CHIRAL TECHNOLOGIES INC
DAICEL GROUP
Innovation Begins Here
Chirality

Asymmetric Enzymatic

Is There a Better Way?

Joseph M. Barendt, Ph.D.
<table>
<thead>
<tr>
<th>Area</th>
<th>Challenges</th>
<th>Key</th>
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<tr>
<td><strong>Discovery</strong></td>
<td>• High volume of candidates</td>
<td>Delivery of material</td>
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<td>• Chirality of drug TBD</td>
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<td><strong>Process Development</strong></td>
<td>• High attrition rate</td>
<td>Speed</td>
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<td>• Chirality is known</td>
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<td><strong>Clinical Trials</strong></td>
<td>• Long-term focus</td>
<td>Scalability</td>
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<td>• Process feasibility</td>
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<td><strong>Commercial Production</strong></td>
<td>• Process robustness</td>
<td>Cost</td>
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<td>• Equipment availability</td>
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Our only focus is enantiomeric purity
  – Custom purification from mgs to 100 kgs
  – Discovery through Phase II Trials

Two Case Studies to exemplify capabilities
  – Process Development
  – Clinical Trials
Case Study #1

• Process Development

• Initial focus was on API
  – Current process; classical resolution
  – Slow process, high cost, not scalable

• Reviewed prior intermediates
  – Developed process to obtain >98%ee
    • Faster than classical resolution
    • 25% of the cost
Case Study #2

• Biogen Idec Drug
The Mannich reaction established the framework for **BIIB042** in the first step producing **BIM-702**, and chiral chromatography was employed to separate the four stereoisomers.
Formation of First Chiral Center

- Attempted both Enzymatic and Classical Resolution to no avail.
- Developed SMB route to obtain >99%ee BIM-752
- Ran 90kg campaign to prove it out
Potential SMB Process

Racemic BIM702

Chiral SMB

90 kg
Potential SMB Process

Racemic BIM702

Chiral SMB

90 kg

BIM 752

>99.5%ee
Potential SMB Process

Racemic BIM702

Chiral SMB

90 kg

Non-Target Enantiomer

BIM 752

>99.5%ee
Potential SMB Process

Racemic BIM702 ➔ 90 kg 

Racemization ➔ Chiral SMB ➔ Non-Target Enantiomer ➔ BIM 752 ➔ >99.5% ee
Potential SMB Process

Racemic BIM702

Racemization

Chiral SMB

90 kg

Non-Target Enantiomer

BIM 752

>99.5%ee
Global Capabilities
• Commercial-scale SMB system at
• Ampac Fine Chemicals plant in Sacramento, CA