Geriatric Rounds:  
Compounds of Medical Need  
March 28, 2014

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Adjunct Asst. Professor of Medicine
My Background at Penn
(Disclosure Slide)

- 1978-1981 Mycobacterial Laboratory Supervisor (H.U.P.)
- 1980-1987 Ph.D. Studies
- 1988-1992 Instructor of self-written course (Grad. Sch. of Education)
- 1994- Instructor, School of Dental Medicine
- 1995-1997 Adjunct Asst. Prof. (Geriatrics – Risa Mourey)
- 2007- Pres Adjunct Asst. Prof. (Geriatrics – Jerry Johnson)

Other:
- 1970-1976 Army National Guard
- 1976-1978 Grad. Teaching Asst for Master’s Degree – West Chester University
- 1982-1988 Smithkline Beecham
- 1996 Founder Of PA Osteoporosis Society
Drug Development Strategy Grid

- Pre-Approval
- Approval Window (DiMasi Window)
- Post-Approval

Average Approval Time: 8-12 years

Average R&D Investment: $800 mil--$1.2 bill.

Return Potential

Other necessary increases over time in R&D expenditures

Discovery

PATENT BEGINS

5

10

15

20

TIME SINCE DISCOVERY (Years)

PATENT ENDS

BILLIONS OF DOLLARS

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Exclusivity Data from DiMasi, Tufts, Sep 2009; Approval Window Data from Tufts, 2007
Generic Presence in 2008 Prescriptions

Source: IMS Data as of February, 2008
Generic Presence in 2013 Prescriptions

Branded: 16%
Generic: 84%

Source: Kaiser Health News as of May 9, 2012

Copyright: A. Giovenella, 2009
Evolved Alternative Pathway for the Drug Discovery Process

Traditional Drug Research Pathway for Pharma

- Laboratory Discovery (In-vitro)
- Pre-Clinical Research
- Phase I
- Phase II
- Phase III
- NDA

Optimal Range of Compound Acquisition

Increasing Risk to Adverse (Unmanageable) Levels

Biotech

Acquisition Drug Research Pathway

Looking for Exit Strategy

Managing Risk

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In the FDA SIA (Safety and Innovation Act) of 2012, in Section 902, the FDA allowed for **BREAKTHROUGH THERAPY DESIGNATIONS** in order to expedite development and review of drugs for life-threatening and serious diseases.

In order for the sponsor to receive this designation for a drug in development, the sponsor must show:

1) Evidence that the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and

2) Preliminary *clinical* evidence indicating that the drug may demonstrate substantial improvement over existing therapies on one or more *clinically significant endpoints*, such as substantial treatment effects observed early in clinical development.

**Source:**
http://orphandruganaut.wordpress.com/2013/12/23/fda-breakthrough-therapy-designation-2013
# FDA CDER & CBER
## Breakthrough Therapy Designations
### (As of March, 2014)

<table>
<thead>
<tr>
<th>Small Molecules</th>
<th>Biologics</th>
<th>Vacc</th>
<th>GSK</th>
<th>Novartis</th>
<th>Roche</th>
<th>Pharmacy</th>
<th>Vertex</th>
<th>USA</th>
<th>Other Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>4(1)</td>
<td>2(1)</td>
<td>3</td>
<td>4</td>
<td>22</td>
<td>13</td>
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<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>NDA Sub</th>
<th>Appr</th>
<th>Kinase Inh</th>
<th>Polym/Prot</th>
<th>B Cell Targets</th>
<th>CFTR</th>
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<tbody>
<tr>
<td>2</td>
<td>10</td>
<td>16</td>
<td>1</td>
<td>5</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td>3</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Mkt Cap ($)</th>
<th>Therap Area</th>
<th>Disease State</th>
<th>Approved:</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;200 BN</td>
<td>Oncology</td>
<td>Cancer</td>
<td>2013</td>
</tr>
<tr>
<td>150-200</td>
<td>Anti-infective</td>
<td>Hepatitis C</td>
<td>Oncology</td>
</tr>
<tr>
<td>100-150</td>
<td>Respiratory</td>
<td>Cyst Fibrosis</td>
<td>Anti-infective</td>
</tr>
<tr>
<td>76-100</td>
<td>Metabolism</td>
<td>Cancer</td>
<td>2014</td>
</tr>
<tr>
<td>51-75</td>
<td>Muscle</td>
<td>Cancer</td>
<td>Oncology</td>
</tr>
<tr>
<td>26-50</td>
<td>Neurology</td>
<td>Cancer</td>
<td>2013</td>
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<tr>
<td>11-25</td>
<td>Cardiology</td>
<td>Cancer</td>
<td>Oncology</td>
</tr>
<tr>
<td>1-10</td>
<td>Dermatology</td>
<td>Cancer</td>
<td>Anti-infective</td>
</tr>
<tr>
<td>&lt;100 MIL</td>
<td>Hematology</td>
<td>Cancer</td>
<td>2014</td>
</tr>
<tr>
<td>PRIV</td>
<td></td>
<td>Cancer</td>
<td>Oncology</td>
</tr>
</tbody>
</table>

*Copyright: A. Giovenella, 2013*
Other Diseases Targeted by Breakthrough Therapy Drugs

- Hepatitis C (3 entries)
- Cystic Fibrosis (2 entries)
- Duchenne Muscular Dystrophy
- Malaria (*Plasmodium vivax*)
- Bleeding Disorder from Factor Xa inhibitors
- Molybdenum Cofactor Deficiency Type A
- Sporadic Inclusion Body Myositis
- Lysosomal Acid Lipase Deficiency (Wolman Dis)
- Epidermolysis Bullosa
- Lambert-Eaton Myasthenic Syndrome
- Bacterial Meningitis Type B
Breakthrough Designations by Therapeutic Area in U.S. Since 2013

N = 35

2013 - 2014

Source: FDA Database, PharmaLive, Evaluate Pharma
& A. Giovenella
March 28, 2014

Copyright: A. Giovenella, 2014
Breakthrough Designations by Therapeutic Area in U.S. Since 2013

\[N = 35\]

Oncology (4 B)
- Onc-13 (2)
- Onc-14 (1)

Antiinfective (6)
- AI-13 (1)
- AI-13 (1)

Metabolism (3)
- Resp-14 (1)

Respiratory (3)
- Resp-14 (1)

Cardiology (1)
- 1 Cardiology

Dermatology (1)
- 1 Dermatology

Hematology (2)
- 2 Hematology

Muscle (1 B)
- 1 Muscle (1 B)

Neurology (1)
- 1 Neurology

BIOLOGICS (5 inc)
- 5 BIOLOGICS (inc)

Total Breakthrough Designations:
- 14 Oncology
- 6 Antiinfective
- 3 Metabolism
- 3 Respiratory
- 2 Muscle
- 1 Neurology
- 1 Cardiology
- 1 Dermatology
- 2 Hematology
- 1 Muscle
- 0 GI
- 0 Anti-inflammatory
- 0 OB-GYN
- 0 Anesthesiology
- 0 Analgesic
- 0 Bone

Source: FDA Database, PharmaLive, Evaluate Pharma & A. Giovenella
March 28, 2014
# Time from Designation to Approval Since 2013

**N = 5**

## Year 2013:
- **4 mo – Hepatitis C**: $91.3 B MC (Ph III) A-I (Gild)
- **6 mo – Chron Lym Leuk**: $171.7 B MC (Ph III) Onc (Roch)
- **7 mo – Mantle Cell Lymph**: $263.2/$9 B MC (Ph III) Onc (Ph/J&J)

## Year 2014:
- **10 mo – Chron Lym Leuk**: $260.4 B/ $10.1 B (Ph III) Onc (Ph/J&J)
- **13 mo – Cyst Fibro (8 mut)**: $20.0 B (Ph III) Resp (Vtx)

Source: FDA Database, PharmaLive, Evaluate Pharma & A. Giovenella

March 28, 2014

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**Bar Chart**

**2013 - 2014**

- **2013**: 3
  - Hep C: 4
  - CLL: 6
  - Mtl Cell Lym: 7
  - Cyst Fib: 2
- **2014**: 2
  - Hep C: 10
  - CLL: 13
  - Mtl Cell Lym: 10
  - Cyst Fib: 7

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Breakthrough Designations by Market Cap in U.S. Since 2013

N = 35

2013 - 2014

Source: FDA Database, PharmaLive, Evaluate Pharma & A. Giovenella
March 28, 2014
Breakthrough Designations by Oncology (Types of Cancer) in U.S. Since 2013

N = 16

Source: FDA Database, PharmaLive, Evaluate Pharma & A. Giovenella
March 28, 2014
Summary

• As biomedical research continues, the FDA has made the “Breakthrough Therapy Designation” (BTD) to expedite development & approval in areas of medical need.

• Approval times for first 5 BTD approvals range from 4 months to 13 months since receiving the designation.

• Oncology research is the dominant therapeutic area receiving BTD thus far.

• In this oncology research, the most BDT designations—and approvals—are for chronic lymphocytic leukemia.