Developing Innovative Therapies for Patients Suffering from Life-threatening Diseases

Corporate Presentation

NasdaqCM: LJPC

January 2015
Forward-Looking Statements

These slides contain "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking terminology such as "anticipate", "believe", "continue", "could", "estimate", "expect", "intend", "may", "might", "plan", "potential", "predict", "should" or "will" and include statements regarding La Jolla Pharmaceutical’s product candidates and clinical trial progress and results. These forward-looking statements are based on our current expectations, speak only as of the date of this presentation and involve risks and uncertainties, many of which are outside of our control, that can cause actual results to differ materially from those in the forward-looking statements. Potential risks and uncertainties include, but are not limited to, our ability to complete our anticipated clinical trials, the time and expense required to conduct such clinical trials, the ability to manufacture clinical or commercial product, issues arising in the regulatory process, use of proceeds from financings and the results of such clinical trials (including product safety issues and efficacy results). Further information is included in La Jolla Pharmaceutical’s periodic reports filed with the SEC at [www.sec.gov](http://www.sec.gov). We disclaim any duty to update any forward-looking statements.
Overview of LJPC
LJPC-501 (Angiotensin II) for CRH
GCS-100 (IV Galectin-3 Inhibitor) for CKD
LJPC-1010 (Oral Galectin-3 Inhibitor) for NASH
LJPC-401 (Hepcidin) for Iron Overload
Financial Position and Milestones
Product Pipeline

**Preclinical**
- CRH
- HRS
- CKD
- ESRD
- NASH
- Iron Overload

**IND**

**Phase 1**
- Phase 1/2

**Phase 2**
- Early 2015 H1 2016
- Extension 2016
- 2a
- 2b H2 2016

**Phase 3**
- Early H2 2015 2016

**Other R&D**
- LJPC-1010 Oral Galectin-3 Inhibitor
- GCS-100 IV Galectin-3 Inhibitor
- LJPC-401 Hepcidin

*Completed*, *Underway*, *Planned*
Overview of LJPC

LJPC-501 (Angiotensin II) for CRH

GCS-100 (IV Galectin-3 Inhibitor) for CKD

LJPC-1010 (Oral Galectin-3 Inhibitor) for NASH

LJPC-401 (Hepcidin) for Iron Overload

Financial Position and Milestones
LJPC-501 for CRH: Overview

- LJPC-501 is a proprietary formulation of angiotensin II, a naturally occurring regulator of blood pressure
- Catecholamine-resistant hypotension (CRH) is an acute, life-threatening condition in which blood pressure drops to dangerously low levels and is unresponsive to current treatments
- LJPC-501 has been shown to raise blood pressure in a pilot RPC clinical trial in CRH, as well as animal models of hypotension
- Initiation of registration Phase 3 planned for early 2015
  - Meeting held with FDA at which agreement was reached that blood pressure can be the primary endpoint for approval
- Orphan Drug Designation application submitted (75,000-100,000 cases/year in U.S.)
- IP licensed from George Washington University; additional LJPC IP filed
What Is CRH?

**Hypotension** = low blood pressure that is below the normal perfusion blood pressure (MAP < 60-65 mmHg)

- Treated with fluids and catecholamines [epinephrine (adrenaline), norepinephrine (noradrenaline) and dopamine]
- Some patients require excessive doses and are found to be resistant

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**All patients at risk for acute hypotension ~1.5M**
(sepsis, cardiogenic shock, trauma, drug reactions)

5-7% catecholamine-resistant

75,000-100,000 estimated patients per year in U.S.
Even Short Periods of Hypotension Are Associated with Serious Adverse Events

Predicted probability of (A) acute kidney injury and (B) myocardial injury by lowest mean arterial pressure (MAP) experienced during surgery.

What Is LJPC-501?

• Proprietary, stable formulation of synthetic angiotensin II

• Endogenous eight-amino acid peptide that is central to the renin-angiotensin system
  ▪ ACE inhibitors lower BP by inhibiting synthesis of angiotensin II

• Currently being investigated in a Phase 1/2 trial in Hepatorenal Syndrome (HRS)
Angiotensin II Raises Blood Pressure in Hypotensive Pig Model

LJPC-501 Raises Blood Pressure in Hypotensive Pig Model

MAP (mmHg)

Baseline | Post-bleed | 30 ng/kg/min LJPC-501

MAP (mmHg)

Baseline | Post-Bleed | 30 ng/kg/min LJPC-501

p <0.00001 vs. baseline

p <0.00001 vs. Post-bleed
Reduced Angiotensin II Creates Catecholamine Resistance

With enalapril = 7 days oral enalapril plus continuous infusion during treatment.
Enalapril inhibits the production of angiotensin II
Angiotensin II Raises Blood Pressure in CRH Pilot Trial

- Randomized, placebo-controlled, double-blind pilot trial
- 20 patients; 10 per arm
- Primary efficacy endpoint
  - Catecholamine dose sparing; surrogate for BP effect
- Safety and other
  - Understand the dose range of safe use
- Published October 2014 in *Critical Care*

Norepinephrine Dose Decreases with Angiotensin II Surrogate Effect on Blood Pressure

% of Patients with Rise in BP: Placebo Group 20% vs. Angiotensin II Group 80%

High Dose Norepinephrine Is Associated with Very Poor Outcome

- Catecholamines cause cardiac toxicity, digital necrosis and metabolic complications leading to higher mortality
- Blocking the cardiac toxicity of norepinephrine improves outcome


JAMA 2013 Oct23/30 310:1683-1691

Percentage

Alive
Dead

Norepinephrine Dose

Low Dose
Hi Dose

Mortality

Control
Esmolol

Study Day

0 5 10 15 20 25 30

0 0.2 0.4 0.6 0.8 1.0
Planned Phase 3 Trial of LJPC-501 in CRH

- Randomized, placebo-controlled, blinded Phase 3 trial
- Patient population: catecholamine-resistant, based on amount of catecholamine required
- Primary endpoint: blood pressure at 3 hours
- Secondary endpoint: change in CV SOFA score
- Size: 300 patients, 25-35 sites
- Start: early 2015

*Cardiovascular Sequential Organ Failure Assessment
Summary of LJPC-501 in CRH

- LJPC-501 is a proprietary formulation of angiotensin II, a naturally occurring regulator of blood pressure

- Catecholamine-resistant hypotension (CRH) is a high, unmet medical need with no approved therapies
  - Catecholamine resistance is due to under production of angiotensin II

- LJPC-501 has been shown to raise blood pressure in a pilot RPC clinical trial in CRH, as well as animal models of hypotension

- Initiation of registration Phase 3 planned for early 2015
  - Meeting held with FDA at which agreement was reached that blood pressure at 3 hours can be the primary endpoint for approval

- IP licensed from George Washington University; additional LJPC IP filed
Overview of LJPC

LJPC-501 (Angiotensin II) for CRH

**GCS-100 (IV Galectin-3 Inhibitor) for CKD**

LJPC-1010 (Oral Galectin-3 Inhibitor) for NASH

LJPC-401 (Hepcidin) for Iron Overload

Financial Position and Milestones
Galectins and Galectin-3

- Galectins are proteins that can bind to specific sugars on other proteins to modulate cellular function and communication.
- Galectin-3 is unique because it has the ability to self-associate (multimerize) up to a pentameric form, allowing it to bind to several receptors at once.
- Galectin-3 is normally present at low concentration, but is up-regulated in organ failure and cancer; increased levels correlated with reduced survival, disease onset.
Galectin-3 and Organ Failure
Epidemiology and Causative Link

Clinical Epidemiology

- Higher galectin-3 levels in normal individuals are associated with reduced survival\(^1\)
- Galectin-3 predicts CKD risk in the general population\(^2\)
- Galectin-3 serum assay is FDA approved to identify patients at risk for death due to heart failure\(^3\)
- Serum galectin-3 levels identify end-stage renal disease patients who are at highest risk for death\(^4\)
- Galectin-3 levels are increased in patients with cirrhosis and negatively correlate with liver function\(^5\)
- Galectin-3 levels are increased in idiopathic pulmonary fibrosis (IPF)\(^6\)

Galectin-3 KO Demonstrates Causative Link*

- Galectin-3 knockout mice develop significantly less kidney fibrosis and kidney failure compared to normal mice
- Fibrosis restored by transfer of wild type (WT) macrophages in Gal-3 KO mice

* Henderson et al, 2008 Am J Pathol

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1. de Boer et al, 2012 J Intern Med
3. de Boer et al, 2011 Ann Med
4. de Boer et al, 2011 AHA Meeting, Presentation
5. Wanninger et al, 2011 Cytokine
• GCS-100 is a well-characterized, complex sugar derived from pectin
• GCS-100 binds to and neutralizes galectin-3; binding activity is localized to the galactose containing side-branches
• Patented manufacturing process required for biologic activity; issued patent claims cover all modified pectin compositions with defined size
Phase 1 Data Validates Galectin-3 as a Target in CKD

- Single-dose, Phase 1 dose escalation trial complete
- 30 mg/m² MTD
- 1/6 patients at 30 mg/m² experienced reversible, self-limited muscle cramps
- Baseline serum galectin-3 levels strongly correlated with reduced kidney function
**Phase 2a CKD Trial Design**

**Screening Visit**

- **Day -1**: GCS-100 Dosing
- **Day -8**: GCS-100 Dosing
- **Day -15**: GCS-100 Dosing
- **Day -22**: GCS-100 Dosing
- **Day -29**: GCS-100 Dosing
- **Day -36**: GCS-100 Dosing
- **Day -43**: GCS-100 Dosing
- **Day -50**: GCS-100 Dosing

**Study Days: Day 1, Day 8, Day 15, Day 22, Day 29, Day 36, Day 43, Day 50, Day 57**

**Randomized, N=121**

- Placebo, n=41
- 1.5 mg/m², n=41
- 30 mg/m², n=39

**Active in retrospective review**

**Day 1**

**Day 57**

**Dosing, IV**

- PBO or GCS-100 at 1.5 or 30 mg/m²

**1° Endpoint:** eGFR change vs. placebo

**2° Endpoint:** safety and tolerability

**Exploratory Endpoints:** circulating galectin-3, markers of inflammation, fibrosis and renal injury

**Key**

- GCS-100 Dosing
Evaluation of Phase 2a Doses
30 mg/m² Is Too High Based on PK/PD

Pharmacologic overdose may lead to adverse off-target effects.
Time Course of Activity Consistent with MoA

Placebo Group Consistent with Natural Hx of CKD

Efficacy Endpoint Also Met at End of Study Time Point (5 Weeks post Last Dose)

Placebo Data Consistent with the Natural History of eGFR in CKD

Published CKD Natural Hx

Nephrol Dial Transplant (2012) 27: 2255–2263

Change in eGFR (mL/min/1.73m²)

End of Dosing

Primary Endpoint

p=0.04

p=0.07

Study Week

0 2 4 6 8 10 12 14

Placebo

1.5 mg/m²

30 mg/m²

Nephrol Dial Transplant (2012) 27: 2255–2263

Placebo Group Consistent with Natural Hx

Efficacy Endpoint Also Met at End of Study Time Point (5 Weeks post Last Dose)

Placebo Data Consistent with the Natural History of eGFR in CKD

Published CKD Natural Hx

Nephrol Dial Transplant (2012) 27: 2255–2263
Phase 2a Predefined Analyses

Diabetic Subset Shows Most Improvement

Effect on eGFR More Prominent in Diabetic Patients in 1.5 mg/m² Group
(From Baseline to Week 8)

- Placebo (n=29)
- 1.5 mg/m² (n=24)
- 30 mg/m² (n=26)

$\text{Mean Change in eGFR (mL/min/1.73m²), Including Standard Error}$

$p=0.029$ NS
Early Terminations

- 117 of 121 patients enrolled completed the study
  - Placebo: 40/41 completed; 1 withdrew consent after the first dose
  - 1.5 mg/m²: 41/41 completed
  - 30 mg/m²: 36/39 completed; 1 withdrew consent before the first dose, 1 withdrew consent after the second dose due to scheduling conflict, 1 subject failed to come back after the 6th dose without explanation

Overall AE profile comparable between groups

- Similar event rate among the groups, although more grade 3 events in the 30 mg/m² group

4 Serious Adverse Events: none at the 1.5 mg/m² dose

<table>
<thead>
<tr>
<th>Dose (mg/m²)</th>
<th>Event Description</th>
<th>Relationship to drug</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Worsening urinary tract infection</td>
<td>None</td>
<td>Resolved</td>
</tr>
<tr>
<td>0</td>
<td>Cerebrovascular accident</td>
<td>None</td>
<td>Resolved with sequelae</td>
</tr>
<tr>
<td>30</td>
<td>Shortness of breath, secondary to congestive heart failure exacerbation</td>
<td>None</td>
<td>Resolved</td>
</tr>
<tr>
<td>30</td>
<td>Progressive chronic kidney disease and volume overload</td>
<td>None</td>
<td>Resolved</td>
</tr>
</tbody>
</table>
ASN Presentation
Additional Confirmatory Data from Extension Study

Statistically Significant Change in eGFR at 16 Weeks vs. 30 mg/m² Group and Placebo

Mean Change in eGFR (mL/min/1.73m²), Including Standard Error

![Graph showing mean changes in eGFR for different groups with p-values](image)
Primary endpoint reached for 1.5 mg/m^2 dose
- eGFR effect correlates with change in galectin-3
- Multiple secondary endpoints improved and consistent with primary endpoint analysis
- No deaths on study, and no Serious Adverse Events (SAE) and no Grade 3/4 events at 1.5 mg/m^2
- No significant adverse effects on other lab parameters
- Data presentation at American Society of Nephrology
  - Extension data confirm Phase 2a
• **Stage**: 3 and 4
• **eGFR**: high baseline variability excluded
• **Other**:
  • Diabetic Etiology

• **OBJECTIVE**
  Compare efficacy of 3 doses versus placebo

• **PRIMARY ENDPOINT**
  Sustained improvement in eGFR versus placebo

• **SECONDARY ENDPOINTS**
  Rate of CV events

• **N** = 340; 85 patients/arm
• 25 sites; US only
• Duration of treatment: 6 months
• Plan to initiate early 2015
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Financial Position and Milestones
LJPC-1010 is a more potent and purified derivative of GCS-100 that can be delivered orally.

Nonalcoholic steatohepatitis (NASH) is the more serious form of nonalcoholic fatty liver disease (NAFLD), which can lead to liver failure; NASH affects 2 to 5 percent of Americans.

In a preclinical study, LJPC-1010 showed a significant reduction in NAFLD activity score, a system of scoring the features of NAFLD.

IND activities for LJPC-1010 in NASH are underway; initiation of Phase 1 trial planned for early 2015.
LJPC-1010: Effect in NASH Model

- In a preclinical model of NASH, comparing LJPC-1010 to placebo, LJPC-1010 showed a significant reduction (p<0.001) vs. control vehicle in NAFLD activity score.

- LJPC-1010 showed a significant impact on steatosis (fat accumulation), lobular inflammation and hepatocyte ballooning (liver cell death), all three measures that encompass the NAFLD score.
LJPC-1010: Oral Delivery Preferred for NASH

Phase 1 Planned for Early 2015

• Intravenous delivery shows little distribution of drug to liver; oral delivery allows direct exposure to liver;

Next Steps:
  • GMP Manufacturing
  • IND and Phase 1 early 2015
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Financial Position and Milestones
LJPC-401 is a formulation of hepcidin, which is an endogenous peptide hormone that controls and regulates iron metabolism.

Several large indications:
- Acquired iron overload
  - Currently treated with chelators; 50% of patients are intolerant to or fail
  - Approximately 25,000 patients in the U.S.
- Hereditary hemochromatosis
  - Disorder of hepcidin production
  - 1,000,000 patients in the U.S.; 5% fail or are intolerant to phlebotomy
LJPC-401: Hepcidin

- **Hepcidin:** *the insulin of iron metabolism*
  - Regulates iron absorption and disposition in all organs
  - Rapid and sustained lowering of blood iron levels

- **Next Steps**
  - Evaluating SQ formulation
  - Phase 1 2015

- Single 50ug IP injection into a mouse

![Diagram of Hepcidin regulation](image)
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Financial Position and Milestones
Financial Position

Condensed Balance Sheet Data | As of Sept 30, 2014 (in millions)
--- | ---
Cash | $54.2
Total liabilities | $1.6
Total shareholders’ equity | $52.8

**Cash resources expected to fund Company through 2016**

| Fully Diluted, As-Converted Shares Outstanding* | 23,879,489 |
--- | --- |

*Includes common stock, preferred stock & outstanding equity awards as of December 31, 2014*
Development Plan

2014 2015 2016 2017

CRH
LJPC-501
H2 2014 H1 2015 H2 2016
IND Phase 1/2 Phase 3

HRS
H2 2015 Not Budgeted
Phase 2/3

CKD
GCS-100
Phase 2a extension Early 2015 H2 2016 Not Budgeted
Phase 2b Phase 3

ESRD
H1 2015 H1 2016
Phase 1

NASH
LJPC-1010
H1 2015 Early 2015 H1 2016 Not Budgeted
Preclinical / IND Phase 1 Phase 2/3

NASH
LJPC-401
Iron Overload
H1 2015 2015 H1 2016
Preclinical / IND Phase 1

Cash resources through 2016

Today

La Jolla Pharmaceutical
Thank You