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Overview

• Founded in 2009 with key assets in the metabolic area; spun out of Merck Serono
• Imeglimin: First-in-Class
  – Differentiated mechanism of action that works at the level of the mitochondria
  – Completed 18 clinical trials in approximately 1,200 subjects
  – T2D Development in Asia
    • Phase 2b trial in 299 patients in Japan met primary and secondary endpoints
    • PMDA meeting planned in Q3’17
    • Phase 3 initiation planned for Q4’17
  – T2D Development in US/EU
    • Seeking partner for Phase 3
• PXL770: First-in-Class
  – New class of “exercise mimetic” in Phase 1 development
  – Most advanced direct AMPK activator
  – Potential to treat metabolic disorders, including liver disease and T2D
• Broad patent portfolio for Imeglimin and PXL770
• $41.5M in cash and cash equivalents as of March 31, 2017
• Listed on Euronext (Paris): POXEL
• Strategy is growth through pipeline development and strategic partnerships
Leadership Team
Highly-Experienced Management Team

Thomas Kuhn (Pharm D, MBA)
CEO and Co-founder

Anne Renevot
Chief Financial Officer

Noah Beerman (MBA)
Executive VP, Business Development and President, US Operations

Sébastien Bolze (Pharm D, PhD)
Executive Vice President, Non-Clinical Development, Co-founder

Sophie Bozec (PhD)
Senior Vice President, R&D Pharmacology, Co-founder

Pascale Fouqueray (MD, PhD)
CDO, EVP Early Development & Translational Medicine, Co-founder

Christophe Arbet-Engels (MD, PhD, MBA)
CMO and EVP Late Development & Medical Affairs

Jonae Barnes
Senior Vice President
Investor Relations & Public Relations
# Pipeline

<table>
<thead>
<tr>
<th>Indication</th>
<th>MoA</th>
<th>Discovery</th>
<th>PC</th>
<th>Ph 1</th>
<th>Ph 2a</th>
<th>Ph 2b</th>
<th>Ph 3</th>
<th>Next Steps</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Imeglimin</strong></td>
<td>Type 2 Diabetes&lt;br&gt;Japan Development</td>
<td>Mitochondrial bioenergetics enhancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• PMDA meeting Q3’17&lt;br&gt;• Phase 3 program initiation Q4’17</td>
</tr>
<tr>
<td><strong>Imeglimin</strong></td>
<td>Type 2 Diabetes&lt;br&gt;EU &amp; US Development</td>
<td>Mitochondrial bioenergetics enhancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Additional differentiation studies ongoing; partnering opportunity for Ph 3</td>
</tr>
<tr>
<td><strong>PXL770</strong></td>
<td>Metabolic disorders, including liver disease and T2D</td>
<td>Direct AMPK activator</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Multiple ascending doses and efficacy</td>
</tr>
<tr>
<td><strong>PXL007 (EYP001)</strong></td>
<td>Hepatitis B</td>
<td>FXR agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Completion of Phase 1 program by Enyo Pharma&lt;br&gt;(EYP001 is advancing through a licensing agreement with Enyo Pharma)</td>
</tr>
</tbody>
</table>

## Discovery Programs

| #2 | Type 2 Diabetes | Oral GLP-1 agonist | |
| #3 | Type 2 Diabetes | GK activator | |
| #4 | Type 2 Diabetes | 11 beta HSD1 inhibitor | |
| 5 | Type 2 Diabetes | | |
T2D: Significant Market Opportunity with a High Unmet Need

Growing Demand

~415M people between the ages of 20 and 79 worldwide in 2015 = ~642M by 2040*

$37B market in 2014 in the top 7 countries = $71B in 2024**

Unmet Needs of Current Type 2 Diabetes Management

- Preservation of pancreatic function
- Reduce insulin resistance
- Decrease cardiovascular and metabolic disease risk factors
- Improve long-term safety

Imeglimin Target Profile

- Sustained efficacy and safety as monotherapy and in combination with other agents
- Improve insulin secretion
- Imeglimin has been observed to slow disease progression by protecting β cell from death and β cell dysfunction
- Imeglimin may prevent micro- & macro-vascular complications through its effect on improving endothelial dysfunction

PXL770 Target Profile

- Improve main T2D CV risk factors: hyperlipidemia, hyperglycemia and weight
- Improve non-alcoholic fatty liver disease
- Additional metabolic disorders

*IDF Atlas 2015  ** Decision Resources, September 2014
Key Potential Value Drivers

Japan is a ~$4B+ market opportunity for T2D with strong growth

Imeglimin Japan Phase 2b 299-patient study met primary and secondary endpoints

Initiate Phase 3 in Q4'17; ability to develop to JNDA 2019

US/EU is a ~$32B market opportunity for T2D

Imeglimin development in the US/EU; includes ongoing preclinical and clinical activities

Phase 3 partnering opportunity

Unique opportunity for metabolic disorders, including liver disease and T2D

PXL770 direct AMPK activator in clinical development

Phase 1b/2a to assess safety, pharmacokinetics, target engagement, and efficacy biomarkers

Discovery research and licensing

Licensing agreement with Enyo to develop FXR agonist for HepB

In-licensing activities focused on metabolic diseases

* Decision Resources, September 2014
Imeglimin

First in a New Class of Potential Anti-diabetic Treatments with a Differentiated Mechanism of Action
Imeglimin: Oral Compound Targeting the Two Main T2D Defects

- Increases insulin secretion
- Improves insulin efficiency
- Increases glucose uptake
- Reduces glucose overproduction
Imeglimin treatment: Restored normal mitochondrial function

Imeglimin: A Differentiated Mechanism of Action in the Mitochondria Enabling ‘Glucose-plus’ Benefits

Diabetic state: Impaired mitochondrial function leading to
- Insufficient insulin secretion from pancreas
- Insulin resistance in liver and muscles
- β-cells dysfunction and death
- Endothelial cell dysfunction and death

Imeglimin treatment: Restored normal mitochondrial function
- Glucose lowering related benefits:
  - Improve β-cells function and survival
  - Increase glucose dependent insulin secretion from pancreas
  - Improve insulin sensitivity in liver and muscles
- Beyond Glucose lowering related benefits:
  - Improve endothelial dysfunction
  - Improve CV complications
Imeglimin Unique Benefits on CV Complications

**Restoration of normal contractility in aortic rings from diabetic mice**

**Preservation of Acetylcholine Induced Vasodilation in diabetic mice**

Imeglimin improves diastolic dysfunction in the Obese Zucker fa/fa rat

Effect on Left Ventricular End-Diastolic Pressure Volume Relation (LV EDPV)

Source: Poster Presented at European Association of the Study of Diabetes, 2016

Source: Internal data – To be presented at upcoming ADA congress
Imeglimin Unique Benefits on Beta Cell Function Preservation

- Imeglimin preserves beta cell mass and beta cell function over time, leading to a potential delay of the disease progression

Human β-cell Protection from Apoptosis

Human β-cell Protection from Apoptosis

β–cell Preservation in a model of β–cell loss

* p< 0.05 vs control

** p< 0.01 vs control

β-CELL MASS
- Control ZDF Rats
- Imeglimin 150 mg/kg bid

ISLET STRUCTURE
- Control ZDF Rats
- Imeglimin 150 mg/kg bid

β-cell function Preservation

INSULINEMIA-OGTT
- Control ZDF Rats
- Imeglimin 150 mg/kg bid

AUC INSULINEMIA // T0
- Control ZDF Rats
- Imeglimin 150 mg/kg bid

* p< 0.05; ** p< 0.01 vs control

World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease, 2016
**Imeglimin: First-in-Class with Potential Differentiated Benefits**

**Goal is to Slow Disease Progression and Reduce Complications**

<table>
<thead>
<tr>
<th>Benefits on Diabetes Pathophysiology</th>
<th>Metformin Biguanide</th>
<th>Pioglitazone Actos® TZD</th>
<th>Sitagliptin Januvia® DPP-4</th>
<th>Empagliflozin Jardiance® SGLT-2</th>
<th>Imeglimin Glimin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin Secretion</td>
<td>++</td>
<td>--</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Glucose Production</td>
<td>+++</td>
<td>--</td>
<td>--</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Glucose Utilization</td>
<td>++</td>
<td>--</td>
<td>+</td>
<td>--</td>
<td>+</td>
</tr>
<tr>
<td>Glucose Excretion</td>
<td>++</td>
<td>--</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

**Benefits on Disease Progression & Complications**

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Metformin Biguanide</th>
<th>Pioglitazone Actos® TZD</th>
<th>Sitagliptin Januvia® DPP-4</th>
<th>Empagliflozin Jardiance® SGLT-2</th>
<th>Imeglimin Glimin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit on CV Complications</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Benefit on Disease Progression</td>
<td>++</td>
<td>--</td>
<td>+</td>
<td>--</td>
<td>++</td>
</tr>
</tbody>
</table>

Company analysis of published and internal data
Poxel Development and Commercialization Strategy

**Imeglimin Japan – Preparing for Phase 3 Program**

- Japan market offers unique high value creation opportunity
- $4B market anticipated to grow to $6B in 2020*
- Ability to independently advance program to JNDA submission targeted in 2019
- Targeting first-line treatment

**Imeglimin Phase 3-ready Program in US/EU**

- Continuing to strengthen Imeglimin differentiated profile for Phase 3 program
- $32B* market opportunity
- Potential for early use in treatment paradigm
- Seeking partner for Phase 3 development

**PXL770 Phase 1**

- First-in-class novel mechanism
- Opportunity to treat metabolic disorders, including liver disease and T2D
- Phase 1 to assess safety, tolerability and pharmacokinetics

**Opportunistic Approach to Early Research Pipeline**

*Decision Resources, September 2014*
• Phase 2b study in Japan met primary HbA1c endpoint and secondary endpoints
• Efficacy and safety in chronic kidney disease patients was similar to patients with normal renal function
• Safe and well tolerated:
  – Rate of observed adverse events similar to placebo at 500 mg and 1000 mg. Slightly higher rate of GI events at 1500 mg (no adverse event greater than 10%)
  – No serious adverse events related to Imeglimin
• No weight gain
• Phase 3 initiation anticipated in Q4’17
Imeglimin Phase 2b Study in Japan Met Primary Endpoint in Reduction of HbA1c vs. Placebo (N=299)

Change in HbA1c from baseline

- 500 mg: 7.94% (N=75, -0.52%, **)
- 1000 mg: 7.85% (N=73, -0.94%, **)
- 1500 mg: 7.91% (N=73, -1.00%, **)

** p < 0.0001
Imeglimin Phase 2b Study in Japan Decrease in Fasting Plasma Glucose and Glycated Albumin (N=299)

Decrease in Fasting Plasma Glucose

<table>
<thead>
<tr>
<th>Dose (mg/dL)</th>
<th>LS mean change from placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg</td>
<td>-24.6 mg/dL</td>
</tr>
<tr>
<td>1000 mg</td>
<td>-24.6 mg/dL</td>
</tr>
<tr>
<td>1500 mg</td>
<td></td>
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</tbody>
</table>

Decrease in Glycated Albumin

<table>
<thead>
<tr>
<th>Dose (mg/dL)</th>
<th>LS mean change from placebo</th>
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<tbody>
<tr>
<td>500 mg</td>
<td>-2.33%</td>
</tr>
<tr>
<td>1000 mg</td>
<td>-4.11%</td>
</tr>
<tr>
<td>1500 mg</td>
<td>-4.23%</td>
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</table>

** p < 0.0001
Imeglimin Phase 2b Study in Japan Improvement in Beta Cell Function and Liver Function (N=299)

Improvement in HOMA-B – Biomarker of Improvement in Beta Cell Function

<table>
<thead>
<tr>
<th>Dose</th>
<th>HOMA Beta (%) - LS mean change from placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg</td>
<td>6.82</td>
<td>p = 0.008</td>
</tr>
<tr>
<td>1000 mg</td>
<td>8.87</td>
<td>p = 0.0008</td>
</tr>
<tr>
<td>1500 mg</td>
<td>11.28</td>
<td><strong>p &lt; 0.0001</strong></td>
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</tbody>
</table>

Improvement in Liver Function
ALT, AST and GGT

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Mean ALT/AST/GGT (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>-0.9</td>
</tr>
<tr>
<td>AST</td>
<td>0</td>
</tr>
<tr>
<td>GGT</td>
<td>-2.2</td>
</tr>
</tbody>
</table>
### Japan Development Strategy: Advance to JNDA Submission in 2019

#### Mechanism of action relevant for Asian patients

#### Close collaboration with PMDA

<table>
<thead>
<tr>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
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<tr>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
<td>Q4</td>
<td>Q1</td>
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<td>Q2</td>
<td>Q3</td>
<td>Q4</td>
<td>Q1</td>
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<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
<td>Q4</td>
<td>Q1</td>
</tr>
<tr>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
<td>Q4</td>
<td>Q1</td>
</tr>
<tr>
<td>Phase 1</td>
<td>Phase 2b N=300</td>
<td>Ph 3 Monotherapy vs Placebo N=300; 6-month treatment</td>
<td>Long term safety Mono &amp; Add-on to oral therapy <em>(Open label)</em> N=600; 12 months</td>
<td>JNDA Subm.</td>
</tr>
</tbody>
</table>

- **Phase 1**
- **Phase 2b** N=300
- **PMDA EOP2**
- **Ph 3 Monotherapy vs Placebo** N=300; 6-month treatment
- **Long term safety Mono & Add-on to oral therapy *(Open label)*** N=600; 12 months
  - **Long term safety add-on to insulin *(Open label)*** N=100; 12 months
  - **Non-pivotal trials planned: T2D patients with CKD, OGTT**

#### Commercial partnering opportunity for Japan / Asia

OGTT: Oral Glucose Tolerance Test
Targeting 1st Line Treatment in Japan: Oral Anti-diabetes Selection

Underlying cause of T2DM

- Increase Insulin Resistance
  - Decrease Insulin secretory capacity
- Inadequate Insulin Action
- Glucotoxicity
- Hyperglycemia
  - Post prandial
  - Fasting

Oral Anti-Diabetes

- Biguanide: Inhibit Hepatic neoglucogenesis
- TZD: Improve insulin sensitivity in muscle and liver
- Glimins (Imeglimin): Improve insulin sensitivity and insulin secretion
  - Sulfonylureas: Promoting glucose independent insulin secretion
  - Glinides: Promoting glucose independent insulin secretion
  - DPPIV Inhibitor: Promoting glucose dependent insulin secretion - glucagon inhibition
  - α Glucosidase Inhibitor: Delaying intestinal glucose absorption
  - SGLT2 Inhibitor: Promoting urinary glucose excretion
Japan: Accessible Market with Solid Growth, $4B+ Anticipated to Grow to $6B in 2020

- 2nd largest diabetes market outside of US/EU
- ~$4B+ (~/year)
- Estimated sales in Japan expected to grow to $6B by 2020; Imeglimin’s anticipated launch year
- Favorable market access conditions
- Clear development path defined by PMDA: all recent new agents approved with ~1,000 patients in Phase 3
- Sitagliptin: ~$1.1B+ annual sales in 3 years*

* Decision Resources, 2015 Report

Source: Oppenheimer & Co. estimates
Poxel Development and Commercialization Strategy

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- Phase 1 to assess safety, tolerability and pharmacokinetics

**Opportunistic Approach to Early Research Pipeline**

*Decision Resources, September 2014*
Phase 2b Monotherapy Results: Primary Endpoint Met (N=382)

**Secondary Endpoints – Imeglimin**

- 33% of patients to reach A1c target (<7%) (p = 0.005)
- -1.25 mM FPG reduction observed (p = 0.001)

- No subject requiring rescue therapy (p = 0.01)
- Neutral effect on weight observed

**Change in A1c vs. Placebo (%)**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Change in A1c (% vs. Placebo)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>500mg</td>
<td>-0.07</td>
<td>NS</td>
</tr>
<tr>
<td>1000mg</td>
<td>-0.29</td>
<td>NS</td>
</tr>
<tr>
<td>1500mg</td>
<td>-0.63</td>
<td>0.006</td>
</tr>
<tr>
<td>2000mg*</td>
<td>-0.50</td>
<td></td>
</tr>
</tbody>
</table>

**Change in A1c Over Time (Week)**

- Dose dependent effect on A1c reduction vs. placebo
- Maximum efficacy from 18-week treatment

<table>
<thead>
<tr>
<th># Patients/group</th>
<th>500mg</th>
<th>1000mg</th>
<th>1500mg</th>
<th>2000mg*</th>
</tr>
</thead>
<tbody>
<tr>
<td>72</td>
<td>77</td>
<td>69</td>
<td>69*</td>
<td></td>
</tr>
</tbody>
</table>

| A1c Baseline     | 7.95  | 8.09   | 7.89   | 8.04    |

* Excluding one subject due to blood sample error
# Imeglimin: Favorable Safety Profile Observed During the Phase 2b Trial (N= 382)

<table>
<thead>
<tr>
<th>Metformin*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea (53%)</td>
</tr>
<tr>
<td>Vomiting (25%)</td>
</tr>
<tr>
<td>Flatulence (12%)</td>
</tr>
<tr>
<td>Asthenia (9%)</td>
</tr>
<tr>
<td>Indigestion (7%)</td>
</tr>
<tr>
<td>Abdominal discomfort (6%)</td>
</tr>
<tr>
<td>Headache (6%)</td>
</tr>
<tr>
<td>Lactic acidosis <em>(black box warning)</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DPP-4 Inhibitors*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sitagliptin</strong></td>
</tr>
<tr>
<td>Nasopharyngitis (5%)</td>
</tr>
<tr>
<td><strong>Saxagliptin</strong></td>
</tr>
<tr>
<td>Upper respiratory tract infection (8%)</td>
</tr>
<tr>
<td>Urinary tract infection (7%)</td>
</tr>
<tr>
<td>Headache (7%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SGLT-2 Inhibitors*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dapagliflozin</strong></td>
</tr>
<tr>
<td>Female Genital infection (8.7%)</td>
</tr>
<tr>
<td>Nasopharyngitis (7%)</td>
</tr>
<tr>
<td>Urinary infection (6%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Imeglimin 1500 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Similar rate of observed adverse events to placebo</td>
</tr>
<tr>
<td>No hypoglycemia observed</td>
</tr>
<tr>
<td>No related CV event observed</td>
</tr>
<tr>
<td><strong>No adverse effects with greater than 5% prevalence</strong></td>
</tr>
</tbody>
</table>

* Extract from Prescribing Information
18-week Phase 2 Efficacy Trial: Balanced Effect on Glucose (N=59)

Change in Post-Prandial Glucose (AUC) Over Time (Week)

- Mean Change in AUC3h Glucose (mmol.h/L) +/- SE:
  - Imeglimin: -564.8 +/- 800.1
  - Placebo: -166.6 +/- 257.3

- Mean Change in HbA1c (%): +/- SE:
  - Imeglimin: -0.03 +/- 0.53
  - Placebo: -1.36 +/- 0.53

Change in Fasting Glucose Over Time (Week)

- Mean Change in FPG (mmol/L) +/- SE:
  - Imeglimin: -0.24 +/- 0.32
  - Placebo: -0.44 +/- 0.44

Change in HbA1c Over Time (Week)

- 0.62 % A1c reduction vs. placebo observed – fully consistent with Phase 2b results

P = 0.001

P = 0.022

P = 0.013

Source: World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease, November 2015, Los Angeles, USA
Combination with Current Standards of Care

Additive Efficacy Observed when Combined with Either Metformin (N=156) or Sitagliptin (N=179)

**Add-on to Metformin (N=156)**

After 12-week treatment in metformin failure patients

**Add-on to Sitagliptin (N=179)**

After 12-week treatment in sitagliptin failure patients

P. Fouqueray et al, Diabetes Care, 2013

P. Fouqueray et al, Diabetes Care, 2014
US/EU: Phase 3 Program Designed Following Constructive Regulatory Authorities Interactions

- End of Phase 2 meeting FDA guidance:
  - 6 placebo-controlled Phase 3 trials required to support NDA filing (1 monotherapy trial, 3 add-on trials, 1 trial in diabetic patients with renal impairment, 1 Cardiovascular Outcome Trial)
  - 1500 mg bid dose to be used for Phase 3 program in patients with normal renal function, subject to approval by regulatory bodies.
  - Further recommendations for operational efficiencies (statistical analysis plan, CV safety analysis, pediatric plan, etc.)

- EMA recommendation for Phase 3 program
  - Similar guidance to FDA on the Phase 3 program required for EU submission
  - Agree on dose adjustment scheme for patients with renal impairment: 1500mg bid in CK1 & 2,750mg bid in CKD3 and 750mg od in CKD4
# Proposed US / EU Phase 3 Development Plan

7 Studies with ~7,000 Patients

<table>
<thead>
<tr>
<th></th>
<th>Y1</th>
<th>Y2</th>
<th>Y3</th>
<th>Y4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>6-month vs. placebo</td>
<td>12-month extension</td>
<td>Subm. US/EU</td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>6-month add on to Metformin</td>
<td></td>
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<tr>
<td>Q3</td>
<td>12-month add on to Metformin vs Sitagliptin</td>
<td>12-month extension</td>
<td></td>
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<tr>
<td>Q4</td>
<td>6-month add on to Glimepiride</td>
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<tr>
<td></td>
<td>6-month add on to basal insulin</td>
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<tr>
<td></td>
<td>6-month in diabetic patients with renal impairment</td>
<td>6-month extension</td>
<td></td>
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<tr>
<td></td>
<td>Cardiovascular Outcome Trial – Stage 1</td>
<td></td>
<td>Cardiovascular Outcome Trial – Stage 2</td>
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</tbody>
</table>

US | EU
Imeglimin Product Profile has the Potential to Enable Early Treatment Use and in Combinations in US/EU Markets

**Typical Progression of Therapeutic Intervention**

1st line

- **Monotherapy**
  - ~ $1B* market (G7 countries**)

- **Metformin**
  - 60% of T2D patients (G7 countries), generic, launched in 1957

2nd line

- **Oral Combination Therapy**
  - ~ $13B* market
  - 2-drug/3-drug combinations with Metformin

- **DPP-4 inhibitors**
  - Sitagliptin: innovative mechanism, 68% market share within its class

- **SGLT-2 inhibitors**
  - Farxiga, Invokana, Jardiance

- **PPAR agonists**
  - Actos

3rd line

- **Injectable Treatments**
  - GLP-1 Agonists
    - Byetta, Victoza
  - Insulin
    - Severe Diabetes and Complications

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* Decision Resources, 2015 Report
** US, France, Germany, Italy, Spain, UK and Japan
PXL770

A Potential Breakthrough Therapy for Metabolic Disorders, including Liver Disease and T2D
**Imeglimin Japan – Preparing for Phase 3 Program**

- Japan market offers unique high value creation opportunity
- ~$4B market anticipated to grow to $6B in 2020*
- Ability to independently advance program to JNDA submission targeted in 2019
- Targeting first-line treatment

**Imeglimin Phase 3-ready Program in US/EU**

- Continuing to strengthen Imeglimin differentiated profile for Phase 3 program
- ~$32B* market opportunity
- Potential for early use in treatment paradigm
- Seeking partner for Phase 3 development

**PXL770 Phase 1**

- First-in-class novel mechanism
- Opportunity to the treat metabolic disorders, including liver diseases and T2D
- Phase 1 to assess safety, tolerability and pharmacokinetics

**Opportunistic Approach to Early Research Pipeline**

*Decision Resources, September 2014*
First-in-Class “Exercise Mimetic” Drug in Phase 1a Development

Opportunity to Treat Metabolic Disorders, Including Liver Disease and T2D

**PXL770 Direct AMPK Activator**

- AMPK increases glucose utilization
- Increases lipid oxidation
- Improves insulin sensitivity

- AMPK reduces glucose production
- Reduces lipid production

**Exercise mimetic**

- Preclinical and Phase 1 activities ongoing
- Broad IP (7 patents)
- PXL770 composition of matter patent (expiry 2033)

- Aim to demonstrate safety and PK
- Designed to evaluate appropriate safety, tolerability and pharmacokinetics in humans
- Single and multiple ascending doses
PXL770 Inhibits Lipid Production via AMPK Activation

AMPK

AMPK Allosterically Activated

AMPK Allosterically Activated & Phosphorylated

Strong inhibition of lipid production

WT mouse hepatocytes

AMPKα1α2-null hepatocytes

- P<0.05 compared with hepatocytes of the same genotype in G5mM
- *P<0.05 compared with hepatocytes of the same genotype in G25mM+insulin
- +P<0.05 compared with wild type hepatocytes treated the same condition
PXL770: Targeting CV Risk Factors
Benefit on Metabolic Parameters in Various Animal Models

Normalization of Glucose Tolerance

Steady Body Weight Loss, Increased Energy Expenditure and Fat Oxidation

High Fat Diet Mouse Model

Mean ± SEM.
€€ P<0.01, €€€ P<0.001 vs. Chow diet group
* P<0.05, ** P<0.01, vs. HFD control group.
$$ P<0.01, $$$ P<0.001 vs. HFD pair fed group
## PXL770 Development Strategy to PoC

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Safety / Pharmacokinetics / Tolerability</strong></td>
<td><strong>Clinical Proof of Efficacy in Patients with Liver Disease and Type 2 Diabetes</strong></td>
</tr>
<tr>
<td>• Safety / tolerability / pharmacokinetics after single and multiple ascending doses</td>
<td>• Glycemic parameters (FPG, OGTT, insulin resistance) and weight</td>
</tr>
<tr>
<td>• Metabolite identification and qualification</td>
<td>• Lipids, liver fat mass and inflammation</td>
</tr>
<tr>
<td></td>
<td>• Safety in target population</td>
</tr>
<tr>
<td></td>
<td>• Target engagement in patients</td>
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</tbody>
</table>
Several Near-Term Catalysts

• Imeglimin
  – Additional data on cardiovascular benefits (Q2/Q3 2017)
  – Presentations for Imeglimin at upcoming scientific meetings, including ADA, ESC, EASD (Q2/Q3 2017)
  – Full Results from Phase 2b study in Japan (2H17)
  – Potential partnership opportunity in Japan and US/EU
  – PMDA End of Phase 2 meeting (3Q 2017)
  – Phase 3 Japan program initiation (4Q 2017)

• PXL770
  – Additional preclinical studies to support clinical program (2017)
  – Phase 1b/Phase 2a studies (2017/2018)

• Licensing
  – Phase 1 program completion for FXR agonist by Enyo Pharma
  – In-licensing activities focused on programs in the metabolic area