



*Due to COVID-19, Poxel is monitoring all developments that might impact the timelines for achievement of our corporate objectives and we will continue to provide updates, as needed.*

### Dear Shareholder,



As part of our year-end update, I would like to take this opportunity to review the significant milestones that we have achieved in 2019. I would also like to thank you for your ongoing support as a shareholder.

Together with our partner Sumitomo Dainippon Pharma, we have successfully completed the Imeglimin Phase 3 TIMES program in Japan, which was major milestone for Poxel. Leading a Phase 3 program in Japan as a European-based company over the last two years was a significant achievement and is strong validation of the internal skills that we have continued to build.

In 2019, we also made meaningful progress in advancing our two NASH programs. Our first program, PXL770, is now in a Phase 2a program. Our second program, PXL065, successfully completed a Phase 1b trial late last year and will be advancing into a single, comprehensive Phase 2 study. These two programs are fundamental to Poxel and represent future growth drivers in an area that has an important unmet medical need.

In 2020, we will continue to leverage our internal expertise to advance our metabolic-focused pipeline. In addition to the clinical studies for PXL770 and PXL065, we are also conducting preclinical combination studies with our NASH drug candidates to explore the potential to show additive or synergistic benefits to treat the root causes of NASH with other agents in development. Also, we are planning for future pipeline growth and evaluating additional research and development opportunities from our internal pipeline as well as external opportunities with a focus on metabolic disorders, including rare diseases.

The year 2020 is already shaping up to be a very busy year and one filled with several important and transformational milestones. These milestones include the results from the PXL770 PK/PD study and Phase 2a trial as well as the initiation of a Phase 2 study for PXL065. We will also be working very closely with Sumitomo Dainippon Pharma on the Japanese new drug application (NDA) submission for Imeglimin and with Metavant in advancing the Imeglimin Phase 3 program in the US and Europe.

I would like to thank you again for your support as a shareholder and look forward to providing you with further updates throughout the year.

Sincerely,  
**Thomas Kuhn**  
Chief Executive Officer

### Poxel at a glance



**Well diversified mid-to-late stage metabolic pipeline** with first-in-class drug candidates



**Highly experienced management team** with extensive metabolic expertise and development experience, and a track record in the US, EU and Japan



**Global multi-billion market** opportunities for type 2 diabetes and NASH



**Strong global partnerships** secured for the most advanced clinical program, Imeglimin



**Two differentiated programs for NASH (PXL770 / PXL065)**, a large growing disease worldwide



As of March 31, 2020, cash and cash equivalents were **EUR 36.9 million (USD 40.4 million)**.



Headquartered in **Lyon, France**, with subsidiaries in **Boston, MA** and **Tokyo, Japan**

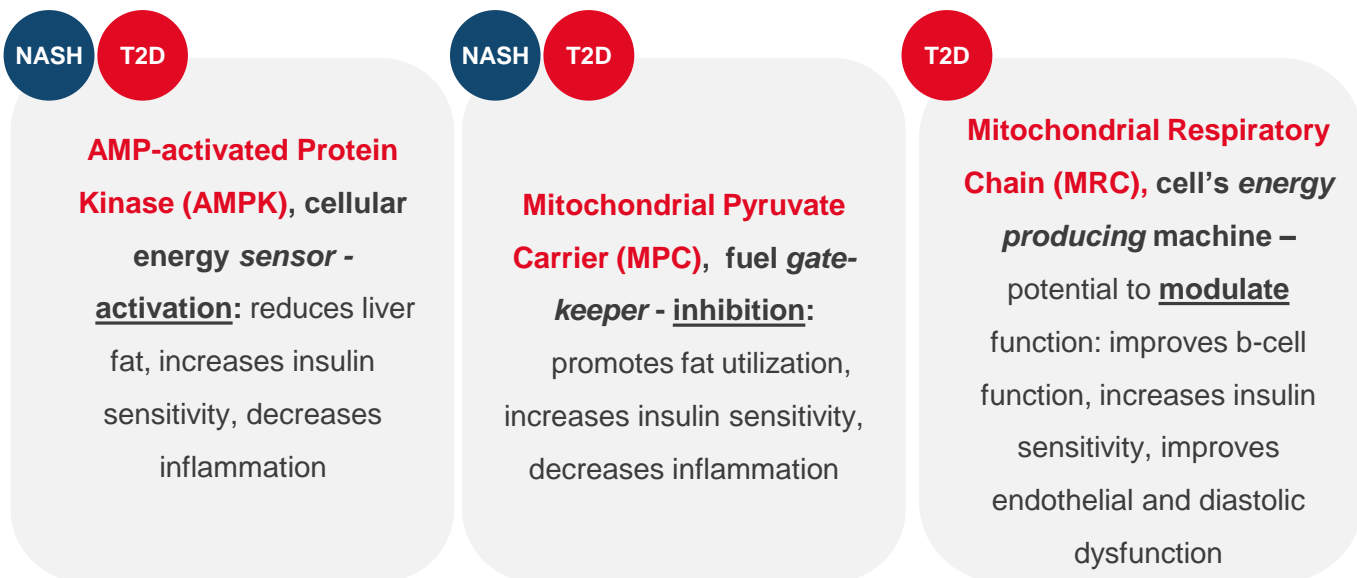
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## Poxel Targets Key Mechanisms that have Distinct Roles in Regulating Cellular Energy Homeostasis

We believe that **targeting cellular energy regulation pathways** for the treatment of metabolic diseases, including type 2 diabetes and NASH are of critical importance as energy imbalances are at the root of these diseases. All three of our clinical stage pipeline programs address key pathways involved in the regulation of energy metabolism. Imeglimin targets mitochondrial dysfunction, mitochondria being the power station of the cell; PXL770 activates the adenosine monophosphate-activated protein kinase (AMPK), an important energy sensor; and PXL065 targets inhibition of the mitochondrial pyruvate carrier (MPC), a key fuel gatekeeper.



## The Company is Developing a well-Diversified Pipeline with Mid-to-Late Stage Programs

	Indication	MOA	Preclinical	Phase 1	Phase 2	Phase 3	Partner/ Rights
<b>Type 2 Diabetes</b>							
<b>Imeglimin</b> Japan / Asia	Type 2 Diabetes (T2D)	MRC Modulator					
<b>Imeglimin</b> US / EU / Other	TD2 patients with CKD stages 3b/4	MRC Modulator					
<b>NASH</b>							
<b>PXL770</b>	NASH	Direct AMPK Activator					
<b>PXL065</b>	NASH	MPC Inhibitor					
<b>PXL007 (EYP001)</b>	Hepatitis B / NASH	FXR Agonist					
<b>Other Metabolic Diseases</b>							
<b>Poxel / DeuteRx Programs</b>	Metabolic (AMN / ALD, NASH, etc.)	Direct AMPK Activator / MPC Inhibitor					



## Type 2 Diabetes – 2019 A Significant Year for Imeglimin in Japan

### Imeglimin, a globally partnered program

*First in a New Class of Potential Anti-diabetic Treatments with a Differentiated Mechanism of Action*

Strategic partnership with **Sumitomo Dainippon Pharma** signed in **October 2017** for Japan, China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, The Philippines, Singapore, Republic of the Union of Myanmar, Kingdom of Cambodia, and Lao People's Democratic Republic.



- **Phase 3 TIMES program successfully completed in Japan**
  - Positive results from TIMES 1, TIMES 2 and TIMES 3
  - Japanese NDA submission anticipated in Q3 2020 (JNDA)
  - Product launch targeted in 2021 in Japan
- Phases 3 in Japan fully funded by Sumitomo

Partnership with **Roivant Sciences**, signed in **February 2018** for the U.S., Europe, and all other countries not covered in the Sumitomo Dainippon Pharma agreement.

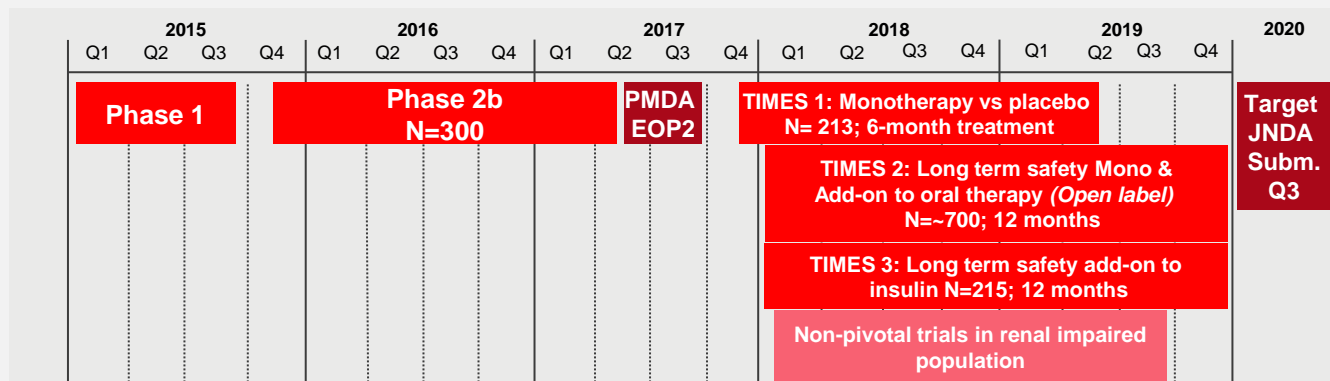


- **Preparation of the Phase 3 program in the U.S. and Europe**
  - Positive results from the PK/PD study in type 2 diabetes patients with chronic kidney disease stages 3b/4
  - Metavant, Roivant's subsidiary dedicated to metabolic diseases, is working with the FDA on the Phase 3 plan prior to initiating a Phase 3 program in this patient population
- Phases 3 fully funded by Roivant in the U.S. and Europe



### 2019 marked the successful completion of the Imeglimin Phase 3 Trials of Imeglimin for Efficacy and Safety (TIMES) program for the treatment of type 2 diabetes in Japan

- Target launch anticipated in Japan in 2021
- Phase 3 TIMES program included over 1,100 patients
- All Phase 3 TIMES trials met endpoints and objectives



### Partnerships cover global diabetes markets

*Potential for up to \$857m (~€705m\*) in development and regulatory milestones, and sales-based payments, and escalating double-digit royalties on net sales*

#### Sumitomo Dainippon Pharma Partnership

- Poxel is entitled to receive future **potential development milestone payments** of up to ¥2.75 billion (approximately €21 million, \$24 million\*)
- After launch, Poxel will receive **escalating double-digit royalties on net sales** and **sales-based payments** of up to ¥26.5 billion (approximately €198 million, \$233 million\*) in accordance with sales goals

#### Roivant / Metavant Partnership

- Poxel is entitled to receive **potential future development and regulatory milestone payments** and **sales-based payments** of up to \$600 million (approximately €486 million\*) subject to the successful clinical development and commercialization of Imeglimin
- After launch, Poxel is entitled to double-digit royalties on net sales
- Roivant is responsible for development and commercialization costs

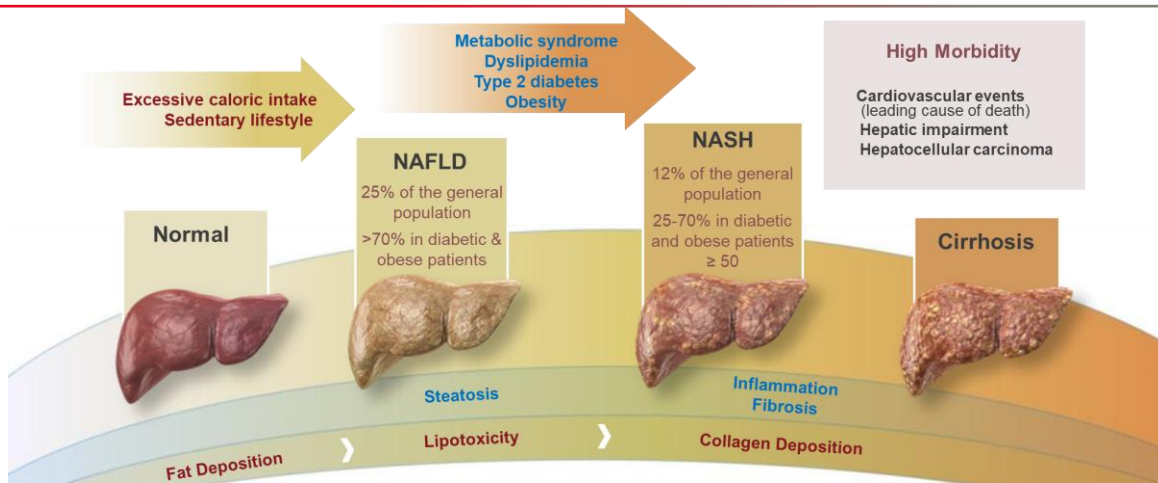
\* Converted at the exchange rate at the date of the agreement



## NASH Portfolio – PXL770 and PXL065

### PXL770 & PXL065 Address Symptoms Across NASH Hallmarks

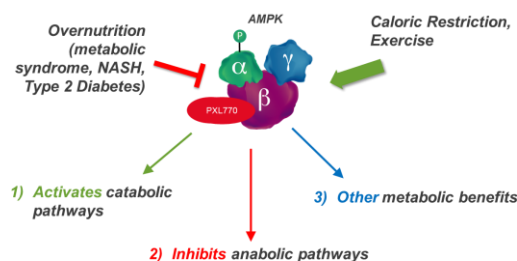
#### NASH is a Complex, Multifactorial Disease



There are no currently approved drugs that treat symptoms & complications across all four categories

### PXL770: A Potential Breakthrough Therapy for Chronic Metabolic Disorders, including NASH

**PXL770** is a novel drug candidate that directly activates adenosine monophosphate-activated protein kinase (AMPK). AMPK serves as a **key cellular energy sensor**; in response to overnutrition and in association with metabolic disease, AMPK activity is suppressed. In contrast, fasting and exercise result in AMPK activation; this then results in regulation of multiple metabolic pathways leading to the control of lipid metabolism, glucose homeostasis and inflammation. Based on its central metabolic role, **we believe that targeting AMPK offers the opportunity to pursue a wide range of indications** to treat chronic metabolic diseases, including diseases that affect the liver, such as NASH.



Specifically, direct activation of the AMPK enzyme has **the potential to treat the root causes of NASH** by triggering benefits affecting the main pathophysiologic processes occurring in the liver and leading to NASH: steatosis, inflammation, ballooning and fibrosis.

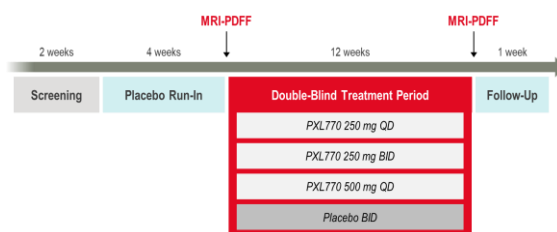
### Activating AMPK has been Observed to Show Beneficial Effects in NASH

STEATOSIS	INFLAMMATION	BALLOONING	FIBROSIS
Improves steatosis by <b>limiting</b> fat flux from adipose tissue and de novo lipogenesis	<b>Decreases</b> inflammation by moving from a pro-inflammatory phenotype to an anti-inflammatory phenotype	<b>Decreases</b> structural degenerative changes and improves cell health	<b>Decreases</b> hepatic stellate cell activation and limits fibrosis

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

### PXL770: Ongoing Phase 2a Program for NASH

- The Phase 2a 12-week, multicenter, randomized, double-blind, placebo-controlled, parallel group trial:  
**Results currently expected late 3Q 20**
  - Objective is to demonstrate PXL770's potential in NASH
  - Phase 2a trial will assess efficacy and safety in approximately 100 likely-NASH patients
- A separate four-week PK/PD study of PXL770:  
**Results currently expected late 2Q 20**

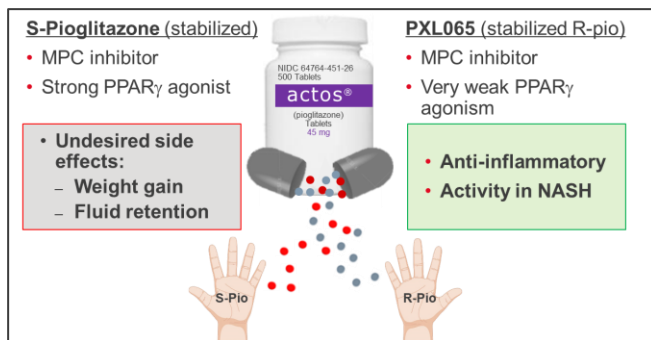




## PXL065: MPC Inhibitor for the Treatment of NASH

### PXL065, a New Approach for the Treatment of NASH

PXL065 is the R stereoisomer (deuterium stabilized single R-isomer) of pioglitazone; its parent molecule has been marketed since 1999 for the treatment of type 2 diabetes. Pioglitazone is a mixture, in equal proportions, of two mirror molecules (R and S stereoisomers) that interconvert *in vivo*. Pioglitazone targets both inhibition of the mitochondrial pyruvate carrier (MPC) and activation of PPAR $\gamma$ . Pioglitazone has been the subject of a large number of Phase 2, 3 and 4 clinical trials for the treatment of NASH, which have demonstrated its ability to produce disease resolution without aggravating fibrosis. Pioglitazone is the **only drug recommended for biopsy-proven NASH patients** by the Practice Guidelines published by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL).



### PXL065 Targets Inhibition of MPC & Modulates Cellular Fuel Utilization

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

STEATOSIS	INFLAMMATION	BALLOONING	FIBROSIS
Increasing fat oxidation <b>decreases</b> liver fat content	Resetting mitochondrial metabolism <b>improves</b> inflammation	Resetting mitochondrial metabolism <b>protects</b> cells from degeneration	Inhibiting MPC <b>decreases</b> HSC activation and markers of fibrogenesis

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

### PXL065: Summary of Phase 1 Study Results

Favorable Safety & PK Support Advancement & Dose Selection

- In December 2019, Poxel announced positive results from a Phase 1b multiple ascending dose (MAD) trial evaluating safety, tolerability and the pharmacokinetic (PK) profile of PXL065 in healthy subjects after repeated administration and provided further details for the Phase 2 clinical trial design.
- In addition, the Company highlighted new preclinical data, a 13-week repeated-dose toxicity study in dogs comparing PXL065 to pioglitazone, in which PXL065 was observed to show an improved safety margin over pioglitazone.

	Phase 1a Single Dose	Phase 1b MAD
<b>Study design</b>	Single oral dose in healthy adults PXL065 <b>capsule</b> (7.5, 22.5, 30 mg) or Actos <sup>®</sup> (45 mg)	Repeated oral doses in healthy adults PXL065 <b>tablet</b> (7.5, 15, 30 mg) vs pbo or Actos <sup>®</sup> (45 mg)
<b>Safety &amp; Tolerability</b>	Well-tolerated at all doses tested	Consistent with Phase 1a
<b>Pharmacokinetics</b>		
<ul style="list-style-type: none"> <li>Stabilization of d-R-pio</li> </ul>	<ul style="list-style-type: none"> <li>Observed at all doses tested, limited interconversion to S-pio</li> </ul>	<ul style="list-style-type: none"> <li>Consistent with Phase 1a</li> </ul>
<ul style="list-style-type: none"> <li>Dose proportionality</li> </ul>	<ul style="list-style-type: none"> <li>Dose proportional up to 22.5 mg</li> </ul>	<ul style="list-style-type: none"> <li>Dose proportional at all doses tested</li> </ul>
<b>Summary</b>	API in capsule increases PK variability PK/PD predicts 15 mg PXL065 will produce efficacy similar to 45 mg pio without weight gain	Tablet formulation improved PK Consistent with Phase 1a



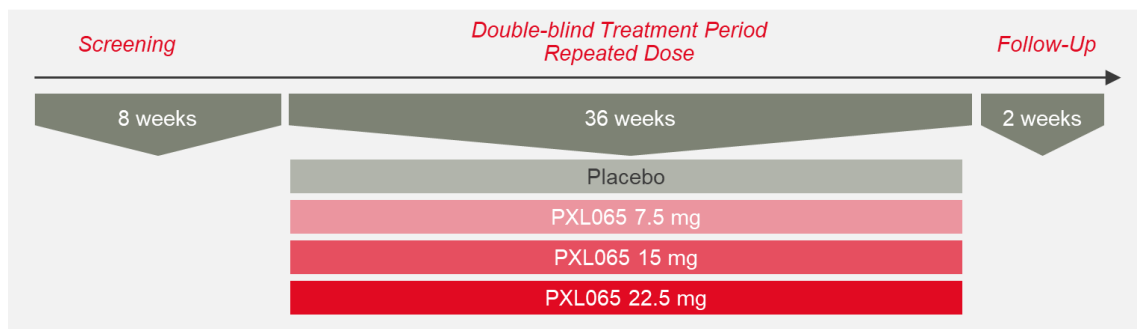


## PXL065: One Phase 2 Trial in Biopsy-Proven NASH Patients Leveraging 505(b)(2) Pathway

### Utilizing 505(b)(2) Regulatory Pathway

Based on the feedback received following the meeting with the FDA, Poxel is advancing PXL065 using a 505(b)(2) regulatory pathway, which will in part reference and rely on the Actos® (pioglitazone) product label and relevant published literature. A 505(b)(2) new drug application (NDA) contains full safety and efficacy reports but permits some of the information required for NDA approval, such as safety and efficacy information on the active ingredient, to come from studies not conducted by or for the NDA applicant. Utilizing this regulatory pathway **has the potential to result in a less expensive and faster route to approval compared to a traditional 505(b)(1) development path.**

A 36-week multicenter, double-blind, placebo-controlled, parallel group, randomized trial to evaluate the safety and efficacy of PXL065 at 3 doses in at least 120 noncirrhotic biopsy-proven NASH patients



- Phase 2 will seek to identify one or two doses for the Phase 3 registration trial
- Primary objective: Assess efficacy of escalating doses of PXL065 by relative change in liver fat (MRI-PDFF)
- Secondary objectives:
  - Assess other efficacy parameters of PXL065 (e.g. ALT, liver histology)
  - Assess safety and tolerability of PXL065 (e.g. body weight gain)
  - Assess pharmacokinetics of PXL065 at pre-specified timepoints and PK/PD correlation

### Combination Therapy

Given the heterogeneity of NASH and its pathophysiology, we believe there is a need for combination approaches that target multiple pathways in the disease's progression. Our two lead products in NASH target distinct pathways, and we believe that the differentiated profiles of PXL770, which allosterically activates AMPK to mitigate metabolic overload in liver cells, and of PXL065, which inhibits MPC to reduce steatosis and prevent liver inflammation and fibrosis, are well-suited for use as a combination therapy. To this end, we are currently conducting preclinical studies for PXL770 and PXL065 in combination together and with other therapies using other mechanisms of action that **we believe could have additive or synergistic benefits for the treatment of NASH.**

### POXEL RECENT CORPORATE UPDATES

- In 2019, Poxel established a **U.S. subsidiary, Poxel Incorporated**, with offices in the **Boston area**, as it continues to expand its presence in the U.S.
- **Quentin Durand** was appointed to the position of **Chief Legal Officer** in 2019 and **David Moller** was appointed to the position of **Chief Scientific Officer** in 2020



## POXEL IN THE MEDIA



### The Future of Diabetes Treatment: Is a Cure Possible?



### Poxel taking two shots at NASH as pharma waits on FDA's OCA verdict



### Novel Agent Imeglimin Improves Glucose Control in Type 2 Diabetes



### Imeglimin shows promise for type 2 diabetes



### Poxel presents detailed positive data for imeglimin at EASD 2019



### Metavant/Poxel prep phase 3 for imeglimin in diabetic kidney disease

*Treatment can help patients with advanced disease, companies say*



### Imeglimin launch in Japan planned for 2021 after more good data



### Sumitomo/Poxel Wraps Up Japan Pivotal Program for Imeglimin with Successful Long-Term Study



### NEWSFLOW

Due to COVID-19, Poxel is monitoring all developments that might impact the timelines for achievement of our corporate objectives and we will continue to provide updates, as needed.

#### IMEGLIMIN

##### 2020

- Metavant discussions with the FDA regarding the Imeglimin Phase 3 program in type 2 diabetes patients with CKD stages 3b/4
- TIMES data publications and presentations
- JNDA submission in Japan targeted for Q3 2020

##### 2021

- Imeglimin target launch in Japan

#### PXL770

##### Q2 2020

- PK/PD data results in NASH

##### Q3 2020

- Phase 2a proof-of-concept data results in NASH

##### 2H 2020

- Presentations and scientific papers published for PXL770

#### PXL065

##### Q2 2020

- Initiation of a Phase 2 clinical program in NASH (timing contingent on safe and stable environment for patient recruitment and availability of clinical trial sites during the COVID-19 outbreak)

##### 2H 2020

- Presentations and scientific papers published for PXL065



### POXEL AND THE STOCK EXCHANGE

#### STOCK EXCHANGE



Market	Euronext Paris since February 2015
Ticker	POXEL
ISIN Code	FR0012432516
Market cap.	€176 million*
Number of shares	26,093,040
Share price	€6.82*
52 week trading range	€4.615 – €13.80

\*as of April 20, 2020

#### 2020 FINANCIAL CALENDAR

##### July 21, 2020

2020 Second Quarter Financial Update

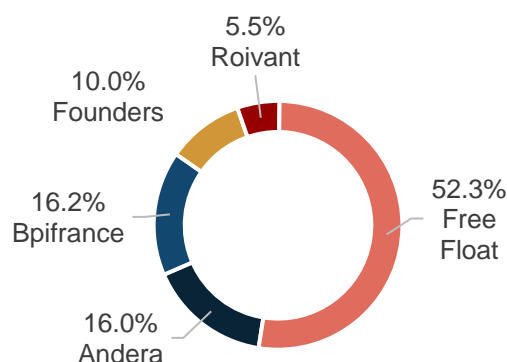
##### September 15, 2020

2020 First Half Results

##### October 20, 2020

2020 Third Quarter Financial Update

#### SHAREHOLDER STRUCTURE AS OF FEBRUARY 10, 2020



#### ANALYST COVERAGE

Degroof Petercam	Benoit Louage
Gilbert Dupont	Jamila El Bougrini
Jefferies	Peter Welford
Kepler Cheuvreux	Arsène Guekam
Oddo BHF	Martial Descoutures

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