Building a Franchise in HDV

Sarasar® (Ionafarnib)  Pegylated Interferon Lambda-1a
Forward-Looking Statements

This presentation and the oral commentary contain “forward-looking” statements that involve substantial risks and uncertainties. All statements other than statements of historical facts, including statements regarding our future financial condition, timing for and outcomes of clinical results, business strategy and plans and objectives for future operations, are forward looking statements. These forward-looking statements include terminology such as “believe,” “will,” “may,” “estimate,” “continue,” “anticipate,” “contemplate,” “intend,” “target,” “project,” “should,” “plan,” “expect,” “predict,” “could,” “potentially” or the negative of these terms. Forward looking statements are our current statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned clinical development, the timing of and our ability to initiate or enroll clinical trials, and our ability to make regulatory filings and obtain and maintain regulatory approvals for Sarasar, PEG IFN Lambda and our other product candidates, our intellectual property position, the potential safety, efficacy, reimbursement, convenience clinical and pharmaco-economic benefits of our product candidates, commercial opportunities, including potential market sizes and segments, our ability to commercialize, expectations regarding clinical trial data and FDA outcomes, our results of operations, cash needs, spending of the proceeds from this offering, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

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Interferon-Lambda: A New Addition to an Old Family

The discovery and initial description of the interferon-λ (IFN-λ) family in early 2003 opened an exciting new chapter in the field of IFN research. There are 3 IFN-λ genes that encode 3 distinct but highly related proteins denoted IFN-λ1, -λ2, and -λ3. These proteins are also known as interleukin-29 (IL-29), IL-28A, and IL-28B, respectively. Collectively, these 3 cytokines comprise the type III subset of IFNs. They are distinct from both type I and type II IFNs for a number of reasons, including the fact that they signal through a heterodimeric receptor complex that is different from the receptors used by type I or type II IFNs. Although type I IFNs (IFN-α/β) and type III IFNs (IFN-λ) signal via distinct receptor complexes, they activate the same intracellular signaling pathway and many of the same biological activities, including antiviral activity, in a wide variety of target cells. Consistent with their antiviral activity, expression of the IFN-λ genes and their corresponding proteins is inducible by infection with many types of viruses. Therefore, expression of the type III IFNs (IFN-λs) and their primary biological activity are very similar to the type I IFNs. However, unlike IFN-α receptors which are broadly expressed on most cell types, including leukocytes, IFN-λ receptors are largely restricted to cells of epithelial origin. The potential clinical importance of IFN-λ as a novel antiviral therapeutic agent is already apparent. In addition, preclinical studies by several groups indicate that IFN-λ may also be useful as a potential therapeutic agent for other clinical indications, including certain types of cancer.

• **First developed by Zymogenetics**
  - Clinical Development into Phase 2 in early 2000's

• **Proposed benefit: improved safety and tolerability vs PEG IFN alfa**

• **Target indication: HCV**

• Acquired by Bristol-Myers Squibb in 2010

• **Greater than 3,000 patients in 17 clinical trials**
  - Phase 2 and Phase 3 studies in HCV and HBV

• **Discontinued following advent of all oral HCV combinations**
PEG IFN Lambda
A targeted interferon for HDV

• A novel, first in class Type III interferon
  - Native Lambda is generated by human immune system in viral infections

• Binds to a unique receptor versus Type I interferons
  - Highly expressed on hepatocytes
  - Limited expression on hematopoietic cells and CNS cells

• Uses similar downstream signaling pathway as Type I interferons

• Anti HCV / Anti HBV activity demonstrated in clinical studies

• Antiviral activity with less of the typical IFN alfa related side effects

• Anti HDV activity demonstrated in humanized liver mouse model
Type I Interferons versus Type III Interferons
alfa, beta, omega versus lambda

潜在的IFN-α受体和Lambda受体分布的影响

IFN-α受体广泛分布在全身。
Lambda受体未广泛分布在全身。

潜在的更多IFN相关的异常情况：
- 血小板减少
- 红细胞减少
- 发热症状
- 肌肉骨骼症状

潜在的更少IFN相关的异常情况：
- 血小板减少
- 红细胞减少
- 发热症状
- 肌肉骨骼症状
## PEG IFN Lambda Safety versus PEG IFN Alfa

### Results of Clinical Study in HBV Infected Patients

<table>
<thead>
<tr>
<th>Type of Event</th>
<th>Event</th>
<th>Lambda 180 mcg (N = 80)</th>
<th>Alfa 180 mcg (N = 83)</th>
<th># of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serious adverse events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 (8.8)</td>
<td>5 (6.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse events leading to discontinuation</strong></td>
<td></td>
<td>6 (7.5)</td>
<td>8 (9.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse events (any grade)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in &gt;15% in any group</td>
<td>Pyrexia</td>
<td>8 (10.0)</td>
<td>38 (45.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alopecia</td>
<td>9 (11.3)</td>
<td>25 (30.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td>26 (32.5)</td>
<td>24 (28.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>11 (13.8)</td>
<td>24 (28.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neutropenia</td>
<td>0</td>
<td>20 (24.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myalgia</td>
<td>3 (3.8)</td>
<td>18 (21.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>5 (6.3)</td>
<td>13 (15.7)</td>
<td></td>
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<tr>
<td></td>
<td>Pruritus</td>
<td>7 (8.8)</td>
<td>13 (15.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ALT Increase</td>
<td>15 (18.8)</td>
<td>8 (9.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse event categories of special interest</strong></td>
<td>Constitutional</td>
<td>28 (35.0)</td>
<td>26 (31.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neurological</td>
<td>18 (22.5)</td>
<td>30 (36.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flu-like</td>
<td>13 (16.3)</td>
<td>45 (54.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Musculoskeletal</td>
<td>5 (6.3)</td>
<td>23 (27.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psychiatric</td>
<td>11 (13.8)</td>
<td>15 (18.1)</td>
<td></td>
</tr>
</tbody>
</table>

Chan, HLY et al, J Hepatology 2016.
### PEG IFN Lambda Safety versus PEG IFN Alfa

**Results of Clinical Study in HBV Infected Patients**

<table>
<thead>
<tr>
<th>Event</th>
<th>Lambda 180 mcg (N = 80)</th>
<th>Alfa 180 mcg (N = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade 3-4 laboratory abnormalities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT increases (&gt;5 x ULN)</td>
<td>33 (41.3)</td>
<td>19 (23.3)</td>
</tr>
<tr>
<td>AST increases (&gt;5 x ULN)</td>
<td>27 (33.8)</td>
<td>15 (18.3)</td>
</tr>
<tr>
<td>Hyperbilirubinemia (&gt;2.5 x ULN)</td>
<td>3 (3.8)</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia (&lt;750 cells / mm³)</td>
<td>2 (2.5)</td>
<td>17 (20.7)</td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;50,000 cells / mm³)</td>
<td>0</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Hemoglobin (&lt;9 g/dL or 4.5 g/dL decrease from baseline)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>ALT flares</strong></td>
<td>13 (16.3)</td>
<td>6 (7.2)</td>
</tr>
<tr>
<td><strong>Dose reductions</strong></td>
<td>12 (15.0)</td>
<td>23 (27.7)</td>
</tr>
<tr>
<td><strong>Dose interruptions</strong></td>
<td>8 (10.0)</td>
<td>4 (4.8)</td>
</tr>
</tbody>
</table>
PEG IFN Lambda Suppresses HDV RNA
Strongly Enhanced Innate Immune Response of Human Hepatocytes

Experimental Design

HDV Viremia

Experimental Design

ISG15 = 6.2 Fold
Rig-I = 1.9 Fold
STAT1 = 6.2 Fold
STAT2 = 11.2 Fold

Dandri et al, EASL 2013 Monothematic Conference, Poster
Sarasar® (lonafarnib) Phase 2 HDV Program
LOWR 1 and LOWR 2 Include PEG IFN α Combination Dosing

- **Proof of Concept**
  - Monotherapy
    - N = 14
    - Complete

- **LOWR HDV – 1**
  - Combinations +/- PEG IFN α
    - N = 15
    - Complete

- **LOWR HDV – 2**
  - Dose Finding +/- PEG IFN α
    - N = 37
    - Dosing

- **LOWR HDV – 3**
  - Duration
    - N = 21
    - Dosing

- **LOWR HDV - 4**
  - Titration
    - N = 15
    - Dosing
PEG IFN Lambda
Plans

- Replace PEG IFN alfa in next Eiger HDV studies

- Efficiently study potential use as:
  - An effective monotherapy in HDV
  - An effective combination therapy with Lonafarnib in HDV

- Identify potential for better tolerability versus PEG IFN alfa in HDV

- Offer a proprietary interferon with more optimal efficacy / tolerability

- Apply for Orphan Designation & Fast Track status

- Create an HDV franchise opportunity at Eiger
PEG IFN Lambda

Expected Timelines

• **Drug Product on hand sufficient for Phase 2**
  – Quantities may supply development through registration

• **Monotherapy study in HDV to begin in 2H2016**
  – Lambda alone dose ranging study

• **Combination study in HDV to begin in 2H2016**
  – Lonafarnib + Ritonavir + Lambda

• **Efficient generation of Phase 2 POC data in 4Q2017**
  – Multiple, international sites
Monotherapy - Phase 2 POC Study in HDV
LMD 120 mcg QW vs LMD 180 mcg QW

Objective: Safety and Efficacy of LMD 120 mcg vs LMD 180 mcg

Arm 1
N = 10
LMD 120 mcg QW  Rx-free follow-up

Arm 2
N = 10
LMD 180 mcg QW  Rx-free follow-up

New Zealand: Ed Gane (Auckland)
Pakistan: Saeed Hamid (Karachi)
PEG IFN Lambda Lambda Monotherapy
Clinical / Regulatory POC Plan

2016

Enroll

Regulatory Filings

2017

Dosing

EOT Data

2018

Post TRx Data
Combination - Phase 2 POC Study in HDV

LNF 50 mg BID / RTV 100 mg BID + LMD 120 mcg QW

Objective: Safety and Efficacy of LNF + RTV + LMD vs LMD Alone

Weeks

EOT

EOFU

2 wk

48 wk

24 wk

Arm 1

N = 10

LNF RTV

LMD 120 mcg QW

LNF 50 mg BID

RTV 100 mg BID

Rx-free follow-up

Arm 2

N = 10

PBO

LMD 120 mcg QW

LNF/RTV PBO

Rx-free follow-up

Planned Sites:

US: NIH Greece Turkey:

Turkey:
**PEG IFN Lambda Combination**

**Clinical / Regulatory POC Plan**

- **2016**
  - Enroll

- **2017**
  - Regulatory Filing

- **2018**
  - Regulatory Filing
  - Dosing
  - EOT Data

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*NIH*  
*American Flag*  
*Regulatory Filing*  
*EOT Data*  
*EASL 2018*
Sarasar® (lonafarnib) in HDV
Phase 2 Results Expected in 2016 / 2017

2015

Phase 2 LOWR HDV – 2

Interim Data

EOT Data

N = 37

2016

Phase 2 LOWR HDV - 3

EOT Data

Post TRx Data

N = 21

2017

Phase 2 LOWR HDV - 4

EOT Data

Post TRx Data

N = 15
## Potential Registration Pathways

**Building an HDV Franchise**

<table>
<thead>
<tr>
<th>HDV Registration Options</th>
<th>Clinical Description</th>
<th>Treatment Option</th>
<th>Treatment Option</th>
<th>Treatment Option</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cure</strong></td>
<td></td>
<td><strong>All Oral</strong></td>
<td><strong>Triple Combo</strong></td>
<td><strong>Mono</strong></td>
</tr>
<tr>
<td>HDV RNA Negativity + ALT Normalization</td>
<td>Lonafarnib + Ritonavir</td>
<td>Lonafarnib + Ritonavir + Lambda</td>
<td>lambda</td>
<td></td>
</tr>
<tr>
<td><strong>Chronic Treatment</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HDV RNA Reduction + ALT Normalization</td>
<td>Lonafarnib + Ritonavir</td>
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</table>
Building a Franchise in HDV

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