Disclaimer

Some of the statements contained in this presentation constitute forward-looking statements. Statements that are not historical facts are forward-looking statements. Forward-looking statements generally can be identified by the use of forward-looking terminology such as “may”, “will”, “expect”, “intend”, “estimate”, “anticipate”, “believe”, “continue” or similar terminology. These statements are based on the Company’s current strategy, plans, objectives, assumptions, estimates and projections. Investors should therefore not place undue reliance on those statements. The Company makes no representation, warranty or prediction that the results anticipated by such forward-looking statements will be achieved, and such forward-looking statements represent, in each case, only one of many possible scenarios and should not be viewed as the most likely or standard scenario. Forward-looking statements speak only as of the date that they are made and the Company does not undertake to update any forward-looking statements in light of new information or future events. Forward-looking statements involve inherent risks and uncertainties. The Company cautions that a number of important factors could cause actual results to differ materially from those contained in any forward-looking statement.

In the context of the COVID-19 outbreak, which was declared a pandemic by the World Health Organization (WHO) on March 12, 2020, the Company is regularly reviewing the impact of the outbreak on its business.

The Company anticipates that the COVID-19 pandemic could have a material negative impact on our business operations. The worldwide impact of COVID-19 may notably affect the Company’s internal organization and efficiency, particularly in countries where it operates and where confinement measures have been implemented by the authorities. In addition, the deteriorating market conditions may impact the Company’s ability to raise additional funding and/or to enter into partnerships. Particularly, delays in the supply of drug substance or drug products, in pre-clinical and/or clinical trials, as well as delays linked to the responsiveness of regulatory authorities could occur, which could potentially have an impact on the Company’s development programs. The Company will continue to proactively monitor the situation.
Mission and Vision

To discover, develop and commercialize innovative therapies for patients suffering from serious chronic diseases with underlying metabolic pathophysiology

• Mid-to-late stage first-in-class pipeline: Type 2 diabetes (globally partnered) and NASH
• Pipeline expansion in chronic and rare metabolic indications
  o Internal AMPK* and D-TZD# Platforms
  o External Opportunities

Targeting Defects in Cellular Metabolism

Leveraging AMPK & D-TZD Platforms

Metabolic Component + Unmet Medical Need

• Hereditary Metabolic Disorders: e.g. adrenoleukodystrophy
• Endocrinopathies
• Renal Diseases: e.g. diabetic nephropathy, polycystic kidney disease, others
• Other: rare, orphan indications

*AMP activated protein kinase; # Deuterium-stabilized thiazolidinediones
Three Mid-to-Late Stage First-in-Class Drug Candidates with Novel Mechanisms and Differentiated Strategies

- **Imeglimin (T2D)**
  - *PLX770 direct AMP-kinase activator (AMPK) from platform*
  - **PXL065 deuterium-stabilized R-pioglitazone (mitochondrial pyruvate inhibitor) from D-TZD (deuterated thiazolidinediones) platform**

- **Type 2 Diabetes**
- **Highly experienced management team; extensive metabolic R&D expertise & track record in US, EU and Japan**
- **Several significant milestones in 2020 including results in NASH & other metabolic indications**

- **Global company with presence in 3 countries** (France, US and Japan); listed on Euronext Paris

- **Anticipated first product launch in Japan in 2021 through Imeglimin partnership with Sumitomo Dainippon Pharma**

- **Global Partnerships**
- **Novel Mechanisms with Platform Expansion**
- **Proprietary Programs**

- **Cash & Equiv. EUR 46M (USD 51.5M) as of 6/30/20**
Poxel Targets Key Mechanisms that have Distinct Roles in Regulating Cellular Energy Homeostasis

Multiple Entry Points Available to Intervene in Metabolic Diseases

AMPK

Activates catabolic pathways

Inhibits anabolic pathways

Inhibits inflammation apoptosis

AMP-activated Protein Kinase (AMPK), cellular energy sensor - activation: reduces liver fat, increases insulin sensitivity, decreases inflammation

Mitochondrial Pyruvate Carrier (MPC), fuel gate-keeper – inhibition: promotes fat utilization, increases insulin sensitivity, decreases inflammation

Mitochondrial Respiratory Chain (MRC), cell’s energy producing machine – potential to modulate function: improves β-cell function, increases insulin sensitivity, improves endothelial and diastolic dysfunction

NASH Other

T2D

NASH Other

AMPK

Mitochondrial Pyruvate Carrier (MPC)

Mitochondrial Respiratory Chain (MRC)

Pyruvate

Acetyl Co-A

TCA cycle

NADH

FADH2

ATP
# Poxel Mid-to-Late Stage Metabolic Pipeline

*Due to COVID-19, the Company Continues to Monitor All Developments that Might Impact the Timelines for Achievement of our Corporate Objectives*

<table>
<thead>
<tr>
<th>Indication</th>
<th>MOA</th>
<th>Discovery/PC</th>
<th>PH 1</th>
<th>PH 2</th>
<th>PH 3</th>
<th>NDA review</th>
<th>Partner/ Rights</th>
<th>Upcoming Milestones</th>
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<tbody>
<tr>
<td>Type 2 Diabetes</td>
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<td>Imeglimin Japan</td>
<td>Type 2 Diabetes (T2D)</td>
<td>MRC Modulator</td>
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<td>Sumitomo Dainippon Pharma</td>
<td>• Target product launch 2021</td>
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<td>Asia*</td>
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<td>Imeglimin US / EU</td>
<td>T2D patients with CKD stages</td>
<td>MRC Modulator</td>
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<td>ROIVANT SCIENCES</td>
<td>• Ongoing Ph3 dialog w/ FDA; initiate Ph 3 post-FDA discussion</td>
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<td>Other**</td>
<td>3b/4</td>
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<td>NASH</td>
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<td>PXL770</td>
<td>NASH</td>
<td>Direct AMPK Activator</td>
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<td>• Ph 2a results late 3Q 20</td>
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<td>PXL065</td>
<td>NASH</td>
<td>MPC Inhibitor</td>
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<td>• Utilize 505(b)(2) pathway</td>
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<td>PXL007 (EYP001)</td>
<td>Hepatitis B / NASH</td>
<td>FXR Agonist</td>
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<td>• 2H 20 Ph 2; initiation subject to COVID-19 environment</td>
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<td>• Complete Ph 2a program by Enyo Pharma 2H 2020</td>
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<td>Other Chronic and Rare Metabolic Indications</td>
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<td>Next-Gen AMPK</td>
<td>Adreno-leukodystrophy</td>
<td>Direct AMPK Activator</td>
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<td>• Complete preclinical studies 2020</td>
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<td>Next-Gen D-TZD</td>
<td>Chronic Kidney Diseases</td>
<td>MPC Inhibitor</td>
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*including: China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, the Philippines, Singapore, Myanmar, Cambodia, and Laos.**

**countries not covered in the Sumitomo Dainippon Pharma agreement.**
Leadership Team

Highly Experienced Management Team; Extensive R&D and Metabolic Expertise

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

Anne Renevat
Chief Financial Officer

Noah Beerman (MBA)
Executive Vice President, Business Development & President, US Operations

David Moller (MD)
Executive Vice President, Chief Scientific Officer (CSO)

Jonae Barnes
Senior Vice President, Investor Relations & Public Relations

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

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

Quentin Durand
Chief Legal Officer

Pascale Fouqueray (MD, PhD)
Executive Vice President, Early Development & Translational Medicine, Co-founder
First in a New Class of Potential Anti-diabetic Therapies with a Differentiated Mechanism of Action
Successful Completion of Phase 3 Program in Japan
JNDA Under Review; Target Launch 2021

Poxel led Phase 3 TIMES program in >1,100 T2D patients; met endpoints and objectives and observed to be safe and well-tolerated

TIMES 1: Monotherapy vs placebo
N= 213; 6-month treatment

TIMES 2: Long term safety Mono & Add-on to oral therapy (Open label)
N=714; 12 months

TIMES 3: Long term safety add-on to insulin
N=215; 12 months

Non-pivotal trials in renal impaired population

<table>
<thead>
<tr>
<th>2018</th>
<th>2019</th>
<th>2020</th>
</tr>
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<tbody>
<tr>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
</tr>
</tbody>
</table>

TIMES 1: Monotherapy vs placebo
N= 213; 6-month treatment

TIMES 2: Long term safety Mono & Add-on to oral therapy (Open label)
N=714; 12 months

TIMES 3: Long term safety add-on to insulin
N=215; 12 months

Non-pivotal trials in renal impaired population

Partnership Details

- Sumitomo commercialization partner for Japan, China and 11 other East and Southeast Asian countries*
- Future potential development milestone payments and sales-based payments of up to approx. $257M
- Double-digit escalating royalties

Business Opportunity Japan: Maximize Product Profile

- Sumitomo #1 diabetes franchise; Guidance FY20 $900M¹
- DPP4i’s are prescribed to 80% T2D patients²
- Limited treatment options for selected populations, incl. elderly and patients with renal impairment
  - Elderly patients account for ~60% of T2D in Japan
- TIMES program observed to show robust efficacy with favorable safety and tolerability profile

* including: South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, the Philippines, Singapore, Myanmar, Cambodia, and Laos. ¹ Sumitomo Fiscal Year April-March. ² IQVIA data FY2016 and NDB data FY2016
Imeglimin Phase 3 TIMES Program Overview (N=1,142)
Robust and Consistent Efficacy in Monotherapy and as an Add-on Therapy

**TIMES 1**
Monotherapy

**TIMES 2**
As an Add-on to Standard of Care

**TIMES 3**
Combination with Insulin

**Change in HbA1c – 24 Weeks**

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Placebo (N=107)</th>
<th>Imeglimin (N=106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>7.93 (0.684)</td>
<td>7.99 (0.764)</td>
</tr>
</tbody>
</table>

**Change in HbA1c (%) – LS Mean Change from Placebo**

- 1000 mg
- HbA1c (%) – LS Mean Change from Placebo:
  - 0.87 (%)
  - p < 0.0001

**Change in HbA1c (vs baseline) – 52 Weeks**

**Change in HbA1c (%) – LS Mean Change from Baseline**

- SU: Sulfonylurea
- GLIN: Glinides
- BIG: Biguanides
- TZD: Thiazolidinediones
- AGI: Alpha-glucosidase inhibitor

**Change in HbA1c – 16 Weeks**

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Placebo (N=107)</th>
<th>Imeglimin (N=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>8.8 (0.8)</td>
<td>8.7 (0.7)</td>
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</tbody>
</table>

**LS Mean Change from Placebo**

- 0.60% (0.10)
- p < 0.0001

*European Association for the Study of Diabetes meeting 2019
Imeglimin Development Strategy for the US & EU
Targeting Type 2 Diabetes Patients with Chronic Kidney Disease (CKD) Stages 3b/4

- Development and commercialization partner in the US, Europe, and other countries*
- Poxel and Roivant will decide on a potential co-promotion prior to commercialization

Initial Development Focus: T2D patients with CKD stages 3b/4

- Demonstrated similar efficacy and was well-tolerated in renally impaired patients (TIMES 1 & Phase 2 data; Japan, US and Europe)
- PK/PD trial met primary objective in this patient population
  - Favorable safety and tolerability profile observed
  - PK/PD data consistent with previous Poxel data
- Given FDA feedback and new draft guidance in March 2020, Metavant is adjusting its Phase 3 plan
- New FDA interactions planned for 2H 2020

Partnership Details

- Upfront payment: $35M
- Equity Investment: $15M at €8.5/share
- Future potential development and regulatory milestone payments and sales-based payments of up to $600M
- Double-digit escalating royalties

*countries not covered in the Sumitomo Dainippon Pharma agreement

1. Poxel contributed $25M (~€20M) to development program over a 2-year period.
2. CKD stage 3b= eGFR 30-44 ml/min/1.73 m² inclusive; CKD stage 4 = 15-29 ml/min/1.73m² inclusive.
Limitations of Current Therapies to Treat T2D by Kidney Disease Stage Drives Metavant Focus for Imeglimin

T2D patients with CKD stages 3b/4
- Diabetes is the most common cause of CKD
- ~ 2.4 million adults in the US
- Increased cardiovascular risk and challenging glucose management

Underserved patient population
- Many therapies require dose reduction or not recommended in the presence of kidney disease
- Insulin and insulin secretagogues most commonly used at suboptimal doses to prevent hypoglycemia risk
- We believe there is a need for a new treatment with robust efficacy and safety profile with no hypoglycemia risk

Please note that references for this slide are in the Appendix section.
PXL770
Proprietary Program

Direct AMPK Activator for the Treatment of NASH
Progression of Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH)

Excessive caloric intake
Sedentary lifestyle

NAFLD
25% of the general population
>70% in diabetic & obese patients

NASH
12% of the general population
25-70% in diabetic and obese patients ≥ 50

Cirrhosis

Estimated Market Opportunity: >$20B by 2025

Metabolic syndrome
Dyslipidemia
Type 2 diabetes
Obesity

Cardiovascular events (leading cause of death)
Hepatic impairment
Hepatocellular carcinoma

High Morbidity

Hepatic impairment
Hepatocellular carcinoma

Normal

Fat Deposition

Steatosis
Lipotoxicity

Inflammation
Fibrosis
Collagen Deposition
PXL770 & PXL065 Aim to Address Hallmarks of NASH Pathology

NASH is a Complex, Multifactorial Disease

**HALLMARKS OF NASH**

- **Steatosis**: Fat gets released from the adipose tissue and accumulates in the liver cells and stays stored there.

- **Inflammation**: Macrophages (MΦ) become activated and lead to inflammation in the liver.

- **Ballooning**: Fat accumulation and inflammation cause degenerative structural changes; ballooning is a sign of cell damage & suffering.

- **Fibrosis**: Hepatic stellate cells become activated and create scar tissue.

There are no currently approved drugs that treat symptoms & complications across all four categories.
AMPK Activation Observed to Restore Metabolic Balance

**PXL770 is a Direct AMPK Activator**

Overnutrition (metabolic syndrome, NASH, Type 2 Diabetes)

1) **Activates** catabolic pathways
   - Fatty acid oxidation
   - Glucose uptake
   - Glycolysis

2) **Inhibits** anabolic pathways
   - Fatty acid & triglyceride synthesis (via ACC inhibition)*
   - Cholesterol synthesis
   - Protein synthesis
   - Mitochondrial biogenesis

3) **Other benefits**
   - Reduces inflammation
     ↓ macrophage and dendritic cell activation
     ↓ pro-inflammatory cytokines
     ↓ NF-κB plus many others
   - Reduces tissue damage (e.g. apoptosis via Caspase 6)
   - Inhibits lipolysis in adipose

*Acetyl CoA carboxylase; a direct AMPK target; clinically validated; GS-0976 [Gastroenterology 155:1463-, 2018].
Activating AMPK Observed to Show Beneficial Effects in NASH

HALLMARKS OF NASH

Steatosis

Improves steatosis by limiting fat flux from adipose tissue and de novo lipogenesis

Inflammation

Decreases inflammation by moving from a pro-inflammatory phenotype to an anti-inflammatory phenotype

Ballooning

Decreases structural degenerative changes and improves cell health

Fibrosis

Decreases hepatic stellate cell activation and limits fibrosis

We believe PXL770 also has the potential to be used in combination with other mechanisms for additive benefits.

These results were observed in mouse model preclinical study.
PXL770: Preclinical Data Observed to Show Potential to Treat Underlying Root Causes of NASH

Data Observed in Multiple Rodent Models Supports Potential for PXL770’s Beneficial Clinical Effects

A. Improved liver steatosis
B. Decreased liver (and adipose tissue) inflammation
C. Decreased profibrogenic pathways in liver
D. Improved plasma liver enzymes (ALT and AST)
E. Improved NAFLD Activity Score (NAS)

**LEANT- Chow vehicle**
**DIO-NASH vehicle**
**DIO-NASH PXL770 75mg/kg bid**
**DIO-NASH PXL770 35mg/kg bid**

**:** p< 0.01, **:** p< 0.001; **** p<0.0001 compared to DIO-NASH vehicle. n=11-12/group

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A. NASH Vehicle
B. Total Liver Macrophages
C. Collagen 1A1 (Liver)
D. Plasma ALT
E. NAS Score

PXL770: Preclinical Data Observed to Show Potential to Treat Underlying Root Causes of NASH

Data Observed in Multiple Rodent Models Supports Potential for PXL770’s Beneficial Clinical Effects

- Improves metabolic syndrome associated with NASH
  - Improves glycemia and lipids in metabolic rodent models:
    ▪ Increased insulin sensitivity
    ▪ Glycemic control: basal glycemia, glucose tolerance and HbA1c
    ▪ Lower circulating lipids (TG’s, FFA’s)
  - Induces a metabolic switch toward preferential fat oxidation

**Insulin Sensitivity**

- **Day 8 WD**
- **Day 22 WD**

**Fat Oxidation**

- WD: Whole Day
- Veh: Vehicle
- PXL770: Preclinical Data Observed to Show Potential to Treat Underlying Root Causes of NASH
- Data Observed in Multiple Rodent Models Supports Potential for PXL770’s Beneficial Clinical Effects

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**Fat Oxidation**

- ob/+ mice: Vehicle
- ob/ob or HFD mice: Vehicle
- ob/ob mice: PXL770 100mg/kg bid
- HFD mice: Pioglitazone 20mg/kg qd

**Statistical Significance**

- ****P<0.0001 vs. veh group.
PXL770: Encouraging Clinical Results Observed (n=148)

*Dose-Dependent PK; Favorable Safety/Tolerability; Target Engagement; Efficacy Signals*

**Phase 1 Healthy Subjects (n=132)**

- Linear, dose-proportional exposure with single and multiple* doses
- Terminal half-life 25h
- No drug-drug interaction with rosuvastatin (OATP and BCRP substrate)
- No SAEs or AEs leading to discontinuation
- Good tolerability; low placebo-like incidence of TAE events
- No effect on ECG parameters (no QT prolongation)

**PK/PD Trial: Obese, Insulin Resistant (n=16)**

- Four-week placebo-controlled study in likely-NASH patients
- Study objectives met:
  - Consistent PK profile
  - **Target engagement & efficacy signals:**
    - **suppression** of *de-novo* lipogenesis (liver synthesis of new lipids)
    - **improved** glucose tolerance and indices of insulin sensitivity
  - Safety and tolerability similar to placebo

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* Results support potential in NASH and for AMPK platform in other chronic and rare metabolic diseases

* Up to 375 mg (less than dose-proportionate at 500 mg); △DNL assessed via fructose loading with D2O labelled palmitate measurements; #oral glucose tolerance test; ^ HOMA-IR, Matsuda, OGIS.
PXL770 PK/PD Study Demonstrated Target Engagement and Efficacy Signals

- **Inclusion criteria**: controlled attenuation parameter (CAP) score >300 db/m (measured by FibroScan®) and HOMA-IR* score >2.5
- **Treatment arm (n=12)**: four weeks PXL770 500 mg QD
- **PXL770 suppressed de-novo lipogenesis◊**, which is responsible for ~25% of liver fat accumulation
- **PXL770 improved glycemia◊** - both total and incremental glucose AUC
- **PXL770 improved insulin sensitivity◊** measured by HOMA-IR (p=0.013); Matsuda# (p=0.014); OGIS∆ (p=0.012)
- **AMPK activation demonstrated**: beneficial impact on key pathways of liver injury and NASH

◊ Versus baseline; no effect in Placebo group

*Homeostatic Model Assessment of Insulin Resistance; # Diabetes Care 1999; 22: 1462–1470; ∆ Oral glucose insulin sensitivity index
PXL770: Ongoing Phase 2a Program for NASH
Phase 2a 12-week, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel Group Trial

- N = 100 likely-NASH patients with and without Type 2 diabetes
- Inclusion criteria: increased hepatic fat (assessed via CAP and MRI-PDFF)
- Trial to assess efficacy and safety
- Primary endpoint: relative change in % liver fat mass (MRI-PDFF) from baseline

Results expected late 3Q 20
Pre-Clinical Data Demonstrate Potential Synergy of PXL770/AMPK Activation with Other Agents in Development

**PXL770 / Semaglutide (GLP-1) Mouse NASH Model**

- Liver lipid content (mg)
  - Vehicle: ****
  - PXL770: ****
  - Semaglutide: ****
  - PXL770 + Semaglutide: ****

- Plasma ALT (U/L)
  - Vehicle: ****
  - PXL770: ****
  - Semaglutide: ****
  - PXL770 + Semaglutide: ****

* p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001, **** p ≤ 0.0001 vs vehicle
# p ≤ 0.05, ## p ≤ 0.01, ### p ≤ 0.001, #### p ≤ 0.0001 vs combination
N=12-13

**Other Mechanisms**

- **PXL770**
  - Low grade inflammation
  - Lipolysis

- **Effects in Adipose Tissue**
  - Low grade inflammation
  - Lipolysis

- **Effects in Liver**
  - De novo lipogenesis / Steatosis
  - Chronic inflammation
  - Stellate cell activation / Fibrosis
  - Apoptosis / cell death

- **Effects in Muscle**
  - Peripheral insulin resistance

---

**Peripheral insulin resistance**

**(Effects in Muscle)**

**(Effects in Liver)**

**(Effects in Adipose Tissue)**

---

**Peripheral insulin resistance**
PXL065
Proprietary Program

MPC Inhibitor for the Treatment of NASH Utilizing the 505(b)(2) Regulatory Pathway
PXL065: Leveraging the Benefits of Pioglitazone
With Reduced PPARγ Activity

• Pioglitazone used in T2D for > 20 years
  >30 million patient-years of exposure
  Established CV outcomes benefit

• Pioglitazone extensively studied and has demonstrated resolution of NASH
  Demonstrated “Resolution of NASH without worsening of fibrosis” in Phase 4 trial
  Only drug recommended for biopsy-proven NASH by AASLD & EASL Practice Guidelines
  Currently prescribed by ~14% of physicians for biopsy-proven NASH patients
  Limited use due to PPARγ-related side effects: weight gain, fluid retention, bone loss

• Pioglitazone, TZDs: both genomic (PPAR) and non-genomic (MPC) mechanisms

• PXL065 is an NCE which selectively mediates non-PPAR effects of Pioglitazone

2. Diab & Vascular Disease Res 2018; 16:133-143
5. Therap Adv Gastroenterol. 2016, 9(1), 4-12
Pioglitazone has Demonstrated Resolution of NASH

Largest Effect of Oral Agents - Use Limited by Weight Gain

Resolution of NASH
without worsening of fibrosis

Patients with Improvement, %

Phase 3 or 4 Trials

- Pioglitazone
- Ocaliva
- Elafibranor
- CVC
- Liraglutide
- Resmetirom
- Aramchol
- Aldaferin
- Semaglutide
- Lanafibranor

Phase 2 Trials

- Pio Cusi Phase 4 trial (30–45 mg, 18 mos) - Ann Intern Med. 2016, 165(5), 305-315 (only completers with definite NASH at baseline). Patients on placebo benefited from 4% weight loss due to hypocaloric diet
- Ocaliva REGENERATE Phase 3 trial (25 mg, 18 mos) - Lancet. 2019, 394(10215): 2184-2196
- Elafibranor RESOLV-IT Phase 3 trial (120 mg, 52 wks) – Press release May 11, 2020
- CVC (Cenicriviroc) CENTAUR Phase 2 trial (150 mg, 2 yrs) – Hepatology 2020, Jan 13 epub
- Liraglutide Phase 2 trial (0.6 increased to 1.8 mg sc weekly 48 wks) - The Lancet, 2016, 387(10019), 679–690
- Resmetirom (MGL-3196) Phase 2 trial (80 mg +/- 20 mg, 36 wks) – Lancet 2019 394:2012-24. Results from per protocol, not intent to treat (ITT) population.
- Aramchol Phase 2 trial (600 mg, 52 wks) – press release June 12, 2018. No effect on "Fibrosis without worsening of NASH".
- Aldaferin (NGM282) Phase 2 trial (1 mg, 24 wks, cohort 4) - Press release Feb 25, 2020. P value not disclosed.
- Semaglutide Phase 2 trial (0.4 mg, 72 wks) – Press release May 6, 2020. P value not disclosed.
- Lanafibranor Phase 2 trial (1200 mg, 24 wks, ITT population) – Press release Jun 15, 2020 (also at 800 mg 33% pts met endpoint, p=0.043)

No head-to-head trials have been conducted. Data derived from different clinical trials with potentially different designs, patient populations, and definition of NASH resolution.
PXL065: A Single Stabilized Stereoisomer of Pioglitazone

Benefits of Pioglitazone for NASH with Reduced PPAR\textsubscript{\gamma} Side Effects

- Pioglitazone is a mixture of 2 stereoisomers with dramatically different properties
- PXL065 is the deuterium-stabilized R-stereoisomer

**S-Pioglitazone (stabilized)**
- MPC inhibitor
- Strong PPAR\textsubscript{\gamma} agonist

**PXL065 (stabilized R-pio)**
- MPC inhibitor
- Very weak PPAR\textsubscript{\gamma} agonism

**Undesired side effects:**
- Weight gain
- Fluid retention

**Activity in NASH**
PXL065 Targets Inhibition of MPC
*Without PPARγ Agonist Activity from S-Stereoisomer*

**MPC Inhibition in HepG2 Cells**

![Graph showing MPC inhibition in HepG2 cells.](image)

**PPARγ Agonist Activity**

![Graph showing PPARγ agonist activity.](image)

PPARγ activation in fluorescence-based TRAP220 coactivator recruitment assay
Results are expressed as % of response of positive control (10µM rosiglitazone)
PXL065 Targets Inhibition of MPC & Modulates Cellular Fuel Utilization

MPC Regulates Transport of Pyruvate Across Mitochondrial Inner Membrane

Regulates cellular fuel selection – Modulates cell signaling

Additional Validation

- MPC inhibition implicated as beneficial for neuroinflammation/neurodegeneration
  - Liver-selective MPC2 -/- mice:
    - Decreased gluconeogenesis; protection from hyperglycemia
    - Protection from diet-induced NASH – transaminase elevations, fibrosis score, stellate cell activation

Inhibiting MPC leads to improvements in NASH and metabolic disease endpoints

Decreasing Entry of Pyruvate by Inhibiting MPC has Desirable Effects in NASH

HALLMARKS OF NASH

Steatosis

- Increasing fat oxidation decreases liver fat content

Inflammation

- Resetting mitochondrial metabolism improves inflammation

Ballooning

- Resetting mitochondrial metabolism protects cells from degeneration

Fibrosis

- Inhibiting MPC decreases HSC\(^1\) activation and markers of fibrogenesis

PXL065 also has the potential to be used in combination with other mechanisms for additive benefits

1. HSC: Hepatic Stellate Cell.
PXL065: Similar Activity to Pioglitazone in NASH Mouse Models

Results Consistent with Potential Beneficial Clinical Effects

- Liver histopathology on day 43 in mice fed a Choline Deficient (CD) or a Methionine/Choline Deficient (MCD) diet

- Pioglitazone (30 mg/kg/day) or PXL065 (15 mg/kg/day), Wilcoxon rank sum test vs vehicle; *p < 0.05, **p < 0.005, ***p < 0.001
Summary of PXL065 Benefits in NASH

PXL065 (R-Pio) Retains Benefits of Pio; S-Pio Drives Weight Gain in Mouse Model

1. NASH rodent models selected based on literature: C57BL/6J mouse model of weight gain & edema (Nat Med 2005, 11, 861-866) and methionine-choline deficient (MCD) model of NASH (Lab Investig. 2007, 87, 56-65). Additional choline deficient (CD) model of NASH was validated with RenaSci. In MCD model both pio and PXL065 reduced ballooning. d-S-pio was only run in the CD model where no effect on ballooning with any compound was observed.

2. Weight gain measured in C57BL/6J mouse model. Pioglitazone dosed at 30 mg/kg, d-S-pio and PXL065 dosed at 15 mg/kg. Statistical significance determined by 1-way (total day 11) or 2-way (% by day) ANOVA with Dunnett’s post average ± SEM; * p < 0.05, ** p < 0.01, *** p < 0.001, **** P < 0.0001

<table>
<thead>
<tr>
<th>NASH Rodent Models¹ Functional Parameters</th>
<th>Pio</th>
<th>PXL-065</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic Triglycerides</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatic Free Fatty Acids</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatic Cholesterol</td>
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</tr>
<tr>
<td>Hepatic Steatosis</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatic Inflammation</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatic Ballooning</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatic Fibrosis</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Weight Gain</td>
<td>✓</td>
<td>-</td>
</tr>
<tr>
<td>Edema</td>
<td>✓</td>
<td>-</td>
</tr>
</tbody>
</table>

Body Weight Gain in Mouse Model²

(0-11 days)
1992 FDA guidance document “Development of New Stereoisomeric Drugs”

- Streamlined development expected for single enantiomers of approved racemic drugs
- Existing nonclinical data from the racemate can be relied upon to support the safety of the single enantiomer, and an abbreviated pharmacology and/or toxicology evaluation and initial clinical characterization may be pursued (Section IV of FDA, 1992)

Ability to rely on data generated by others in

- Product label for parent drug
- Published literature

Potential opportunities to bridge to data from parent drug

- Fewer animal toxicity studies
  - Example: 28 day and 90-day studies in 1 species instead of 2
  - Example: no need for 2-year rat carcinogenicity study
- Potential for fewer clinical trials for submission of NDA
- Safety database with <1500 subjects
**PXL065: Phase 1 Study Results**

15 mg PXL065 vs. 45 mg Actos®: Similar R-Pio Exposure; S-Pio Exposure Decreased ~5-fold

- Single (SAD) and repeated (Ph1b) oral dose studies completed
- Stabilization and sustained higher exposure to R-pio (limited conversion to S-pio)
  - PK dose proportionality; no food effect
  - tablet formulation qualified in Ph1b study
- Well tolerated at all doses tested
PXL065: One Phase 2 Trial in Biopsy-Proven NASH Patients
Leveraging 505(b)(2) Pathway

36-week multicenter, double-blind, placebo-controlled, parallel group, randomized trial to evaluate the safety and efficacy of 3 doses in ~120 noncirrhotic biopsy-proven NASH patients

- Phase 2 objective: identify one or two doses for Phase 3 registration trial
- Primary objective: Assess efficacy of escalating doses by relative change in liver fat (MRI-PDFF)
- Secondary objectives:
  - Assess other efficacy parameters (e.g. ALT, liver histology)
  - Assess safety and tolerability (e.g. body weight gain)
  - Assess pharmacokinetics at pre-specified timepoints and PK/PD correlation
PXL770 & PXL065 Aim to Have the Following Effects for NASH
Potential for Use in Combination with Other Agents in Development

- **Effects in Adipose Tissue**
  - PXL770
  - PXL065
  - Low grade inflammation
  - Lipolysis
  - Peripheral insulin resistance

- **Effects in Muscle**
  - De novo lipogenesis

- **Effects in Hepatocytes**
  - Steatosis
  - Chronic inflammation
  - Fibrosis
  - Gluconeogenesis

- **Effects on Mitochondria Structure and Function**
  - Fibrogenesis
  - Hepatic stellate cell activation

- **Effects in Liver**
  - PXL770
  - PXL065
  - Steatosis
  - Chronic inflammation
  - Fibrosis
  - Gluconeogenesis
Pipeline Expansion

Chronic and Rare Metabolic Indications

Next Generation AMPK Activators

Next Generation D-TZD’s*

*Deuterium-modified thiazolidinediones
AMPK and MPC Dysregulation are Implicated in the Biology of Various Metabolic Diseases

Exploring applications of current and next generation AMPK activators and MPC inhibitors in biologically relevant metabolic diseases

**Rare Metabolic**
- Adrenoleukodystrophy (ALD; AMN)
- Mitochondrial disorders

**Renal**
- Diabetic kidney disease
- Polycystic kidney disease

**Endocrine**
- Type 2 diabetes
- Polycystic ovary syndrome
Potential of AMPK Activation to Treat Adrenoleukodystrophy

Why AMPK?

- AMPK is suppressed in brain from ALD patients\(^1\)
- **ABCD2/3 could replace** function of missing ABCD1; AMPK activation with metformin elevates ABCD2 levels in patient cell lines and ABCD1-KO mice\(^1\)
- Deletion of AMPK\(\alpha1\) in glial cells of ABCD1-null mice (AMN model) → mitochondrial dysfunction/low ATP \(^2\)

PXL770 reduces VLCFA & induces ABCD2/ABCD3 in cells from human AMN-ALD patients

---

2. Singh J, Med Inflamm, 2015
Potential for AMPK Activation to Treat Renal Diseases

**Diabetic Kidney Disease**
- Multiple pathways engaged; anti-inflammatory, anti-apoptotic, anti-fibrotic effects of AMPK
- AMPK activity is *reduced* in human/rodent DKD tissue samples
- **Preclinical efficacy** reported with indirect and direct AMPK activation

**Polycystic Kidney Disease**
- Autosomal dominant; fourth leading cause of CKD
- Significant unmet medical need
- **AMPK activation validation:**
  - AMPK pathways linked to pathophysiology (eg mTOR; CFTR)
  - *In vivo* efficacy with both indirect and direct AMPK activators

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**DKD**

**PKD**

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Upcoming Milestones
Cash Through Significant Upcoming Milestones into 2022

Appendix
Key Financial & Shareholder Information

Market data

Ticker: POXEL
ISIN: FR0012432516
Number of shares: 28,471,523*

Key financials

- As of 6/30/20 cash & cash equivalents: EUR 46.0 million (USD 51.5 million)
- Cash runway into 2022

Shareholder ownership*

- 14.6% Andera Partners
- 16.7% Bpi France
- 9.5% Founders
- 5.0% Roivant Sciences Ltd
- 54.2% Floating

Analyst coverage

- Degroof Petercam: Benoit Louage
- Gilbert Dupont: Guillaume Cuvillier
- Jefferies: Peter Welford
- JMP Securities: Jason Butler
- Kepler Cheuvreux: Arsene Guekam
- Oddo: Martial Descoutures

* at June 2020.
References for Slide 12


Imeglimin Observed to Restore Normal Mitochondrial Function in Type 2 Diabetes (T2D)

Diabetic state is caused by an impaired mitochondrial state

Mitochondrial Respiratory Chain (MRC) becomes activated

Activating the MRC has these desirable downstream effects in T2D:

- Increases glucose-dependent insulin secretion from pancreas
- Improves β-cell dysfunction and survival
- Improves insulin sensitivity in muscle cells and liver cells
- Improves endothelial and diastolic dysfunction
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 diastolic dysfunction

ROS: reactive oxygen species  mPTP: mitochondrial permeability transition pore
Imeglimin Phase 2b Trial In Japan Met Primary and Secondary Endpoints (N=299)

- Full Phase 2b data presented at the European Association of the Study of Diabetes, Lisbon (Sept. 2017)
- Phase 2b trial in Japan met primary HbA1c endpoint and secondary endpoints
- Demonstrated efficacy in chronic kidney disease patients was similar to patients with normal renal function
- Observed to be 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
- Optimal dose for Phase 3 program in Japan is 1000 mg
Imeglimin Phase 2b Trial in Japan Met Primary Endpoint in Reduction of HbA1c vs. Placebo (N=299)

Change in HbA1c from Baseline

<table>
<thead>
<tr>
<th>Dose</th>
<th>LS Mean Change from Placebo</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg</td>
<td>-0.52%</td>
<td>75</td>
</tr>
<tr>
<td>1000 mg</td>
<td>-0.94%</td>
<td>73</td>
</tr>
<tr>
<td>1500 mg</td>
<td>-1.00%</td>
<td>73</td>
</tr>
</tbody>
</table>

HbA1c (%) - Baseline

** p < 0.0001

European Association of the Study of Diabetes, in Lisbon (Sept. 2017)
Phase 2b Trial in Japan: Similar Efficacy Demonstrated in T2D Patients with Renal Impairment vs with Normal Kidney Function

Change in HbA1c – 24 Weeks

- **500 mg**
  - eGFR ≥ 80: -0.53%
  - eGFR < 80: -0.44%
  - N=24
  - N=51

- **1000 mg**
  - eGFR ≥ 80: -0.92%
  - eGFR < 80: -0.83%
  - N=24
  - N=49

- **1500 mg**
  - eGFR ≥ 80: -0.89%
  - eGFR < 80: -0.92%
  - N=23
  - N=50
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