Feeding the Pipeline VII: Clearing the Innovation Bar

Ed Saltzman
Defined Health

LES 2006 Annual Meeting
New York
The information in this presentation has been obtained from what are believed to be reliable sources and has been verified whenever possible. Nevertheless, we cannot guarantee the information contained herein as to accuracy or completeness.

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The Presenter’s Challenge

“The ear tends to be lazy, craves the familiar, and is shocked by the unexpected: the eye, on the other hand, tends to be impatient, craves the novel and is bored by repetition.”

-- W.H. Auden
I. Still stuck in the No-Fun Zone
II. Are the fun times coming back?
III. Licensing to the rescue (again!)
IV. But an ever-increasing list of challenges for those in L&BD:
   – The Typical: The Perennial Late Stage Opportunity Shortage
   – The New: Spiraling Cost of Early Stage Deals
V. Implications and Predictions
   – Lessons from the M&A Space: When Pipelines are Worth More than Products
   – Reverberations from a brutal Biotech IPO market
VI. OK, but I still Need to Find a Product! Take-Homes from the “No-Spin Zone”
   – The New Regulatory Bar: Safety, Efficacy and Medical Necessity
   – Unmet Needs: Let’s Get Serious!
   – Broader isn’t Better: The Coming of the Less Impersonal Blockbuster
The No Fun Zone
Pharma Continues to Dwell in a No Fun Zone

EvaluatePharma, Cowen & Company, June 2006; Defined Health analysis
Pharma Continues to Dwell in a No Fun Zone

Pharma Industry – Trend in Return on Equity

Pharma Industry ROE

EvaluatePharma

EvaluatePharma; Defined Health Analysis

Feeding the Pipeline VII
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Pharma Continues to Dwell in a No Fun Zone


*Through June 20, 2006
Cowen & Company, June 2006; Defined Health analysis
Spiraling R&D Expense and Decreasing Output

Parexel's Pharmaceutical R&D Statistical Sourcebook 2005/2006; DH analysis
The Innovation Deficit Is Making Things Worse

Innovativeness of FDA Approved Drugs (1989-2000)

FIGURE 6
Only 15% of new drugs approved in 1989–2000 were highly innovative priority NMEs.

Distribution of NDAs, 1989–2000
TOTAL = 1,035 NEW DRUGS

MOST INNOVATIVE
15%

LEAST INNOVATIVE
46%

Old Active Ingredients = 65%

Increasing Level of Innovation

NIHCM Foundation, FDA

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FDA OKs pearly pigments to color pills
By ANDREW BRIDGES, Associated Press Writer
Thu Jul 20, 11:03 PM ET

AP Photo: In this photograph provided by EMD Chemicals, Inc., Candurin Pearl Effect Color coated tablets are...

If you think beauty can't go more than skin deep, swallow this: Health officials on Thursday said drug companies could start gussying up their pills with pigments like those that give cosmetics a pearly sheen.

The pearlescent pigments can be used in any drugs that are swallowed, including pills, tablets and liquids, the Food and Drug Administration said. As a result, drugs may never look the same again.

The pigments can produce sparkly metallic, satiny and shimmery finishes, as well as different hues of red and gold, depending partly on the color of the underlying drug.
Though Better than Pharma, Biotech Has Its Own Innovation Gap

Innovativeness of FDA Approved Drugs (2001-2004)

*Distribution of NDAs, Pharma vs. Biotech*  
(Total=619 New Drugs)

Pharma

<table>
<thead>
<tr>
<th>Priority NME</th>
<th>Standard NME</th>
<th>Priority IMD</th>
<th>Standard IMD</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>11%</td>
<td>16%</td>
<td>6%</td>
<td>60%</td>
<td>7%</td>
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Old Active Ingredients = 73%

Biotech

<table>
<thead>
<tr>
<th>Priority NME</th>
<th>Standard NME</th>
<th>Priority IMD</th>
<th>Standard IMD</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>29%</td>
<td>16%</td>
<td>6%</td>
<td>43%</td>
<td>6%</td>
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</tbody>
</table>

Old Active Ingredients = 55%

*NDA sponsors were designated either Biotech or Pharma; includes BLAs
USFDA; DH analysis*
New Biotech Products are Smaller than Current Ones

**WW Peak Sales by Originator**
Top 10 Products per Group

- **Pharma**
- **Biotech**
- **2nd Generation Biotech**

- 2nd Generation Biotech: Alexion, Myogen, Threshold, Antigenics, Telik, Basilea, Dendreon, Keryx and Xenoprot

EvaluatePharma; DH analysis
Is Biotech Facing its Own Innovation Gap?

Biotechnology Companies – Average Peak Year Sales Forecast for First Marketed Product

Company reports; DH analysis

Year of Company Formation

$ Millions

1975-1979: $1,493
1980-1984: $1,079
1985-1989: $299
1990-1994: $971
1995-1999: $397
The Strong Biotechs Are Getting Stronger

Market Cap for Top 10 Biotechs as a Fraction of All Biotechs

- 1995: 90%
- 1996: 82%
- 1997: 78%
- 1998: 73%
- 1999: 73%
- 2000: 63%
- 2001: 62%
- 2002: 73%
- 2003: 71%
- 2004: 71%
- 2005: 76%

EvaluatePharma; Yahoo! Finance
But Very Few New Big Biotechs

Biotech Companies That Have for the First Time Surpassed $3 Billion in Market Cap

EvaluatePharma; Yahoo! Finance
Ligand to Sell Oncology Line to Eisai

© 2006 The Associated Press

SAN DIEGO — Ligand Pharmaceuticals Inc. said Friday it agreed to sell its oncology product line and related assets to Eisai Inc. and Eisai Co. for $205 million in cash.

Teaneck, N.J.-based Eisai and its Tokyo-based unit develop drugs to treat Alzheimer's, acid reflux and convulsions. The sale includes Ligand's four marketed oncology drugs — Ontak, Targretin capsules, Targretin gel and Panretin gel. Ontak is FDA-approved to treat persistent or recurrent cutaneous T-cell lymphoma, while Targretin has proven effective as a treatment for cutaneous T-cell lymphoma.

In February 1999, the FDA granted marketing clearance for Panretin gel for the topical treatment of cutaneous lesions of patients with AIDS-related Kaposi's sarcoma.

Ligand said Eisai will assume all future royalty payment obligations for the products. Eisai will receive all rights to the products worldwide, including related intellectual …

On Thursday, Ligand agreed to sell U.S. and Canadian rights to its Avinza pain drug to King Pharmaceuticals Inc.

"We have now sold our two commercial operations for total cash consideration of $518 million. With the sale of our commercial operations, Ligand will become a dynamic and highly-specialized R&D and royalty company, said Henry F. Blissenbach, Ligand chairman and CEO.

"By the end of 2006, Ligand expects to have new corporate leadership, to have restructured and narrowly focused its research and development endeavors in order to focus on our most promising compounds, and to minimize its expense structure with a goal to be both earnings and cash-flow positive," added Blissenbach.

Shares closed Thursday at $9.95 on the Nasdaq.
Ligand to Sell Oncology Line to Eisai

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When Life Just Blows... FUKIDOL!

http://www.office-humour.co.uk/g/i/1992/
Are the Fun Times Coming Back?
“The science has exploded and all sorts of things are happening… I’m going to stay for a while because I’ve been around for all the crummy stuff, and this is going to be good.”

-- John L. LaMattina, President, Pfizer Global Research and Development
July 18, 2006
The richness of the early-stage pipeline illustrates the replacement power of the Novartis pipeline and demonstrates the continuing high performance of the research organization.

Company press release, January 2005
Early-Stage Pipeline Update

The Company announced that it continues to make progress advancing its early-stage pipeline. Since the start of 2006, five new molecules, two in oncology solid tumors, two for diabetes and one for idiopathic pulmonary fibrosis have been advanced into clinical development. Additionally, two new molecules, one for diabetes and one for pain, have entered the clinic for introduction into humans. During this period, three early-stage programs have been terminated.
…clear improvements in the company's product flow capability and early stage pipeline have been achieved in the past two years.

Company press release, November, 2005
Takeda Pharmaceuticals North America, Inc. (TPNA) is a new kind of pharmaceutical company. We are dedicated to serving patients by providing innovative products that improve their lives with better healthcare. With a foundation built on the tremendous success of ACTOS® (pioglitazone HCl) as well as a robust, early-stage pipeline, TPNA is poised to realize its vision of becoming a world class pharmaceutical company.
More Shots on Goal Have Not Scored More Goals

Index Based on 2001 Status

Number of Compounds in Each Phase of Development By Year

- Phase I
- Phase II
- Phase III

2001 2002 2003 2004 2005

1539 1371 1218 1139 1486 1647 1694 754 781 1485

Phase II Attrition is Skyrocketing

Phase II Failure Rate

- 1991-2000: 60%
- 2005: 80%

Parexel; Robert Ruffolo in Wall Street Journal, Sept. 30, 2005
Licensing to the Rescue (Again)!
In-Licensed Products Will Soon Dominate in Both Number of Top Selling Products & Revenue Contribution

EvaluatePharma, Sept 2006
In-Licensed Revenue to Double Between 2000 & 2009
From 2000 – 2009, Revenues From In-Licensed Drugs will Grow 1.6X Faster Than for Internal Compounds

EvaluatePharma; DH analysis
In-Licensed Drugs are More Likely to be Approved the First Time Around

Approval Rate by Drug Origin

Self-Originated

N=60

55%

42%

In-Licensed

N=17

35%

65%

Big Biotech Would Be Less “Big” Without Externally-Sourced Products

**Amgen**

Self marketed products for which sales are booked only, excludes royalties from out-licensed products not booked as sales.

*EvaluatePharma; Defined Health analysis*
Big Biotech Would Be Less “Big” Without Externally-Sourced Products

Genentech

Self marketed products for which sales are booked only, excludes royalties from out-licensed products not booked as revenues.

EvaluatePharma; Defined Health analysis
Big Biotech Would Be Less “Big” Without Externally-Sourced Products

Genzyme

Self marketed products for which sales are booked only, excludes royalties from out-licensed products not booked as revenues.

EvaluatePharma; Defined Health analysis
Big Biotech Would Be Less “Big” Without Externally-Sourced Products

Medimmune

Self marketed products for which sales are booked only, excludes royalties from out-licensed products not booked as revenues.

EvaluatePharma; Defined Health analysis
But an Ever-Increasing List of Challenges...
An Ever-Increasing List of Challenges

The Usual:
The Perennial Late-Stage Opportunity Shortage

The New:
The Spiraling Cost of Early-Stage Deals
An Ever-Increasing List of Challenges

The Usual:
The Perennial Late-Stage Opportunity Shortage
“Hey, I said this in 2000!”

“Of course, we’d all like low-priced, low-risk Phase III products with wonderful programs, but there are very few of them, and when they do exist, you end up spending top-dollar.”

-- John Patterson, Executive Director, Development, AstraZeneca
Quoted in Chemical & Engineering News
March 6, 2006
“There are Very Few of Them…”

Trend in Number of Phase III Deals

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Deals</th>
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<tbody>
<tr>
<td>2002</td>
<td>11</td>
</tr>
<tr>
<td>2003</td>
<td>10</td>
</tr>
<tr>
<td>2004</td>
<td>11</td>
</tr>
<tr>
<td>2005</td>
<td>13</td>
</tr>
<tr>
<td>Q1-3/06</td>
<td>6</td>
</tr>
</tbody>
</table>

Company reports; ReCap; DH analysis
“…and you end up paying top dollar”

Index of Deal Upfronts for Phase II & Greater Deals
1994 - 2006

CPI: Consumer Price Index
DPI: Deal Price Index

Note: Includes deals signed in Phase II, III, and after filing; only those with ascertainable upfront payments
DH analysis based on data presented by Oxford Bioscience Partners
(*): Projection applying historic trend
An Ever-Increasing List of Challenges

The Usual:
The Perennial Late-Stage Opportunity Shortage

The New:
The Spiraling Cost of Early-Stage Deals
Early Stage Deals Have Only Recently Become Expensive: The Early Stage DPI vs. The CPI

Index of Deal Upfronts For Phase I Deals 1994-2006

CPI: Consumer Price Index
DPI: Deal Price Index

Note: Includes deals signed in Phase I; only those with disclosed/ascertainable upfront payments
DH analysis based on Recap Data
(*) as of September 06
Skyrocketing Ph I Prices but Pharma’s Still Buying!

* Includes 2006 deals completed to-date (September 11, 2006)

EvaluatePharma, Recombinant Capital; Defined Health analysis
“In spite of the cost of living, it's still popular.”

-- Kathleen Norris
Pay Now or Pay Later? The Biggest Pharmas are Not the Biggest Buyers of Phase I Products

Phase I Deals by Selected Pharmacos 2002-2006

Company reports; Recap; DH analysis

Roche  Novartis  Pfizer  GlaxoSmithKline  AstraZeneca  sanofi-aventis
Big Phase I Deals: The New Sticker Shock

**Roche/Actelion**
- July 2006: $630 MM
- $75 MM upfront, $550 MM milestones, royalties, profit share
- Autoimmunity, multiple indications
- WW single compound license (S1P1 receptor agonist), plus platform
- Actelion to fund into Phase II for 2 indications

**Infinity/Medimmune**
- August 2006: $500 MM
- $70 MM upfront, $430 milestones
- Cancer (multiple types)
- WW single compound license (hedgehog inhibitor), and agreement to jointly develop compounds against hh and Hsp 90
- Shared development costs

Company reports; Recap; DH analysis
Big Phase I Deals: The New Sticker Shock

Sankyo/Ajinomoto

- August 2006: Yen 4.6 B
- $39 MM upfront, undisclosed milestones, royalties
- Diabetes
- WW Single product license (new pathway activates the insulin signaling pathway), plus platform
- Joint development for certain programs
Deal Nostalgia Quiz # 1

Date: 1996
Financials: Upfront $20 MM for US, $5 MM for ROW, $170 MM milestones; Total Deal $200 MM
Territory: WW
Phase: III
Therapeutic Area: Cardiovascular
Product: ?/?/?
Peak Year (2008) Consensus Forecast = $12.6 B

Analyst Consensus Forecasts, Evaluate Pharma
Deal Nostalgia Quiz # 2

Date: 1997

Financials: Upfront $15 MM, $85 MM

Milestones

Territory: North America

Phase: III

Therapeutic Area: Rheumatoid Arthritis

Product: ?//?/?
2010 Consensus Forecast = $6.8 B

Analyst Consensus Forecasts, Evaluate Pharma
Deal Nostalgia Quiz # 3

Date: 1998
Financials: Upfront $85 MM for US, $155 MM
Milestones
Territory: North America
Phase: III
Therapeutic Area: Pain
Product: ?/?/?
2010 Consensus Forecast = $3.3 B

Analyst Consensus Forecasts, Evaluate Pharma
Deal Nostalgia Quiz # 4

Date: 2001
Financials: Upfront $11 MM, $27 MM
Milestones
Territory: North America
Phase: III
Therapeutic Area: Supportive Oncology
Product: ?/?/?
2010 Forecast = $383 M

Analyst Consensus Forecasts, Evaluate Pharma
Deal Nostalgia Quiz # 5

Date: 2001
Financials: Upfront $200 MM, $800 MM
Milestones
Territory: WW
Phase: III
Therapeutic Area: Oncology
Product: ?/?/?
2010 Consensus Forecast = $2.9 B

Analyst Consensus Forecasts, Evaluate Pharma
Deal Nostalgia Quiz # 6

Date: 2002

Financials: Upfront $110 MM, $335 MM

Milestones

Territory: WW

Phase: III

Therapeutic Area: Diabetes

Product: ?/?/?
2010 Consensus Forecast = $1.3 B

Analyst Consensus Forecasts, Evaluate Pharma
Implications and Predictions
"Those who have knowledge, don't predict. Those who predict, don't have knowledge."

-- Lao Tzu, 6th Century BC Chinese Poet
Ed: Circa 1985
Ed: Circa 1995
Ed: Present Day
<table>
<thead>
<tr>
<th></th>
<th>Very Comfortable</th>
<th>Less Comfortable</th>
<th>Very Uncomfortable</th>
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<tr>
<td><strong>80’s</strong></td>
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<tr>
<td><strong>Comfort Factor</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Ph III Inventory</td>
<td>Plentiful</td>
<td>Scarce</td>
<td>Extinct!</td>
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<tr>
<td>Late Stage Deal Cost</td>
<td>Inexpensive</td>
<td>Getting pricy</td>
<td>Priceless</td>
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<tr>
<td>Commercial Risk for</td>
<td>Nil</td>
<td>Increasing</td>
<td>Forget about it!</td>
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<tr>
<td>Follow-Ons</td>
<td></td>
<td></td>
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<tr>
<td>Biotechs Willing to</td>
<td>Most</td>
<td>Few</td>
<td>None</td>
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<tr>
<td>Cede Complete Control</td>
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<td></td>
<td></td>
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<tr>
<td>Early Inventory</td>
<td>Who cared?</td>
<td>Who cared?</td>
<td>Generous</td>
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<tr>
<td>Early Stage Deal Cost</td>
<td>Dirt cheap</td>
<td>Cheap</td>
<td>Getting very pricey</td>
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<tr>
<td>Revenue Bar</td>
<td>$500mm</td>
<td>$1b</td>
<td>Lipitor</td>
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<tr>
<td></td>
<td>80’s</td>
<td>Early-Mid 90’s</td>
<td>Late 90’s-Present</td>
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<tr>
<td><strong>Comfort Factor</strong></td>
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<tr>
<td>Number of Potential</td>
<td>Numerous</td>
<td>Shrinking</td>
<td>Shrinking more</td>
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<td>Big Pharma Partners</td>
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<tr>
<td>Big Pharma’s</td>
<td>Bring ‘em on</td>
<td>First or second</td>
<td>Hopefully, it’s</td>
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<td>such an</td>
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<td>on Commercially</td>
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<td></td>
<td>innovation that</td>
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<tr>
<td>Challenging Products</td>
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<td>it doesn’t</td>
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<td>Need to In-License as</td>
<td>I’m a genius.</td>
<td>How much will</td>
<td>How soon can</td>
</tr>
<tr>
<td>Well as Out-License</td>
<td>Why would I</td>
<td>that sales force</td>
<td>you guys find us</td>
</tr>
<tr>
<td></td>
<td>want somebody</td>
<td>cost??</td>
<td>products?</td>
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<tr>
<td></td>
<td>else’s stuff?</td>
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<td></td>
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<tr>
<td>Competition for</td>
<td>I'm not a buyer,</td>
<td>Still not buying</td>
<td>How do I</td>
</tr>
<tr>
<td>Prime In-Licensing</td>
<td>I’m a seller</td>
<td></td>
<td>compete with</td>
</tr>
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<td>Assets</td>
<td></td>
<td></td>
<td>Pfizer for</td>
</tr>
<tr>
<td>To Keep or Not to</td>
<td>Say what?</td>
<td>Still mostly a</td>
<td>Must keep even</td>
</tr>
<tr>
<td>Keep</td>
<td></td>
<td>no-brainer</td>
<td>if you don’t want</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>to!</td>
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*Defined Health*
### Comfort Factor

<table>
<thead>
<tr>
<th>IPO Bar</th>
<th>Very Comfortable 80’s</th>
<th>Less Comfortable Early-Mid 90’s</th>
<th>Very Uncomfortable Late 90’s-Present</th>
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</thead>
<tbody>
<tr>
<td>VCs Willingness to Finance Early Stage Development</td>
<td>Any sexy sounding science</td>
<td>Anything high throughput, combinatorial or genomic</td>
<td>At least 2 Phase III and 4 Phase II products</td>
</tr>
<tr>
<td></td>
<td>As long as it sounds cool</td>
<td>As long as it targets a big market</td>
<td>Let’s just say the terms are very unpleasant and leave it at that</td>
</tr>
</tbody>
</table>

Feeding the Pipeline VII  
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Implications and Predictions

Lessons From the M&A Space: When pipelines are worth more than products

Reverberations from a brutal Biotech IPO market
Implications and Predictions

Lessons From the M&A Space: When pipelines are worth more than products

Reverberations from a brutal Biotech IPO market
FOR IMMEDIATE RELEASE

Geneva, Switzerland, November 8, 2005 – Serono (virt-x: SEO and NYSE: SRA)

Following the information published by the Wall Street Journal today, the Company confirms that Goldman Sachs has been retained to explore various strategic alternatives for the Company.

There can be no assurances that any transaction will be consummated.

The Company has no further comment.
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…..15 Billion CASH!
SERONO ANNOUNCES TERMINATION OF DISCUSSIONS CONCERNING A SALE OF THE COMPANY

The Company will actively pursue opportunities for acquisitions

Geneva, Switzerland, April 10, 2006 – Serono (vitr-x: SEO and NYSE: SRA) announced today that its controlling shareholder, the Bertarelli family, has terminated discussions concerning a sale of the Company. The family has indicated that the offers it received did not adequately reflect the future prospects of the Company.

“Moving forward, Serono will invest in its existing businesses and will actively pursue opportunities for growth through acquisitions,” said Ernesto Bertarelli, Chief Executive Officer. “I take this opportunity to thank our employees for their loyalty and commitment to Serono.”

As previously announced, to provide the Company with the financing capacity to pursue such alternatives, the Board of Directors will propose to the forthcoming annual Shareholders meeting on April 25, 2006 an increase in the authorized share capital of the Company. As and when required, the authorized share capital will enable the Board of Directors to obtain financing rapidly through the issuance of additional shares.
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Market Cap: $12.58 B (9/7/06)

Yahoo! Finance

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http://finance.yahoo.com/
Current Portfolio Will Demonstrate Decent Growth through 2010

EvaluatePharma

<table>
<thead>
<tr>
<th>Year</th>
<th>WW Sales: US $ (mln)</th>
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<tbody>
<tr>
<td>2005</td>
<td>0</td>
</tr>
<tr>
<td>2006</td>
<td>1,000</td>
</tr>
<tr>
<td>2007</td>
<td>1,500</td>
</tr>
<tr>
<td>2008</td>
<td>2,000</td>
</tr>
<tr>
<td>2009</td>
<td>2,500</td>
</tr>
<tr>
<td>2010</td>
<td>3,000</td>
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- HuMax-CD4
- Raptiva
- Saizen
- Gonal-F/Gonalef
- Rebif
Future Pipeline Contribution is Debatable

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperglycosylated FSH in infertility</td>
<td>Oxytocin receptor antagonist in pre-term labor</td>
<td>Oral cladribine in multiple sclerosis</td>
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<tr>
<td>MMP-12 inhibitor in multiple sclerosis</td>
<td>JNK inhibitor in multiple sclerosis</td>
<td>Phenoptin in phenylketonuria</td>
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<tr>
<td>Atacicept (TACI-Ig) in rheumatoid arthritis</td>
<td>Atacicept (TACI-Ig) in relapsed / refractory B-cell malignancies</td>
<td>Zanolimumab (HuMax-CD4) in cutaneous T-cell lymphoma</td>
</tr>
<tr>
<td>Atacicept (TACI-Ig) in systemic lupus erythematosus</td>
<td>Atacicept (TACI-Ig) in multiple myeloma</td>
<td>Adecatumumab in prostate cancer</td>
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<tr>
<td>NI-0401 anti-CD3 monoclonal antibody in Crohn's disease</td>
<td>Adecatumumab + docetaxel in metastatic breast cancer</td>
<td>Adecatumumab in metastatic breast cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zanolimumab (HuMax-CD4) in non-cutaneous T-cell lymphoma</td>
</tr>
</tbody>
</table>

Company website

Feeding the Pipeline VII
September, 2006 - Pg. 84
Imclone Systems Engages Lazard to Review Strategic Alternatives for the Company;

IMCLONE SYSTEMS ANNOUNCES JOSEPH L. FISCHER, DIRECTOR, NAMED INTERIM CHIEF EXECUTIVE OFFICER

NEW YORK--(BUSINESS WIRE)--Jan. 24, 2006--ImClone Systems Incorporated (NASDAQ:IMCL) announced today that the Board of Directors has engaged Lazard to conduct, in conjunction with management, a full review of the Company's strategic alternatives to maximize shareholder value. These alternatives could include a merger, sale or strategic alliance. The Company is proceeding in consultation with its existing partners as the process moves forward. The Company also announced today that Joseph L. Fischer, a member of ImClone Systems' Board of Directors since 2003 as well as a member of its Audit and Compensation Committees, has been named Interim Chief Executive Officer, replacing Philip Frost, M.D., Ph.D. Mr. Fischer brings over 20 years of global managerial and operational experience to the Company. As a result of being named Interim Chief Executive Officer, Mr. Fischer will no longer serve on the Audit and Compensation Committees of the Board of Directors. Dr. Frost will remain as Executive Vice President and Chief Scientific Officer.
Growth Forecasts for Erbitux are Respectable

EvaluatePharma
**But No Potential Pipeline Payoff for 10 Years**

<table>
<thead>
<tr>
<th>Oncology Product Research</th>
<th>Pre-Clinical</th>
<th>IND Filing</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>FDA Approval</th>
<th>Phase IV</th>
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<tbody>
<tr>
<td>Flt-3 MAb</td>
<td></td>
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<td>VEGFR-3 MAb</td>
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<td>VE-cadherin MAb</td>
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<td>Ron MAb</td>
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<td>TRP-1 MAb</td>
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</tbody>
</table>

**GROWTH FACTOR BLOCKERS**

- INDICATION: AML, ALL
- INDICATION: Solid tumors
- INDICATION: Solid tumors
- INDICATION: Solid tumors
- INDICATION: Solid tumors
- INDICATION: Solid tumors
- INDICATION: Solid tumors
- INDICATION: Solid tumors
- INDICATION: Solid tumors
Imclone Systems Completes Review of Strategic Alternatives and Decides to Remain Independent; Transaction Alternatives Did Not Provide Sufficient Premium to Shareholders

Joseph L. Fischer to Continue to Lead Company While Board Searches for Permanent CEO

Company Announces Annual Meeting Date and Invites Carl Icahn to Join Company's Board of Directors

NEW YORK--(BUSINESS WIRE)--Aug. 10, 2006--ImClone Systems Incorporated (NASDAQ: IMCL): ImClone Systems Incorporated (NASDAQ: IMCL) announced today that its Board of Directors has completed a review of the Company's strategic alternatives and has made the decision to remain independent. The strategic review, conducted by the Board in conjunction with the Company's financial advisors and management, was initiated in January and included the evaluation of a number of alternatives, including a merger, sale or strategic alliance. In reaching its decision, the Board noted that the Company possessed a number of significant near- and long-term value drivers, including improving revenue and earnings performance; increasing sales of ERBITUX(R) in its approved indications, a successful launch in head and neck cancer and increased market penetration in colorectal cancer; the prospects for important clinical trial results toward the end of this year and beginning of 2007; and significant potential for the Company's pipeline product candidates. Commenting on the Board's decision, Joseph L. Fischer, Interim Chief Executive Officer of ImClone Systems, stated: "The Board concluded that the alternatives available, including bids received for the acquisition of the Company, did not match the value potential of ImClone Systems as an independent company. This decision was made in light of significant improvements in the top- and bottom-line performance of the Company over the review period and from the Company's numerous opportunities for growth. The Board, management team and I look forward to continuing to grow and improve ImClone Systems as a business, so that we can continue to be industry leaders in developing novel products for the benefit of the oncology community."

Company website; August 10, 2006 press release
Market Cap: $2.36 B (9/7/06)

Yahoo! Finance

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http://finance.yahoo.com/
Imclone Systems Announces Slate of Directors for Annual Meeting of Shareholders

NEW YORK--(BUSINESS WIRE)--Aug. 23, 2006--ImClone Systems Incorporated (NASDAQ: IMCL) announced today the slate of nominees recommended by the Board of Directors for election at the 2006 Annual Meeting of shareholders scheduled for September 20, 2006 at 10:00 AM at the Company's offices in Branchburg, New Jersey. This slate of twelve individuals comprises the nine current members of the Board together with Richard Mulligan, Ph.D., Charles Woler, Ph.D. and Carl Icahn.

The Company's Board of Directors believes that Drs. Mulligan and Woler, who were both suggested by Mr. Icahn, are highly qualified to serve as independent directors and it is confident that they will make valuable contributions to the Board as it focuses on continuing to grow the Company. The agreement with Mr. Icahn regarding the composition of the Board slate also avoided a proxy contest that would have been distracting for the Company.

David Kies, Chairman of ImClone Systems' Board of Directors, stated: "We are fortunate to have Joe Fischer serve as interim Chief Executive Officer. He has managed the Company effectively during a challenging time and has agreed to continue to serve ImClone Systems while we search for a permanent Chief Executive Officer. We welcome the input of all of our directors into the process of naming a permanent Chief Executive Officer. We look forward to Mr. Icahn's further input with regard to the Company's governance, and hope that it will be productive and given in a manner that maximizes the value of the Company for all shareholders."

Dr. Charles Woler is CEO of Neuro3D, a biopharmaceutical company focused on discovery and development of treatments for psychiatric disorders such as schizophrenia, depression and anxiety, and is Operating Partner Healthcare at Duke Street Capital. He has also served as CEO of Cadus Corporation, as CEO of Roche, France, an affiliate of F. Hoffmann-LaRoche Ltd., and as Chairman, Europe Pharmaceuticals, SmithKline Beecham.

Mr. Icahn is the principal equity holder and a director.
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Altana Considers Sale of Pharmaceuticals Division Amid Delays

Oct. 30 (Bloomberg) -- Altana AG, the German drugs and chemicals maker controlled by the billionaire Quandt family, is considering a sale of its pharmaceuticals business amid delays in the introduction of new drugs, its chief executive said.

The Bad Homburg-based company hired Goldman Sachs Group Inc. to explore strategic options for the business, spokesman Thomas Gauly said, confirming a report in the Financial Times Deutschland that cited a letter by Chief Executive Officer Nikolaus Schweickart to employees. All options regarding the future of the business are still open, Gauly said today. ``The letter refers to strategic gaps in our portfolio that will require action,'' Gauly said in an interview. ``If all options are open, then that also includes a sale.''

A sale of the business would depart from Schweickart's strategy, announced in August, to strengthen the drugs business through strategic partnerships and collaborations after he budgeted 1 billion euros ($1.2 billion) for investments in the unit. Altana is struggling to move new products onto the market as sales of its asthma drug Alvesco are trailing earlier projections.
Sales development since 1985 (m€)

- **1994** Pantozol® launched in Germany
- **2000** Protonix™ launched in USA
Some Costs Could Surely Be Taken Out of Altana
To that end, the company established the Herbert Quandt Foundation and the Altana Cultural Forum. Twice a year, at the foundation’s invitation, leading figures from politics, industry, science, and religion meet at the Sinclair House in Bad Homburg to discuss key social issues.

The Cultural Forum, also headquartered in the Sinclair House, collects and exhibits international works of art of the 20th and 21st centuries. Altana’s annual report displays some of that art and a quote from Nikolaus Schweickart, chairman of Altana AG: “Culture is intellectual nourishment. It reflects society’s degree of civilization. That is why the arts must not flounder but flourish.”

In celebration of the holding company’s 25th anniversary, the Munich Symphony Orchestra and a well known choir from Munich traveled with Altana’s management around the world to host management meetings and celebrations in Frankfurt, Sao Paulo, New York, Mexico City, and Shanghai. The company invited customers and employees at every level of the company to attend.
A place in society

Altana believes in building bridges between industry and culture.

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But with a Weak Pipeline, No Rush of Interested Buyers

No update on strategy and spending on Daxas/early stage pipeline continues

We obviously did not expect any “breaking news” on the search for a strategic partner in the pharmaceutical division to conveniently coincide with the results. Any definitive progress in this area would clearly have to be communicated to the market immediately. However, it is now a year since Altana first informed investors that it planned to separate its chemicals and pharmaceuticals businesses and 9 months since the announcement that it was looking for a strategic partner for pharmaceuticals (although the phrase “opening of the pharmaceutical business to a change in the shareholder structure” was the one used yesterday).Although the written guidance on this process remains unchanged with Altana purely stating that it expects to make a decision on both processes during the course of this year, previous comments by the CEO Dr Schweickart that the chemicals separation would happen in autumn are looking a little ambitious.

But with a Weak Pipeline, No Rush of Interested Buyers

Citigroup analyst report Aug 3, 2006
## But with a Weak Pipeline, No Rush of Interested Buyers

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism Of Action</th>
<th>Drug Development Phase (Indication : Phase : Country)</th>
<th>Originator</th>
<th>Licensee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roflumilast</td>
<td>PDE IV inhibitors</td>
<td>COPD : Preregistration : EU Asthma : Phase III : EU, USA COPD : Phase III : Australia, Brazil, India, South Africa, USA Asthma : Phase II : Japan COPD: Phase II : Japan Psoriasis : Preclinical : EU</td>
<td>ALTANA Pharma</td>
<td>Tanabe Seiyaku</td>
</tr>
<tr>
<td>Lusupultide</td>
<td>Membrane integrity antagonists Membrane permeability enhancers</td>
<td>ARDS : Phase III : EU, NA, South Africa</td>
<td>Scios</td>
<td>ALTANA</td>
</tr>
<tr>
<td>Soraprazan</td>
<td>Potassium-competitive acid blockers</td>
<td>GERD : Phase II : Germany GERD : Phase I : USA</td>
<td>ALTANA</td>
<td></td>
</tr>
<tr>
<td>GERD therapy</td>
<td>Potassium-competitive acid blockers</td>
<td>GERD : Phase I : EU</td>
<td>ALTANA</td>
<td></td>
</tr>
</tbody>
</table>

*Adis R&D Insight*
Market Cap: $7.8 B (9/11/06)

Yahoo! Finance
On the Other Hand, Schering AG Gets Fought Over!

Apr 13/06: Bayer offers €86 per share, for Schering, a premium of 61% over 12 months, and 39% pre takeover, as a “White Knight”

Schering Board recommends Bayer

Jul 26-06: Bayer offers €89 per share for all remaining shares and buys out Merck, successfully acquiring Schering

Mar 13/06: Merck offers €77 per share for Schering, a premium of 24%.

Mar-Jun/06: Merck declares it will not increase its offer, but acquires a large stake, 21%, in Schering.

Company reports; DH analysis

Merck sells Schering stake, pocketing €400 gain

Bayer acquires Schering
• KPMG value for Schering was E88 per share
• Bayer final offer E89 per share, valuing Schering at E17 B ($21 B)

3 x 2006E Sales
13 x 2006E EBITDA
16 x 2006E Earnings
Schering Pipeline has Lots of Near Term Shots on Goal

Company reports; EvaluatePharma; DH analysis
## At $15 Billion Was Serono Overpriced?

<table>
<thead>
<tr>
<th></th>
<th>Schering</th>
<th>Serono</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3 X Sales</strong></td>
<td>$22 B</td>
<td>$8 B</td>
</tr>
<tr>
<td><strong>13 X EBITDA</strong></td>
<td>$22 B</td>
<td>$9 B</td>
</tr>
<tr>
<td><strong>16 X Earnings</strong></td>
<td>$22 B</td>
<td>$12 B</td>
</tr>
<tr>
<td><strong>Market Cap</strong></td>
<td>$22 B</td>
<td>$10 B</td>
</tr>
</tbody>
</table>

Serono takes itself off the block

*MarketWatch Apr 10, 2006*

After six months on the block, Switzerland's Serono SA on Monday gave up on the idea of selling itself and instead said it was considering making acquisitions to expand.

Serono said its controlling shareholder, the Bertarelli family, decided the offers it received didn't adequately reflect its true value.

Published reports had indicated that bids for Europe's largest biotech from suitors including GlaxoSmithKline and Novartis were closer to $12 billion than the $15 billion that Serono had sought.

---

Company reports; Deutsche Bank; DH analysis
Growth Forecasts for Marketed Portfolio are Very Nice

EvaluatePharma; DH analysis
But Any Pipeline Payoff Looks Like a Longshot

**Pharmaceutical Pipeline**

<table>
<thead>
<tr>
<th>NDA FILED/UNDER FDA REVIEW</th>
<th>COMPOUND: Arformoterol</th>
<th>COPD</th>
<th>MECHANISM: Long-acting β-agonist</th>
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<tbody>
<tr>
<td>PHASE I</td>
<td>COMPOUND: SEP-225289</td>
<td>Depression</td>
<td>MECHANISM: Serotonin, Norepinephrine, Dopamine Reuptake Inhibitor</td>
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<tr>
<td></td>
<td>COMPOUND: SEP-227162</td>
<td>Depression</td>
<td>MECHANISM: Serotonin, Norepinephrine Reuptake Inhibitor</td>
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<td>IND-TRACK</td>
<td>COMPOUND: SEP-226330</td>
<td>Parkinson’s Disease</td>
<td>MECHANISM: Norepinephrine, Dopamine Reuptake Inhibitor</td>
</tr>
<tr>
<td>RESEARCH COLLABORATION</td>
<td>ACADIA Pharmaceuticals</td>
<td>Neuropsychiatric and Other Conditions Sleep Related</td>
<td>MECHANISM: Muscarinic Receptor Agonists and Antagonists MECHANISM: 5-HT&lt;sub&gt;2A&lt;/sub&gt; Antagonist and Eszopiclone Combination</td>
</tr>
</tbody>
</table>
Will Pfizer Buy Sepracor?

Largest contribution to growth occurs with immediate accretion in year of acquisition

- Note: Impact of any FTC mandated divestitures is not included in this analysis

EvaluatePharma; Defined Health analysis
Forest Laboratories Inc.

New President for FRX

What Happened. FRX today announced that Lawrence Olanoff will succeed Kenneth Goodman as President and COO as Goodman retires after 26 years with the company. Olanoff, an M.D., Ph.D, previously served as Executive Vice President and Chief Scientific Officer for ten years at Forest. He left in July of 2005 to become President and CEO of Celsion Corporation.

Our Takeaway. Ken Goodman has been a very strong leader for the company and this is a material loss for Forest. Larry Olanoff did a great job in R&D for Forest for years and is interestingly returning to take over but at this point he has little experience running the full operations. It is our understanding that Ken Goodman has been considering this move for some time, but we think he has waited for the company to move through the Lexapro patent situation and for a time when the company is on strong footing. We also believe that Dr. Olanoff is very well respected within the company and many of the division leaders who will report to him are very experienced and stable at the company. Hence we don’t expect any missteps.

We have always gotten questions about whether Forest was a take out candidate. While CEO Howard Solomon remains, he is close to eighty years old. It was always assumed that when he retired Ken Goodman would take over the company. With this move today, we would have to say that a potential sale of Forest is a higher likelihood than we had previously thought.

CSFB
Forest Laboratories Inc. (FRX)
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CSFB
Will Pfizer Buy Forest?

*Note: Impact of any FTC mandated divestitures is not included in this analysis

EvaluatePharma; Defined Health analysis

© Defined Health 2006
That Decision Would Appear to Depend on One’s View of the Pipeline

<table>
<thead>
<tr>
<th>The Forest Pipeline</th>
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<tbody>
<tr>
<td><strong>Preclinical</strong></td>
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<tr>
<td>mGLUR1/5 for various CNS conditions</td>
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</table>
Implications and Predictions

Lessons From the M&A Space: When pipelines are worth more than products

Reverberations from a Brutal Biotech IPO Market
Biotech is Under Water

2006 IPO Performance
(US Market, Through Q2)

% Change in Market Cap Post IPO

Adapted from BioCentury, The Bernstein Report, July 3, 2006
Some Biotech Haircuts Are Just A Light Trim…
A Little Off the Top, Please

Xenoport
Proposed $14-16
IPO January 2005 at $10.50
Raised $53 MM
Day 1 Close: $10.39
Current Share Price: $21.03

Haircut ≈ 35%

Somaxon
Proposed $13-15
IPO October 2005 at $11.00
Raised $55 MM
Day 1 Close: $11.00
Current Share Price: $14.11

Haircut ≈ 37%

Burrill & Company newsletter, April 2006; DH analysis
Today’s Biotech Haircuts are a Bit More Severe
<table>
<thead>
<tr>
<th>Company</th>
<th>Proposed Range</th>
<th>IPO Year</th>
<th>Raised</th>
<th>Day 1 Close</th>
<th>Current Share Price</th>
<th>Haircut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accentia Biopharma</td>
<td>$11-13</td>
<td>February 2005</td>
<td>$19 MM</td>
<td>$7.25</td>
<td>$3.06</td>
<td>≈40%</td>
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<tr>
<td>Advanced Life Sciences</td>
<td>$11-13</td>
<td>April 2005</td>
<td>$35 MM</td>
<td>$6.00</td>
<td>$2.99</td>
<td>≈60%</td>
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</table>
## Biotech Pulled IPOs (2005)

<table>
<thead>
<tr>
<th>Company</th>
<th>Ticker</th>
<th>File Date</th>
<th>Proposed Offering</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voyageur Pharma</td>
<td>VYGR</td>
<td>9/9/2005</td>
<td>$89-112M</td>
</tr>
<tr>
<td>Reliant Pharma</td>
<td>RRX</td>
<td>5/20/2005</td>
<td>TBA</td>
</tr>
<tr>
<td>Predix Pharmaceuticals</td>
<td>PRDX</td>
<td>8/3/2005</td>
<td>$50-60M</td>
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<tr>
<td>Peninsula Pharma</td>
<td>PPRX</td>
<td>12/16/2003</td>
<td>$69-81M</td>
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<td>Xcel Pharma</td>
<td>XCEL</td>
<td>1/7/2002, 8/22/2003</td>
<td>$75M</td>
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<tr>
<td>Intarcia</td>
<td>ITCA</td>
<td>2/7/2005</td>
<td>$86M</td>
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<tr>
<td>SkinMedica</td>
<td>SKMD</td>
<td>4/27/2005</td>
<td>TBA</td>
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<td>Cymabay Pharmaceuticals</td>
<td>CDEX</td>
<td>4/8/2004</td>
<td>$50M</td>
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<td>Synta Pharma</td>
<td>SNTA</td>
<td>1/18/2005</td>
<td>$115M</td>
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<td>EpiCept</td>
<td>EPCT</td>
<td>1/10/2005</td>
<td>$75M</td>
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<td>Targacept</td>
<td>TRGT</td>
<td>5/14/2004</td>
<td>$86M</td>
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<td>Cyclacel</td>
<td>CYCC</td>
<td>7/2/2004</td>
<td>$44-52M</td>
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<td>TolerX</td>
<td>TLRX</td>
<td>8/26/2003</td>
<td>$75M</td>
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<tr>
<td>Adesis</td>
<td>ADPX</td>
<td>8/27/2003</td>
<td>$75M</td>
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</table>
Biotech Start-Ups Increasingly Opt For a Sale to Drug Firms Over an IPO

By DAVID P. HAMILTON  July 13, 2006

Biotechnology start-ups long have followed a simple playbook: Go public at an early stage, keep raising money for a decade or more and …

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Trend in Big Pharma-Biotech Mergers & Acquisitions

Signals Magazine; DH analysis

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<th>Summary of Biotech Pipeline / Technology Platform on Date of Transaction</th>
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| **AstraZeneca**     | KuDOS Pharma             | Dec 2005            | $210 M Cash     | • The DNA repair platform includes several different approaches towards inhibition of enzymes involved in the responses to various types of DNA damage. DNA repair inhibitors have the potential to kill cancer cells either as stand-alone therapy or by enhancing the efficacy of chemo- and radio-therapies  
• The acquisition of KuDOS Pharmaceuticals augments AstraZeneca's portfolio with clinical and pre-clinical compounds and programmes. An innovative, targeted compound, KU 59436, an oral poly-ADP-ribose polymerase (PARP) enzyme inhibitor, is currently in phase I clinical development | • Largely unpartnered  
– 11 Dec 2003: Banoxantrone licensed to Novacea in North America |
| **Pfizer**          | Angiosyn                 | Jan 2005            | $527 M Cash     | • Angiosyn (now Pfizer), is developing a proprietary angiostatic agent for the potential treatment of ophthalmic diseases, such as age-related macular degeneration (AMD) | • All unpartnered |
| **Pfizer**          | Idun Pharma              | Feb 2005            | $298 M          | • Idun's technology is focused on the control of caspase activity. Caspases are a group of cellular proteases involved in the pathway of apoptosis and inflammation. Idun has developed therapeutic applications focused on inhibiting caspase activity as potential treatments for liver disease and inflammation. Idun also has programs targeting the activation of caspases as potential treatments for cancer  
• Idun's lead compound, IDN-6556, a first-in-class pan caspase inhibitor, is in Phase II clinical trials in liver transplantation and in patients infected with Hepatitis C virus.  
• In addition to IDN-6556, Idun has a robust preclinical pipeline including a number of programs in inflammation and oncology | • Largely unpartnered  
– Abbott holds exclusive worldwide rights for clinical compounds from research programs for Bcl-2 antagonists & Akt inhibitors |

_ADIS R&D Insight; Company reports; Company websites; IDdb; Recombinant Capital; Signals Magazine; DH analysis_
Big Pharma Now Acquires Pre-IPO Private Biotech with Relatively Unencumbered Pipelines


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<tr>
<td>Pfizer</td>
<td>Vicuron</td>
<td>Jun 2005</td>
<td>$1.9 B Cash</td>
<td>• Vicuron has two products currently under New Drug Application (NDA) review at the FDA: anidulafungin for fungal infections and dalbavancin for Gram-positive infections. Recently, Vicuron announced positive Phase III results on anidulafungin, demonstrating superiority versus fluconazole in invasive candidiasis/candidemia</td>
<td></td>
<td>• All unpartnered</td>
</tr>
</tbody>
</table>
| Pfizer              | Rinat                    | Apr 2006            | Not disclosed   | • Rinat’s most advanced compound is RN624, a potential new treatment for acute and chronic pain entering Phase II clinical trials.  
• Developing RN1219, a humanized monoclonal antibody for the treatment of Alzheimer’s disease. RN1219 has been shown to reduce amyloid plaque in pre-clinical studies  
• Compounds in late pre-clinical development for migraine prophylaxis and cachexia as well as discovery programs in obesity, pain, neuropathy and Parkinson’s disease |                      | • Lead compound partnered, others unpartnered            |
| Merck               | Aton                     | Feb 2004            | Acq. for Cash Upfront and Contingent | • Aton’s lead product candidate, suberoylanilide hydroxamic acid (SAHA), has been studied in Phase I clinical trials in cancer patients and is currently in Phase II clinical trials for the treatment of cutaneous T-cell lymphoma (CTCL).  
• SAHA is also in Phase 1 for treatment of patients with other types of cancer, including leukemia, multiple myeloma and solid tumors, such as breast and colorectal cancer |                      | • All unpartnered                                           |

ADIS R&D Insight; Company reports; Company websites; IDdb; Recombinant Capital; Signals Magazine; DH analysis
Biotech/Biotech Deals are Producing Fewer but Bulkier Pipelines More Ripe for M&A

Phase I Deals by Company Type

Company reports; Recap; DH analysis
Genzyme to pursue rare hostile biotech bid
August 31, 2006
Cambridge, MA-based Genzyme says it will pursue its hostile takeover of AnorMed with a tender offer of $8.55 per share, a 70 percent premium on the Canadian biotech's trading price. The New York Times' Andrew Pollack polled a group of industry execs, none of whom could recall any recent example of a hostile takeover in the biotech industry. Analysts say that a successful hostile takeover could trigger a walkout by key people in a biotech outfit, significantly reducing its value. AnorMed, though, may be a special case. Baker Brothers Advisers engineered a board coup at the company last April. The new board, meanwhile, has brought in Goldman Sachs to evaluate "strategic alternatives," a sign for some that they just want a higher offer before agreeing to sell.
OK, But I Still Need a Product! Take-Homes from the “No-Spin Zone”
OK, But I Still Need a Product! Take-Homes from the “No-Spin Zone”

The New Regulatory Bar: Safety, Efficacy and Medical Necessity

Unmet Needs: Let’s get serious!

Broader isn’t better: The Coming of the Less Impersonal Blockbuster
OK, But I Still Need a Product! Take-Homes from the “No-Spin Zone”

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Broader isn’t better: The Coming of the Less Impersonal Blockbuster
Cephalon drug a victim of ADHD debate: experts

"The FDA has come under fire and gotten more conservative," said Dr. Doris Day, assistant professor of dermatology at New York University School of Medicine. "There are so many drugs out there that can cause Stevens Johnson Syndrome, and at a higher level than this one."

Sparlon was made up mainly of psychiatrists. The only dermatologist on the panel was Dr. Michael Bigby, associate professor of dermatology at Harvard Medical School. He voted in favor of the drug, and other dermatologists say they would have voted the same way. "The FDA has come under fire and gotten more conservative," said Dr. Doris Day, assistant professor of dermatology at New York University School of Medicine. "There are so many drugs out there that can cause Stevens Johnson Syndrome, and at a higher level than this one."
Cephalon ADHD drug effective but not safe: pane

Cephalon Inc.'s Provigil drug is not safe enough to win approval for treating attention deficit hyperactivity disorder (ADHD) in children and teenagers, even though data showed it worked, a U.S. advisory panel said on Thursday. The Food and Drug Administration group of outside experts said it was most concerned about the risk of skin rashes that can lead to hospitalization and called on the drug maker to conduct more clinical trials. "I think we're dealing with some fuzzy information," said panel chairman Wayne Goodman, a psychiatrist at the University of Florida, adding that more patients needed to be studied before approval. "I don't want to do that experiment in the post-marketing arena," Goodman said.

Provigil is already approved to treat sleep disorders, but Cephalon is seeking to sell it under the name Sparlon for children and teenagers with ADHD. The ADHD version of the drug, known generically as modafinil, would be smaller and come in more than 20 dose levels. FDA granted conditional approval for ADHD in October 2005, but sought expert advice over lingering concerns about rashes as well as mania, aggression and other possible psychiatric effects. "I don't want to do that experiment if it's not going to be marketed" if the skin risk showed up in future studies, FDA's Director of Psychiatry Products Thomas Laughren told reporters after the meeting.

Cephalon officials said the concern was unexpected. "We were surprised by the degree to which this relatively benign case led to such apparent turmoil in the minds of the committee today," said Dr. Paul Blake, executive vice president of Cephalon's medical and regulatory operations. "We were surprised by the degree to which this relatively benign case led to such apparent turmoil in the minds of the committee today," said Dr. Paul Blake, executive vice president of Cephalon's medical and regulatory operations.

Cowen and Co. analyst Eric Schmidt said the panel's 12-1 vote against the drug's safety was "definitely disappointing." Thursday's vote follows the action of another FDA panel that called on Wednesday for all ADHD drugs to include new information about psychiatric and heart risks although data are still unclear. "This is a medication that looks likely to be slightly less effective than the other options available," panelist Dr. Marsha Rappley of Michigan State University added.
NPS Provides Update on Preos NDA Process and Timing

SALT LAKE CITY, February 7, 2005 -- NPS Pharmaceuticals, Inc. announced today that the company will extend the time it will take to prepare the U.S. new drug application (NDA) for its osteoporosis drug candidate Preos in light of European deadlines and filing requirements of its partner Nycomed, and the complex process of incorporating data from multiple clinical studies into different regulatory submission documents.

The company noted that Nycomed intends to submit a marketing authorization application in Europe next month for approval to sell Preotact (the European brand name for Preos or PTH), and that NPS and Nycomed are cooperating to meet the submission deadline designated by the European Medicines Agency. Because U.S. requirements are more extensive, NPS will submit its NDA following the Nycomed submission as soon as it has electronically formatted all of the additional documentation necessary for a successful U.S. marketing application.

Hunter Jackson, Ph.D., Chairman, President, and CEO of NPS, said, "We are nearing completion of the NDA for Preos and believe we have a very strong data package to support the approval of this investigational therapy for postmenopausal osteoporosis. Although we will extend our submission date beyond the end of February, we expect the delay will be brief and that the extra effort and time will facilitate productive regulatory reviews in the U.S. and in Europe, which will allow us to achieve a timely and coordinated global Preos launch."

About Preos
Preos is recombinant full-length human parathyroid hormone (PTH 1-84). NPS has studied Preos in a number of clinical settings to assess its safety and its effect on bone. The pivotal Phase 3 study, known as TOP (Treatment of Osteoporosis with PTH), was a multi-center, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the potential of PTH (1-84) to reduce the risk of vertebral fractures in post-menopausal women. In the TOP study Preos demonstrated a statistically significant reduction in the risk of new or worsened vertebral fractures in women with and without osteoporosis-related fractures prior to entering the study. Results from the TOP study will be the foundation of the U.S. and European marketing applications.
NPS Pharmaceuticals Reports Second Quarter and Six Month Operating Results

8/3/2006 4:53:00 PM

PARSIPPANY, N.J., Aug. 3 /PRNewswire-FirstCall/ -- NPS Pharmaceuticals, Inc. (Nasdaq: NPSP) today provided a general business update and reported its operating results for the three and six months ended June 30, 2006.

Business and Pipeline Update

In the second quarter of 2006 NPS recognized increased royalty revenue from sales of Sensipar(R)/Mimpara(R) (cinacalcet HCl) by Amgen, celebrated the European launch of PREOTACT(R) (parathyroid hormone [rDNA origin] for injection) by its partner, Nycomed, and continued to advance its proprietary and partnered product candidates through research and development.

NPS reported that it expects to complete enrollment of its Phase 3 study with teduglutide in patients with short bowel syndrome (SBS) by year-end 2006. Currently over 80% of the patients required by the trial protocol have been randomized into the study. The SBS protocol calls for six months of dosing. NPS expects to file a new drug application (NDA) for SBS in 2008. The company also reported that it expects to complete a double blind dose escalating PK and tolerability study of teduglutide to support dose range selection for the next study in Crohn's disease.

Based on an analysis of the existing clinical data and additional communications with the FDA, NPS has determined that the likelihood of success in addressing the agency's specific concerns regarding PREOS with an analysis of the existing data is low. As a result, NPS does not expect to file an amendment based on existing clinical data.

N. Anthony Coles, M.D., president and CEO of NPS said, "We continue to believe that PREOS is an important and valuable global asset to NPS and are working to ensure that PREOS returns value to our shareholders and patients."

Company website
Merck's Possible Vioxx Successor Draws Mixed Results in Study

By HEATHER WOON TESORIERO
August 24, 2006; Page D6

Merck & Co. released preliminary results of a large-scale study that suggested that an arthritis medicine it hopes will replace Vioxx on pharmacy shelves may not carry any more heart risks than an older, widely prescribed drug. But the company's statement, which didn't include some basic information about the study, also flagged some potential worries for the drug, including higher rates of hypertension and other conditions that caused some patients who were taking it to drop out of the trial. And some scientists raised questions about the study's design. The painkiller, Arcoxia, is sold in Europe and Latin America but hasn't been approved for sale in the U.S. In October 2004, the FDA examinined cardiovascular effects of Arcoxia and Cox-2 inhibitor, as are Vioxx and Celebrex, made by Pfizer Inc., and which are meant to be safer on the stomach than aspirin and other painkillers.

If Merck gets the green light to sell Arcoxia in the U.S., the drug could replenish lost Vioxx sales -- though its overseas sales in the first half of this year were only $126 million. Merck's preliminary findings suggested that there is no significant difference in the cardiovascular risks of Arcoxia and diclofenac. But Merck also said that greater numbers of certain Arcoxia patients had to discontinue treatment due to problems related to high blood pressure, edema and congestive heart failure. The drug's European label carries a warning about these conditions.

Merck said it plans to release the full results of the study once they are published in a peer-reviewed journal. Critics also questioned the study's design, especially the use of diclofenac as the comparison treatment. Diclofenac, Dr. Nissen said, acts in the body more like Cox-2 inhibitors than painkillers such as naproxen. The Cox-2 drugs have harmful effects and this study documented that diclofenac is no safer."

---- Ron Winslow contributed to this article

Wall Street Journal
US FDA staff question rash risk with Oscient drug

Mon Sep 11, 2006 8:41am ET

WASHINGTON, Sept 11 (Reuters) - Data for Oscient Pharmaceuticals Corp.'s (OSCI.O: Quote, Profile, Research) Factive antibiotic show a higher risk of skin rashes compared with other similar drugs, U.S. regulatory staff said in documents released on Monday.

Oscient is seeking Food and Drug Administration approval of the drug for the five-day treatment of acute sinus infections. Factive is already approved to treat other infections.

The documents were released ahead of an FDA advisory panel scheduled for Tuesday.

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What's This?

Soaring Penny Stock Pick
Cutting Edge Technology, Big Gains. Remember RIMM, $3 To $105
PennyStockMasters.com

3 Stocks Ready to Soar
Atypical Antipsychotic Approved by FDA in 2001

Geodon is contraindicated in patients with a known history of QT prolongation, recent acute myocardial infarction, or uncompensated heart failure, and should not be used with other QT-prolonging drugs. Geodon has a greater capacity to prolong the QTc interval than several antipsychotics. With some drugs, QT prolongation has been associated with torsade de pointes, a potentially fatal arrhythmia.

Hyperglycemia related adverse events, sometimes serious, have been reported in patients treated with atypical antipsychotics. There have been few reports of hyperglycemia or diabetes in patients treated with Geodon, and it is not known if Geodon is associated with these events. Patients treated with an atypical antipsychotic should be monitored for symptoms of hyperglycemia.
Cholesterol Drug Crestor Poses Risks, Journal Says
Study Suggests Use Only as Last Resort

By Marc Kaufman
Washington Post Staff Writer
Tuesday, May 24, 2005; Page A01

Crestor, which was approved by the FDA in 2003, is agreed to be the most potent statin on the market. Its higher strength, however, does not make a dramatic difference in studies. While statins such as Lipitor, Zocor and Pravachol lower LDL -- or harmful -- cholesterol by 50 to 55 percent, Crestor decreases it by 55 to 60 percent, said Grundy and Karas.

In the new study, doctors of patients taking Crestor were significantly more likely to report complications of kidney disease and rhabdomylosis, a muscle deterioration that releases toxins into the blood that can cause renal failure. The overall number was small -- 145 muscle or kidney problems out of 5.2 million prescriptions during the drug's first year on the market -- but the number was substantially higher than for other statins.

In 2001, the FDA took Baycol, a considerably more powerful statin than Crestor, off the market because of similar side effects. In a congressional hearing last December, FDA drug safety officer and whistle-blower David Graham identified Crestor as one of five drugs now on the market that he believed posed serious safety problems that were not balanced by their benefits.

The FDA yesterday referred callers to its March conclusions that Crestor is no more hazardous than other statins.
OK, But I Still Need a Product! Take-Homes from the “No-Spin Zone”

The New Regulatory Bar: Safety, Efficacy and Medical Necessity

Unmet Needs: Let’s get serious!

Broader isn’t better: The Coming of the Less Impersonal Blockbuster
Strategy

Will focus on …
Pipeline and products in selected disease areas of **unmet medical need**.
Considered the founder of the biotechnology industry, Genentech has been delivering on the promise of biotechnology for almost 30 years, using human genetic information to discover, develop, commercialize and manufacture biotherapeutics that address significant unmet medical needs.
In Discovery, our scientists work together across boundaries to exchange ideas, to promote best practice and to maximise the opportunities that are offered by our size and global reach. We focus on finding novel medicines for targeted unmet medical needs in our chosen areas of activities.

Verus is dedicated to identifying, developing and delivering solutions to address the **unmet medical needs** of children and those who care for them.
Indiplon: Two formulations with a novel, more selective approach for treating the various types of insomnia

Preparing for the Indiplon Launch:
In December 2002, Neurocrine and Pfizer entered into a global agreement for the exclusive worldwide development and commercialization of indiplon. Neurocrine and Pfizer expect to submit New Drug Applications (NDA) with the U.S. Food and Drug Administration (FDA) in 2004. Pfizer will collaborate with Neurocrine on the development and marketing of indiplon in the U.S. and will have exclusive marketing and development rights to indiplon outside of the U.S.

Insomnia remains a disorder with high unmet medical needs, including the inability to fall asleep, maintain sleep throughout the night and middle of the night awakenings with failure to return to sleep.
Myriad is a leading biopharmaceutical company. Our strategy is to develop novel healthcare products in areas of critical need and to address some of the most pervasive diseases of our time.

Myriad website

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“Unmet Needs Met”

Q2 06 Sales by Therapeutic Area

- Neurology: 58%
- Reproductive Health: 27%
- Dermatology: 11%
- Growth and Metabolism: 1%
- Other: 3%

Company website

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The New Regulatory Bar: Safety, Efficacy and Medical Necessity

Unmet Needs: Let’s get serious!

Broader isn’t better: The Coming of the Less Impersonal Blockbuster
How many of the 25 best-selling albums in American history can you name?
How many of the 25 best-selling albums in American history were recorded in this century?
“If the 20th century entertainment industry was about hits, the 21st will be equally about niches.”
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“Patients feel entitled to have personalized medicine.”

-- Susan Desmond-Hellman, President of Product Development, Genentech
CEO Henry McKinnell said Tuesday that although 2005 will be a transition year, he expects the drug giant to return to double-digit earnings growth starting in 2006. "We have reinvented ourselves many times, and it's clearly time to do it again," McKinnell said during a meeting with analysts and investors.

The company offered guidance for 2005 that was lower than analysts had expected. Pfizer said it expects to earn $2.00 a share, excluding items, down from $2.12 a year ago. On a GAAP basis, the drug giant expects net income of about $8.6 billion and EPS of about $1.16.

McKinnell said 2005 would be a transition year due to the expiration of patents on certain products and "a number of uncertainties," which include the company's arthritis drugs, "continued pricing pressures, and market acceptance of new products."

The Cox-2 Dilemma
One uncertainty is how Bextra and Celebrex will fare once the Food and Drug Administration acts on recommendations made by two advisory committees in mid-February to place restrictions on all arthritis drugs known as Cox-2 inhibitors. McKinnell said the benefits outweighed the risks for Vioxx and Bextra. The committees gave Celebrex overwhelming support. McKinnell said Celebrex and Bextra are "very important options" to millions of patients, adding that he expects "renewed growth" from currently depressed sales levels of the Cox-2 drugs if the FDA gives the company a relatively broad label for these drugs.

Early in the second half of 2005, Shedlarz added, Pfizer will consider another buyback. Now trading in the mid-$20s range, Pfizer's stock is much closer to its 52-week low of $21.99, than its 52-week high of $37.90.

TheStreet.com
CEO Henry McKinnell said Tuesday that although 2005 will be a transition year, he expects the drug giant to return to double-digit earnings growth starting in 2006. “We have reinvented ourselves many times, and it’s clearly time to do it again,” McKinnell said during a meeting with analysts and investors.

The company offered guidance for 2005 that was lower than analysts had expected. Pfizer said it expects to earn $2.00 a share, excluding items, down from $2.12 a year ago. On a GAAP basis, the drug giant expects net income of about $8.6 billion and EPS of about $1.16.

McKinnell said 2005 would be a "transition year" due to the expiration of patents on certain products and "a number of uncertainties," which include the company’s arthritis drugs, "continued pricing pressures, and market acceptance of new products."

**The Cox-2 Dilemma**

One uncertainty is how Bextra and Celebrex will fare once the Food and Drug Administration acts on recommendations made by two advisory committees in mid-February to place restrictions on all arthritis drugs known as Cox-2 inhibitors. ..., said the benefits outweighed the risks for Vioxx and Bextra. The committees gave Celebrex "overwhelming support."

McKinnell said Celebrex and Bextra are "very important options" to millions of patients, adding that he expects "renewed growth" from currently depressed sales levels of the Cox-2 drugs if the FDA gives the company a relatively broad label for these drugs.

Early in the second half of 2005, Shedlarz added, Pfizer will consider another buyback. Now trading in the mid-$20s range, Pfizer's stock is much closer to its 52-week low of $21.99, than its 52-week high of $37.90.

TheStreet.com
So, Pharma’s Future is in Personalized Medicine, Right?

Lipitor
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Springfield, IL 95523
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So, individualized medicines, tailored to you based on your genetics, are something people have been ranting about for a while now. The field is called pharmacogenomics. But, the sort of idea they're selling - that your physician will prick your finger, sample your DNA with some GATTACA-style palm-pilot and print out a list of prescriptions for designer drugs to take to the pharmacy - well, that's mostly bull. For now, anyway.

We're a hell of a long way from being able to look at someone's genes, derive their physiology and use the information to formulate any specialized medication. We're even a long way from being able to locate genetic reasons for why a drug might be efficacious in one population and not in another.

Here's how pharmacogenomics is actually starting out: trial and error, quite literally. After the heart medication, BiDil failed in trials, Nitromed - the company developing the drug - decided to cut their losses and try a new drug trial in African Americans only, based on some preliminary evidence that it worked better in this population. Today it was reported, the same is happening with Xyotax. Cell Therapeutics, a pharmaceutical company is going to start women-only trials of the lung cancer drug after initial trials failed.

These companies know nothing about the underlying genetic or environmental conditions that might make the drug more or less effective in different people - they're merely cutting their losses after trials fail by re-trying the drug in a unique subpopulation. And this is going to be an increasing trend, as companies realize that FDA approval doesn't have to be an all-or-nothing game. Eventually, through trial and error, they'll divide up the population into promising FDA trial groups and we may get to something approaching individualized medicine.

Linking genetic markers to drug efficacy is a really hard problem. I'm not saying pharmacogenomics won't eventually come around. But it's unlikely that we're going to see a bottom up approach of identifying genes, and designing drugs to match. It's much more likely we'll see a gradual subdivision of the drug market into increasingly specific groups, until separating patient groups by genetic markers becomes the next logical step.
Less Impersonal Medicine: Clinical Segmentation Instead of Pharmacogenetic Segmentation

- Empiric therapy Non-responders
- Pt. subsets (e.g., aspirin-induced asthma)
- Drug-drug interactions
- Contra-indications
- Co-morbidities
- Age Sex Race
- Tolerability/Safety

Profiling Clinical Chemistry Data Mining
Impersonal Medicine

Personalized Medicine

Lipitor
Personalized Medicine
Less Impersonal Medicine
Less Impersonal Medicine

Impersonal Medicine

Personalized Medicine

Less Impersonal Medicine
“When one door closes another door opens; but we so often look so long and so regretfully upon the closed door, that we do not see the ones which open for us.”

-- Alexander Graham Bell
"...anything but another conference"

"Therapeutic Insight brings together a sophisticated, knowledgeable audience along with outstandingly qualified speakers addressing a variety of defining topics/issues challenging the pharmaceutical/biotechnology industry and is anything but another conference. It is a forum that one leaves with new thought and ideas that are useful and provocative for your own organization."

Frederick Frank
Vice Chairman
Lehman Brothers, Inc.

"In a world with so many licensing, M&A and strategy meetings, yet such limited discretionary budget and time, how do we choose? The answer - go with the meeting that offers unconventional insight into matters that sometimes cannot even be discussed candidly at internal company meetings. Hands down, the choice is Defined Health's famous annual Therapeutic Insight Conference."

Clive A. Meanwell, MD, PhD
Chairman & CEO
The Medicines Company
"...anything but another conference"

“I used to attend this conference for the networking and insights into therapeutics. While that is still a valuable benefit, Ed Saltzman has amplified this value through his thoughtful, highly insightful, frequently controversial approach to addressing the complex issues reshaping our industry. No other conference offers this combination of benefits.”

Michael J. DuBois
Senior Vice President, Global Licensing
Schering-Plough Corporation

"Therapeutic Insight is a unique forum that brings together an array of thoughtful and diverse biopharmaceutical stakeholders in an intimate setting. Panelists speak on state-of-the-art issues, deliver content that is objective and not commercial, and don’t refrain from engaging in controversial debates. Defined Health moderators provide informative overviews and lead balanced discussions. Even the most sophisticated biopharmaceutical professional would advance his or her thinking by attending this conference."

Robert H. Glassman, PhD
Managing Director, Healthcare Investment Banking
Merrill Lynch
"The annual Therapeutic Insight conference by Defined Health offers fresh insights into complex issues facing the pharmaceutical and biopharmaceutical industry. Carefully chosen topics are discussed by panels of experts who have very diverse views and broad experience. I always learn something new and profound and meet someone interesting and important, who I would have been unlikely to encounter anywhere else, in an atmosphere that is ideal for mind-bending."

Mary C. Tanner
General Partner
Life Sciences Partner

"The Defined Health annual conference, Therapeutic Insight, brings together biotech and pharmaceutical thought leaders and business professionals in an intimate, interactive, highly informative setting. The candid open debate on key issues is, in itself, worth the price of admission."

Leonard P. Shaykin
Chairman and CEO
Tapestry Pharmaceuticals
"...anything but another conference"

“The conference is excellent. Extremely informative. A great networking opportunity with seasoned business professionals. Exceptional, knowledgeable speakers. I’ve attended Therapeutic Insight every year since it began. It is definitely a must-attend conference!”

Harry Loveys
Principal
Capital Royalty L.P.

“Over the years Defined Health has managed to attract many of the absolutely top flight pharmaceutical industry, academic, health economic, and health ethics experts to their Therapeutic Insight conference. It is a privilege to participate in these meetings not simply from a networking viewpoint but more especially, to learn from one’s respected peers.”

Brian Leyland-Jones, MD, PhD
Minda de Gunzburg Professor of Oncology
Founding Chairman, Department of Oncology
McGill University
"...anything but another conference"

“The most compelling aspect of Therapeutic Insight is the therapeutic area panel discussions. 2006 was my first time to attend, and I was very impressed with the quality and diversity of the speakers and the different perspectives they brought to the issues. I especially appreciated the oncology panel. The discussion had tremendous clinical relevance regarding state-of-the art views with no “pie-in-the-sky” attitudes, just the reality of what is actually happening in this therapeutic area right now.”

Phyllis Whiteley, PhD
Senior Vice President
Business Development & Licensing
Perlegen Sciences, Inc.

“The Defined Health Therapeutic Insight meeting always delivers on its promise: a large dose of insight. Ed and the Defined Health team put together the experts and the program that delivers the goods.”

John M. Siebert, PhD
Chairman & Chief Executive Officer
CyDex Inc.