GNI Ltd.

Ying Luo, Ph.D.

President and CEO

www.gnipharma.com
History Background


Mission: Develop new therapeutic agents for disease prevalent in Asia
Research service for western biotech

Campus: R&D facility in Shanghai;
Headquarter in Tokyo.

R&D: 2001-2004: Target identification and drug discovery (public projects, grants)


Clinical Pipeline

F647 IPF

F647 RP

F351 LF
- New candidate drug for acute liver failure. Licensed from Epicept.

F1013
- Lead compound for liver and lung cancer. CDK inhibitor.

C45

Pre-IND IND Phase I Phase II Phase III NDA

All product candidates are small molecule Class I drugs in China.
Conducting Clinical Trials in the Reputable Hospitals in China to Take Advantage of the Cost Efficiency

- Peking Union Medical College Hospital
- Capital University of Medical Sciences Affiliate of Beijing Chaoyang Hospital
- Beijing Cancer Hospital
- First Hospital Affiliated to China Medical University
- General Hospital of Shenyang Military Command
- Shanghai Tongji University Affiliated Pulmonary Hospital
- Zhongshan Hospital, Fudan University
- Shanghai Ruijin Hospital
- Shanghai 6th People’s Hospital, Shanghai Jiaotong University
- The First Affiliated Hospital of Wenzhou Medical College
- Union Hospital, Tongji Medical College
- People’s Hospital of Henan Province
## Therapeutic Product 1: F647/Pirfenidone

### Background of the Phase II Disease Indications

<table>
<thead>
<tr>
<th>Idiopathic Pulmonary Fibrosis (IPF)</th>
<th>Radiation Pneumonitis (RP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPF is a fatal disease</td>
<td>65% of NSCLC (Non-small cell lung cancer) cases require radiation therapy in the course of the illness</td>
</tr>
<tr>
<td>Etiology of IPF is still unknown</td>
<td></td>
</tr>
<tr>
<td>The mean length of survival from the time of diagnosis: 2.8 years</td>
<td>30-50% of the lung cancer patients undergo radiotherapy develop acute lung injury (radiation pneumonitis), which may lead to subsequent fibrosis and fatality</td>
</tr>
<tr>
<td>There is currently no effective treatment for IPF</td>
<td>Chemotherapy agents increase the susceptibility of radiation pneumonitis</td>
</tr>
<tr>
<td>Prevalance: 14.0-42.7/100,000 population*</td>
<td>Radiation therapy for breast and esophageal cancer caused acute lung injury</td>
</tr>
<tr>
<td>Incidence: 6.8-16.3/100,000 population*</td>
<td></td>
</tr>
</tbody>
</table>


### Market in China

- **IPF**: up to 555,000 patients
- **RP**: 1.3 million patients
F647’s IND and Clinical Development

F647 Belongs to Category 1.1 Novel Chemical Compound Drug

- Class I novel drug status, 29 documents submitted in Dec. 2004
- SFDA review meeting on March 22, 2005
- SFDA issued IND approval on May 11, 2005
- Phase I plan and ethics approval on May 30, 2005
- Phase I initiated in June, 2005
- Phase I completed with 86 healthy volunteers on Oct 7, 2005

SFDA Certified Clinical Base: Institute of Clinical Pharmacology, Union Hospital, Tongji Medical College, Wuhan

Qualified Lead Investigator: Dr. Fandian Zeng, Head of Pharmacology and Clinical Base
Phase I Trial Conclusions

- PK parameters demonstrate a good linearity over the single oral dosage of 200, 400, 600mg of F647.
- Compare with the PK parameters after an overnight fast and after meal, $T_{\text{max}}$ and $C_{\text{max}}$ of F647 concentration show a significant differences ($P<0.01$). $T_{\text{max}}$ was prolonged and $C_{\text{max}}$ was decreased after meal, which indicate the absorption of F647 was impacted by food.
- After multiple oral dosing for 7 consecutive days, no significant changes on PK characteristics of F647 was observed, which means there was no accumulation of F647 in the course of repeated dosing.
- In single dosing study, there were no ADR in 200 mg and 400 mg groups. There were 5 subjects in 800 mg group and 8 subjects in 1200 mg group with mild ADRs.
- In multiple dosing study, there was no ADR in 400 mg group; 6 subjects in 600 mg group occurred mild ADRs.
- According to the outcome of this test, the recommended dosage is 400 mg tid administering after meal.
F647/Pirfenidone Phase II Trials

- Treatment of Idiopathic Pulmonary Fibrosis (IPF)
- Prevention/Treatment of Radiation Pneumonitis (RP)
## Results (Efficacy : FAS)

### Changes of SaO2 (%) from baseline to 12 months after treatment (Primary End Point 1)

<table>
<thead>
<tr>
<th></th>
<th>600mg</th>
<th>400mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD (%)</td>
<td>-2.57 ± 5.10</td>
<td>-0.30 ± 3.05</td>
<td>-3.83 ± 4.02</td>
</tr>
<tr>
<td>P value</td>
<td>&lt; 0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Changes of SpO2 after 6 minute walk test (%) from baseline to 12 months after treatment (Primary End Point 2)

<table>
<thead>
<tr>
<th></th>
<th>600mg</th>
<th>400mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD (%)</td>
<td>-5.17 ± 7.75</td>
<td>0.22 ± 7.30</td>
<td>-9.08 ± 10.66</td>
</tr>
<tr>
<td>P value</td>
<td>&lt; 0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Results (Efficacy : FAS)**

Changes of DLco (%) from baseline to 12 months after treatment

<table>
<thead>
<tr>
<th></th>
<th>600mg</th>
<th>400mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD (%)</td>
<td>-2.79±9.34</td>
<td>-10.93±14.03</td>
<td>-14.92±16.40</td>
</tr>
<tr>
<td>P value</td>
<td>&lt; 0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comparison of pulmonary function effective rate after 12 months treatment

<table>
<thead>
<tr>
<th></th>
<th>600mg</th>
<th>400mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total effective rate (%) (improved + stable)</td>
<td>62.50</td>
<td>56.52</td>
<td>41.67</td>
</tr>
<tr>
<td>P value</td>
<td>&gt; 0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Changes of walking distance of 6 minute walk test from baseline to 12 months after treatment

<table>
<thead>
<tr>
<th></th>
<th>600mg</th>
<th>400mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD (Meter)</td>
<td>-120.44±195.90</td>
<td>-116.47±153.23</td>
<td>-164.62±184.06</td>
</tr>
<tr>
<td>P value</td>
<td>&gt;0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Therapeutic Product Line 2: F351 (NCE)**

**Background and Disease Indication**

- Liver fibrosis is a wound-healing process that occurs in response to chronic stimuli such as excessive alcohol exposure, viral infection (HCV/HBV)
- Hepatic stellate cells proliferate, increase type I collagen production, liver acquires a “fibrotic” appearance
- Can lead to cirrhosis, liver failure, or death
- Possible therapeutic targets: TGF-β pathways, etc.

---

**China:**

- Chronic hepatitis carrier: 26 mil.
- Liver fibrosis: 5.98 mi.
- Alcohol addiction: 15 mil.
- Liver fibrosis: 0.45 mil.

**Japan**

- Liver fibrosis: 2 mil.
- Outpatient: 0.584 mil.
F351 Ameliorates Liver Fibrosis in DMN Model (Rats)

<table>
<thead>
<tr>
<th>Experiment design</th>
<th>DMN</th>
<th>w1</th>
<th>w2</th>
<th>w3</th>
<th>w4</th>
<th>w5</th>
<th>w6</th>
<th>w7</th>
<th>w8</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F351</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Normal

DMN model

F351 50mg/kg

F351 100mg/kg

F351 250mg/kg

Legalon 50mg/kg

Liver Fibrosis Histology: Masson Staining 50×
**Therapeutic Product Line 3: F1013, a Di-Peptide Caspase Inhibitor for Acute-on-Chronic Liver Failure at Pre-IND**

F1013 Treatment Prevents Liver Cell Death and Neutrophil Accumulation

Gal/ET+Vehicle  
Gal/ET+F1013, 10mg/kg

7hr post-Gal/ET; H&E and Esterase stain for PMN  
Gal/ET: galactosamine/endotoxin

Summary:
I. Molecular target: Broad spectrum caspase inhibitor.  
II. Patents: Composition and usage patent granted in China and other territories. Rights in Asia licensed to GNI.  
III. Pharmacology: Efficacious in two animal models of liver fibrosis:  
   A. Endotoxin  
   B. Fas  
IV. Dipeptide orally active small compound  
V. IND expected in 2010.

F1013 Increases Survival of Fas-Induced Hepatitis in Mice

![Graph showing survival rates](image)

Vehicle  
F1013 10mg/kg  
F1013 1mg/kg  
F1013 0.5mg/kg  
F1013 0.25mg/kg

(N=6)  
Minimum effective 50% dose: ~0.25 mg/kg
Future Pipeline with an Emphasis on Co-development

License-in/Co-development

Pre-clinical → Phase I → Phase II → Phase III

Internal Discovery (New Indication, Structural Modification)

Partner with pharma to develop in US/Europe after proof-of-concept

Contact:
Dr. Ying Luo
N30F Shinjuku Park Tower
Nishishinjuku 3-7-1
Shinjuku-ku, Tokyo 160-1030
Japan
+86-13817698961
+81-80-3487-6010
yluo@shanghaigenomics.com
www.shanghaigenomics.com