: Strategic; 5-10 year ROI horizon</td>
<td>2004</td>
<td>12</td>
<td>$0.1-10MM / round $10MM total</td>
</tr>
<tr>
<td>Novartis Option Fund</td>
<td>10</td>
<td>90</td>
<td></td>
<td>$200mm: Early stage, high-risk, high return with limited term option to specific product/technology. Capital gains</td>
<td>2007</td>
<td>6</td>
<td>$1-3MM / round</td>
</tr>
<tr>
<td>Merck-Serono Ventures</td>
<td>60</td>
<td>40</td>
<td></td>
<td>$51mm: Enabling technologies, drug candidates. Long term capital gains</td>
<td>2009</td>
<td>2</td>
<td>$1-3MM / round</td>
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</tbody>
</table>

**Pharma Corporate Venture Groups 2009**

Takeda Research Investment, Inc.
Role for invested companies

- As a minority investor, TRI assists a passive role in management
  - Board observer, not director
  - provide knowledge as an integrated pharma
  - **endorse** product/tech. through DD
- TRI introduces product/technology to TAKEDA, potential **end user** of them
Investment Portfolio 2008

CA, USA (Seed + Series A): Oncology focused, product-oriented, novel targets, biotherapeutics

Cambridge, UK (Seed + Series A): Enabling platform for proteomics-based ion channel screening, novel small molecule modulators with improved selectivity

NC, USA (Series B-1 + Series C + Series D): Enabling platform, product-oriented, novel oncology targets, small molecules

Copenhagen, Denmark (Series E): Polyclonal antibodies discovery and development

Vancouver, Canada (Series E): Clinical genetics-based drug R&D, novel targets for CNS and CVS diseases

Melbourne, Australia (Seed + IPO): Human antibody development with emphasis on IgM antibodies for cancer
Cambridge, UK (Series A): Unique “hub and spoke” model with multiple exclusive agreements with leading researchers focused on epigenetics and mechanisms that determine cell fate.

Success or Failure?

<table>
<thead>
<tr>
<th>Year</th>
<th>Action</th>
<th>Result</th>
<th>Comment</th>
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</thead>
<tbody>
<tr>
<td>1st year</td>
<td>access</td>
<td>MTA→Go</td>
<td>Profit Return</td>
</tr>
<tr>
<td>2nd year</td>
<td>MTA→NoGo</td>
<td>Sold</td>
<td>Sold Buyer’s shares</td>
</tr>
<tr>
<td>3rd year</td>
<td>access</td>
<td>MTA→NoGo</td>
<td>Change the direction</td>
</tr>
<tr>
<td>4th year</td>
<td>access</td>
<td>MTA→NoGo</td>
<td>Out of our focus</td>
</tr>
<tr>
<td>5th year</td>
<td>access</td>
<td>MTA→NoGo</td>
<td>Out of our focus</td>
</tr>
</tbody>
</table>
CVC helps the Start-UP

Scrip’s biotechnology correspondent talks to Dr. Will West, CEO of CellCentric, a UK company whose business strategy involves making epigenetics the next big thing in drug discovery. Since its formulation in 2004, CellCentric has been building an international network of the principal researchers to pool the latest knowledge in the epigenetic arena. One of its investors is Takeda Research Investment, the venture capital arm of Japan’s largest drugs firm, which invested $2MM in exchange for around 15% of the company. CellCentric is in discussion with Takeda and other pharmaceutical companies to enter collaboration based around families of targets and target classes. Dr. West expects CellCentric to reach a crossroads in the next 18 months.

Scrip Dec 5, 2007  3317, p11
In the current economic downturn where 1) VC money is tight and 2) the IPO market is at a standstill, startups are increasingly looking at corporate venture as a means to growth -- or even just survival. What I found interesting in the past few months is "corporate partnerships": what is innovative in a startup's technology or business model is evaluated both in terms of the potential value for the corporation but also in terms of what the corporation can help that startup further develop. (Anne-Marie Roussel 3/24/2009)

CellCentric’s strategy is to develop a broad portfolio of epigenetic-related intellectual property generated with leading epigenetic researchers Worldwide

Through TRI investment, Takeda researchers enjoy not only early access to multiple potential drug target opportunities in the field of epigenetics, but also access to wide network of relationships with opinion leaders in epigenetics. This type of access itself is our strategic return.

In return, Takeda provides the integrated R&D with marketing needs knowledge to help the start-up makes the right decision to develop.