Full Year 2020
Financial and Corporate Update

March 25, 2021

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 outbreak of the COVID-19, which has been declared a “pandemic” by the World Health Organization on March 12, 2020, the Company has undertaken a full review of the impact of such outbreak on its business. Considering the rapidly evolving situation, the Company is updating this assessment on a regular basis.

As of the date of this presentation, and based on publicly available information, the Company has not identified the occurrence of a material negative effect on its business due to the COVID-19 pandemic.

However, the Company anticipates that the COVID-19 pandemic may have a material negative impact in the near future. First, the worldwide deteriorated economic environment may notably impact the Company’s internal organization and efficiency, particularly in countries where it operates and where confinement measures have been implemented by the authorities, as well as its ability to raise additional funding and / or to enter into partnerships. Secondly, while the Company’s timelines for its manufacturing, pre-clinical and clinical operations remain unchanged on the date hereof, the COVID-19 outbreak is likely to have an impact on the Company’s operations, in the same way as for any company operating within the healthcare industry. 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 certain or all of the Company’s development programs.

Corporate Update During Coronavirus (COVID-19) Pandemic

Proactive Corporate Initiatives

- Continuous monitoring of the situation worldwide and its impact on our people, operations and plan
- Employees used to working remotely due to global locations, supported by appropriate IT infrastructure

Imeglimin – T2D

- J-NDA process on track, Target launch expected in 2021[1] in JP, as planned, by Sumitomo Dainippon Pharma, #1 diabetes company in Japan
- Business Opportunity for Imeglimin in US, EU & Other Countries

PXL770 & PXL065 - NASH

- Significant progress of both programs in 2020
- Positive Phase 2a results for PXL770, leading to Phase 2b preparation
- Phase 2 recruitment ongoing for PXL065, following study initiation in Sept. 2020 due to Covid-19 context in the US

Manufacturing

- Imeglimin: DSP responsible for manufacturing; Batches available for progress in US & EU. We are currently not aware of COVID-19 disruptions
- NASH programs: we rely on outsourcing and have options for alternative venders, as needed

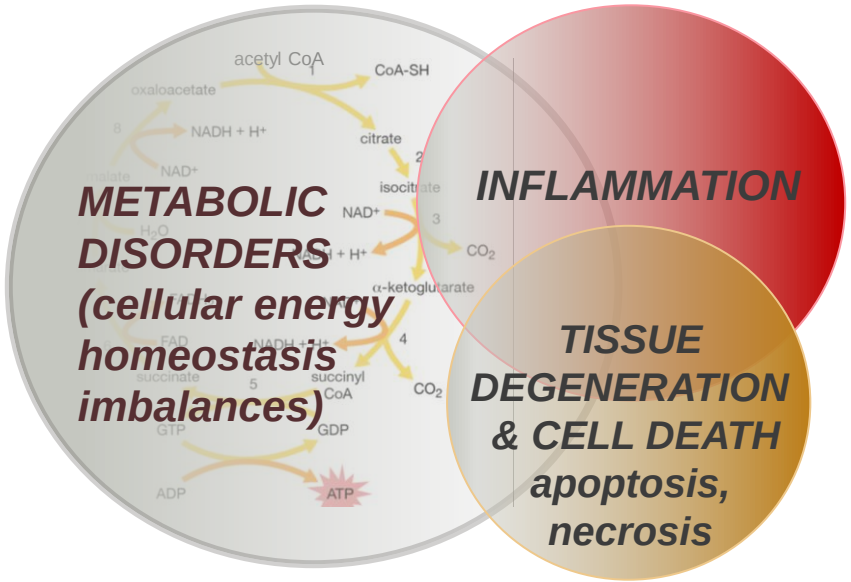
Finance

- Financial position strengthened through capital increase of EUR 17.7 million in May 2020 and EUR 6 million in Oct. 2020 in non-dilutive funding in the form of a French Government Guarantee Loan in the context of the COVID-19 pandemic.

1. Sumitomo fiscal year April-March.

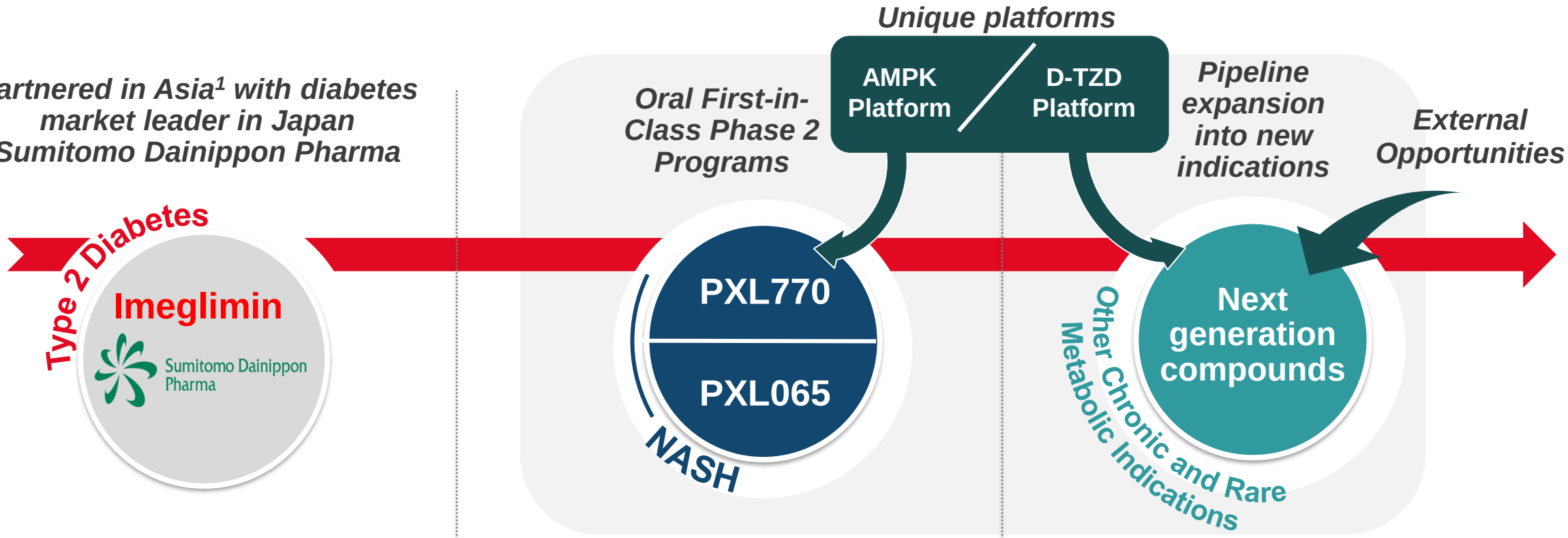
Poxel's Mission and Vision

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



Three Pillars of Poxel's Strategy

First-in-Class Programs Leading to Key Value Inflection Points



Expected approval in 2021[2] triggering milestones

Phase 3 ready partnership opportunity in US/EUR

Phase 2 biopsy data for both programs in 2022-2023

Combination potential

New clinical programs in next 12-24 months

Further strengthening product pipeline

1. Including: Japan, China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, the Philippines, Singapore, Myanmar, Cambodia, and Laos. 2. Sumitomo fiscal year April-March.

Robust Mid-to-Late Stage Metabolic Pipeline

	Indication	MOA	Discovery/PC	PH 1	PH 2	PH 3	NDA review	Partner/ Rights	Upcoming Milestones
Type 2 Diabetes (T2D)									
Imeglimin Japan / Asia[1]	T2D	MRC Modulator						Sumitomo Dainippon Pharma	▪ Target product launch in 2021[2] in Japan
Imeglimin US / EU / Other	T2D with CKD stages 3b/4	MRC Modulator						poxel	▪ Exploring options to move the program forward into Phase 3
NASH									
PXL770	NASH with T2DM	AMPK Activator						poxel	▪ Initiate Phase 2b study in 2H 2021
PXL065	NASH	MPC Inhibitor						poxel	▪ Phase 2 results mid-2022 ▪ 505(b)(2) pathway
PXL007 (EYP001)	Hepatitis B / NASH	FXR Agonist						ENYO PHARMA	▪ Complete Ph 2a program by Enyo Pharma mid-2021
Other Chronic and Rare Metabolic Indications									
Next-Gen AMPK	ALD/AMN, ADPKD, CKD, other	AMPK Activator						poxel	▪ Complete PC studies in 2021 ▪ Select lead candidate(s)
Next-Gen D-TZD	ALD/AMN, other	MPC Inhibitor							

1. Including: China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, the Philippines, Singapore, Myanmar, Cambodia, and Laos. 2. Sumitomo fiscal year April-March.

Financial Update

Full Year 2020

Revenue

Mostly reflecting the JNDA filing of Imeglimin in Japan

In K€	FY 2020 12 months	FY 2019 12 months
Sumitomo Agreement	6 787	26 179
Roivant Agreement	18	276
Other	1	101
Total revenues	**6 806**	**26 556**

- Includes the JPY 500 million milestone payment received from Sumitomo Dainippon Pharma for the submission of the Imeglimin J-NDA
- In a less extent, reflects the residual allocated portion of the EUR 36 million upfront payment received from Sumitomo Dainippon Pharma in 2017 and the TIMES program costs re-invoiced to Sumitomo Dainippon Pharma .
- TIMES program fully completed, explaining the decrease in revenue in 2020

Statement of Comprehensive Income as of Dec. 31, 2020*

Decrease in revenue and Opex, mostly reflecting the completion of the TIMES program

	In K€	December 31, 2020	December 31, 2019
1	**Revenue**	**6 806**	**26 557**
	Research and development		
2	Research and development expenses	(29 235)	(44 550)
	Tax credit	2 517	4 373
3	General and administrative	(9 935)	(11 051)
	Operating profit	**(29 847)**	**(24 671)**
4	Financial loss	(1 975)	(1 071)
	Profit before tax	**(31 822)**	**(25 742)**
	Income tax	(36)	(1)
	Net income	**(31 858)**	**(25 743)**

1. Mostly reflects the JPY 500 million (EUR 4.0 million) milestone payment that Poxel received from Sumitomo Dainippon Pharma for the submission of the Imeglimin J-NDA
2. Clinical costs incurred for the ongoing Phase 2 programs of PXL770 and PXL065
3. Decrease in G&A costs reflects non-recurring costs incurred in 2019
4. Mainly reflects interest expenses for EUR 1.3 million

*IFRS.

Statements of Financial Position as of December 31, 2020*

Assets

In K€	December 31, 2019	December 31, 2019
Intangible assets	16 642	16 614
Property, plant and equipment	2 224	2 323
Other non-current financial assets	246	477
Deferred tax assets	-	-
Total non-current assets	19 113	19 414
1 Trade receivables and related accounts	281	6 593
2 Other receivables	5 480	9 107
Current tax receivables	-	-
3 Cash and cash equivalents	40 203	37 187
Total current assets	45 964	52 888
Total assets	**65 077**	**72 302**

1. Decrease reflects the end of the TIMES program (and reinvoiced costs to Sumitomo Dainippon Pharma)
2. Mostly reflects lower Tax Credit in 2020 compared to 2019
3. Change in cash (+€3m) reflects €29m coming from financing activities in 2020 and the net loss of the year (see slide 12)

*IFRS.

Statements of Financial Position as of Dec. 31, 2020*

Shareholders' Equity and Liabilities

	In K€	December 31, 2020	December 31, 2019
1	**Total shareholders' equity**	**26 879**	**39 142**
	Non-current liabilities		
	Employee benefits	581	375
2	Non-current financial liabilities	20 986	1 842
	Provisions	172	94
	Non-current liabilities	**21 739**	**2 311**
	Current liabilities		
2	Current financial liabilities	2 866	8 941
	Derivative liabilities	691	1 766
3	Provisions	2 409	-
4	Trade payables and related accounts	8 362	16 406
	Other current liabilities	2 131	3 736
	Current liabilities	**16 459**	**30 849**
	Total liabilities	**65 077**	**72 302**

1. Reflects the 2020 net loss and the €17.7m fund raising in 2020
2. Includes IPF loan (€16.5m) and PGE (€6m)
3. Includes the amount due to Merck as a result of the arbitral procedure
4. Mostly reflects the end of the TIMES program and related CRO payables

*IFRS.

Statements of Cash Flow as of Dec. 31, 2020*

In K€	December 31, 2020	December 31, 2019
Cash flows from operating activities before change in WC	(26 040)	(23 111)
(-) Changes in working capital requirements	(292)	2 582
Cash flows from operating activities	**(25 749)**	**(25 693)**
Acquisitions of assets	(281)	(113)
Other investments cash flows	332	465
Cash flows from investing activities	**52**	**352**
1 Share capital increase	16 808	1 031
2 Other financing operations	11 904	(5 239)
Cash flows from financing activities	**28 712**	**(4 208)**
Increase (decrease) in cash and cash equivalents	**3 016**	**(29 549)**

1. Reflects the €17.7m fund raising in May 2020
2. Mostly reflects the €10m 2nd tranche of IPF loan and the €6m PGE

*IFRS

Key Financial & Shareholder Information

Market data

Ticker: POXEL

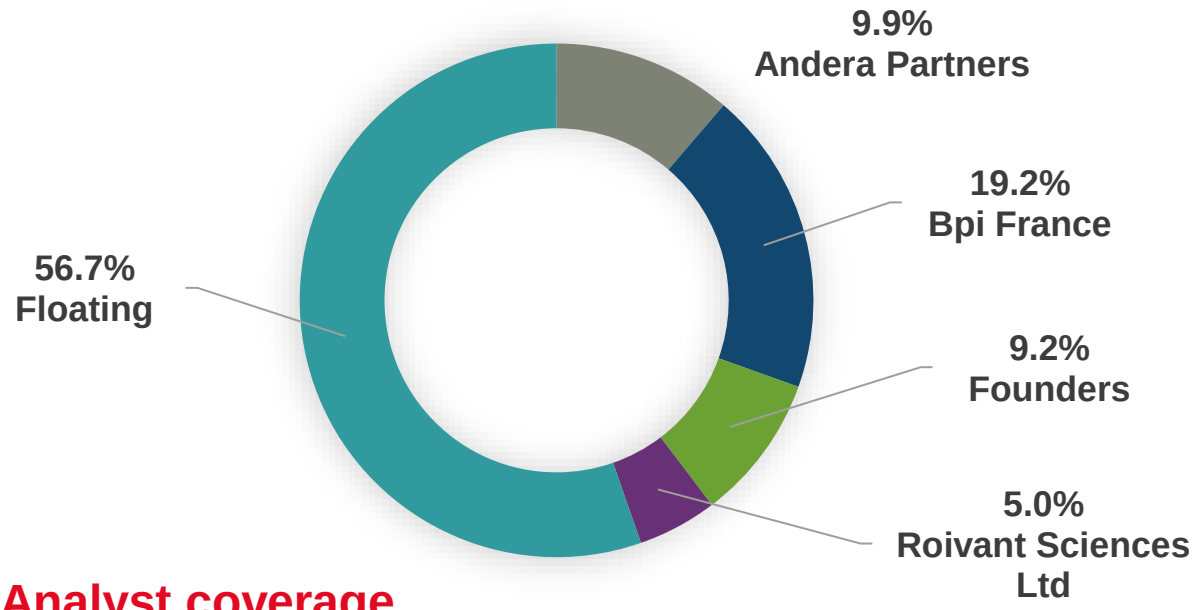
ISIN: FR0012432516

Number of shares: 28,611,254[1]

Key financials

- As of 12/31/20 cash & cash equivalents: **40.2 million (USD 49.4 million)**
- Cash runway extends through 2022 based on our current business plan[3]

Shareholder ownership2



Analyst coverage

Bryan Garnier	Jean-Jacques Le Fur
Degroof Petercam	Benoit Louage
Jefferies	Lucy Codrington
JMP Securities	Jason Butler
Oddo	Martial Descoutures

1. At January-end 2021. 2. At the date of the presentation, based on the Company's knowledge. 3. Taking into account ~€13.8M (based on the JPY/€ exchange rate at December 31, 2020) milestone payment by Sumitomo Dainippon Pharma, and €13.5M from IPF loan, which are both subject to the marketing approval of Imeglimin in Japan, expected in 2021 (Sumitomo Dainippon Pharma's fiscal year), and not including the financing of the Ph.2b study for PXL770.

Type 2 Diabetes

Imeglimin

Key Partnership for Japan & Asia

Sumitomo Dainippon Pharma

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

Expected Regulatory Approval in Japan in 2021

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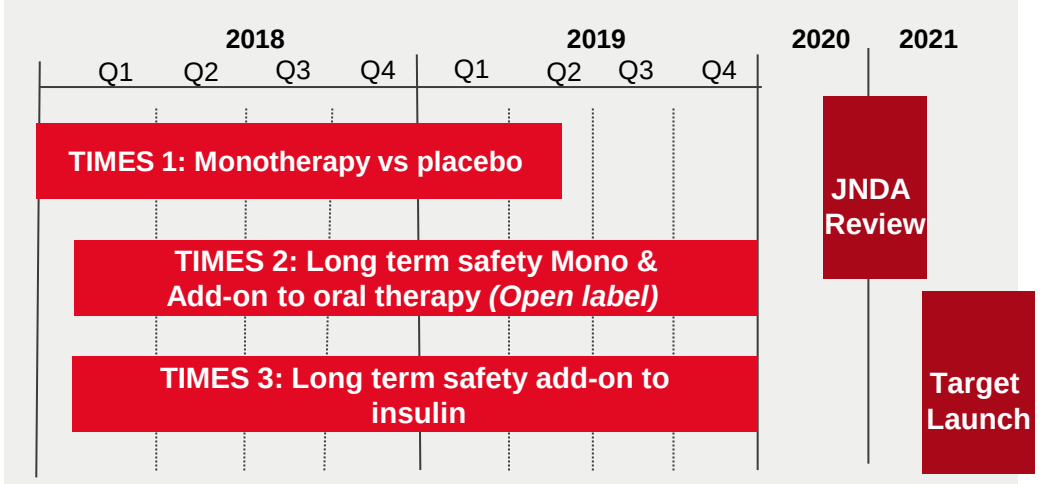
Imeglimin: Novel Mechanism - Nearing Approval in Japan

Partnered in Asia[1] with Diabetes Market Leader, Sumitomo Dainippon Pharma

- Successful Completion of Phase 3 Program in Japan
- J-NDA approval triggers **milestone payment of ~€13.8M ($16.9M)**[2] and ability to draw down **€13.5M** from IPF loan
- **Target launch expected in 2021**[3]; Future potential **development milestone payments and sales-based payments** of up to **approx. $237M**[4] and double-digit escalating royalties



Business Opportunity Japan: Maximize Product Profile

- Sumitomo #1 diabetes franchise; Guidance **FY20 $900M**[3]
- DPP4i's are prescribed to 80% T2D patients[5]
- Limited treatment options for selected populations, including 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***

1. Including: Japan, China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, the Philippines, Singapore, Myanmar, Cambodia, and Laos.
2. Based on the JPY/€ exchange rate at December 31, 2020.
3. Sumitomo fiscal year April-March.
4. Currency exchange rate is at the date of the agreement.
5. IQVIA data FY2016 and NDB data FY2016.

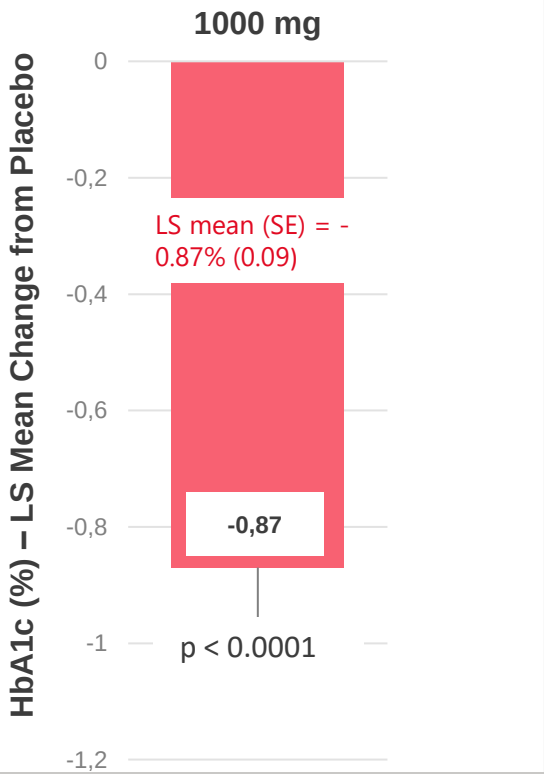
Imeglimin Phase 3 TIMES Program Overview (N=1,142)

Robust and Consistent Efficacy in Monotherapy and as an Add-on Therapy

TIMES 1* Monotherapy

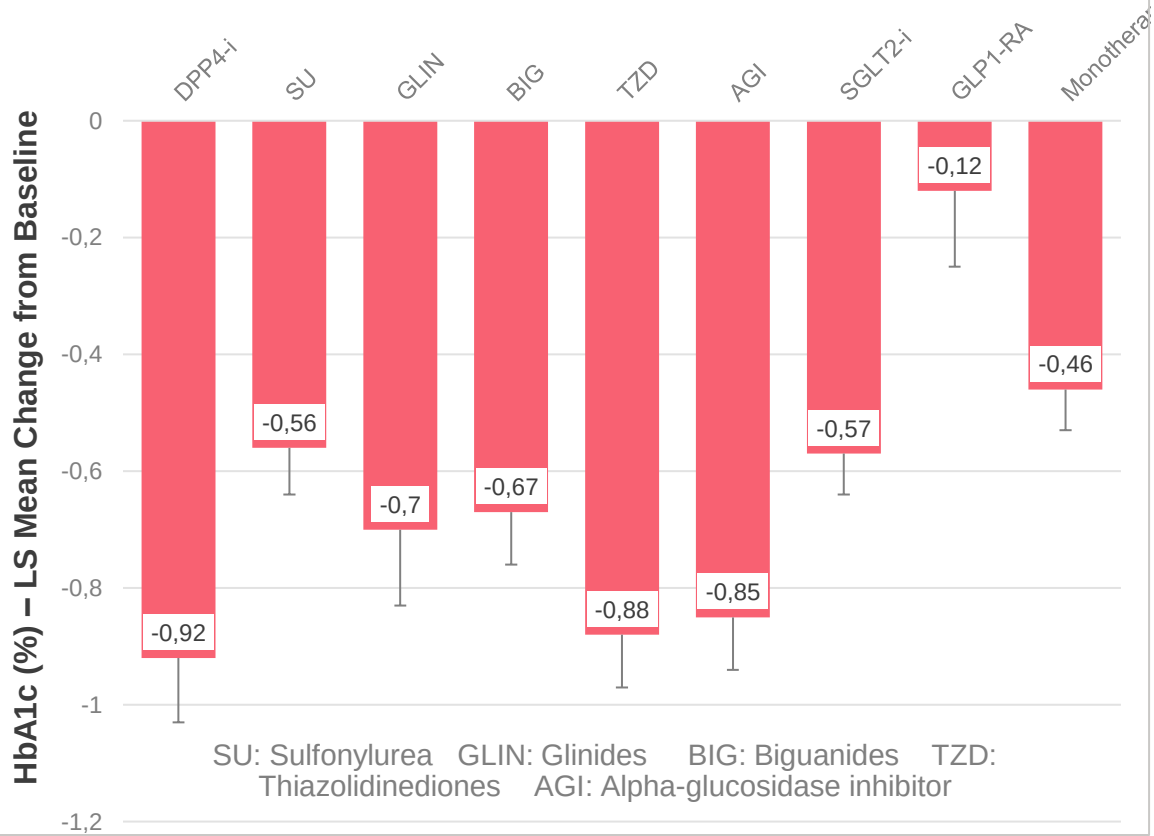
Change in HbA1c – 24 Weeks

Patients (n)	Placebo (N=107)	Imeglimin (N=106)
HbA1c (%), mean (SD)	7.93 (0.684)	7.99 (0.764)



TIMES 2 As an Add-on to Standard of Care

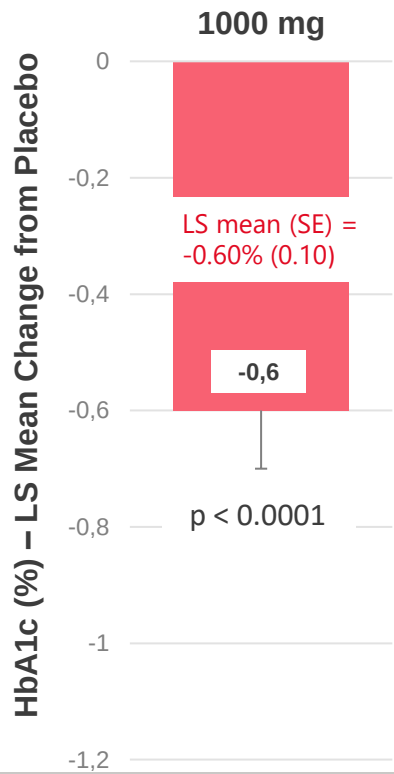
Change in HbA1c (vs baseline) – 52 Weeks – 714 patients



TIMES 3 Combination with Insulin

Change in HbA1c – 16 Weeks

Patients (n)	Placebo (N=107)	Imeglimin (N=108)
HbA1c (%), mean (SD)	8.8 (0.8)	8.7 (0.7)



*European Association for the Study of Diabetes meeting 2019.

Business Opportunity for Imeglimin in US, EU, Other Countries[1]

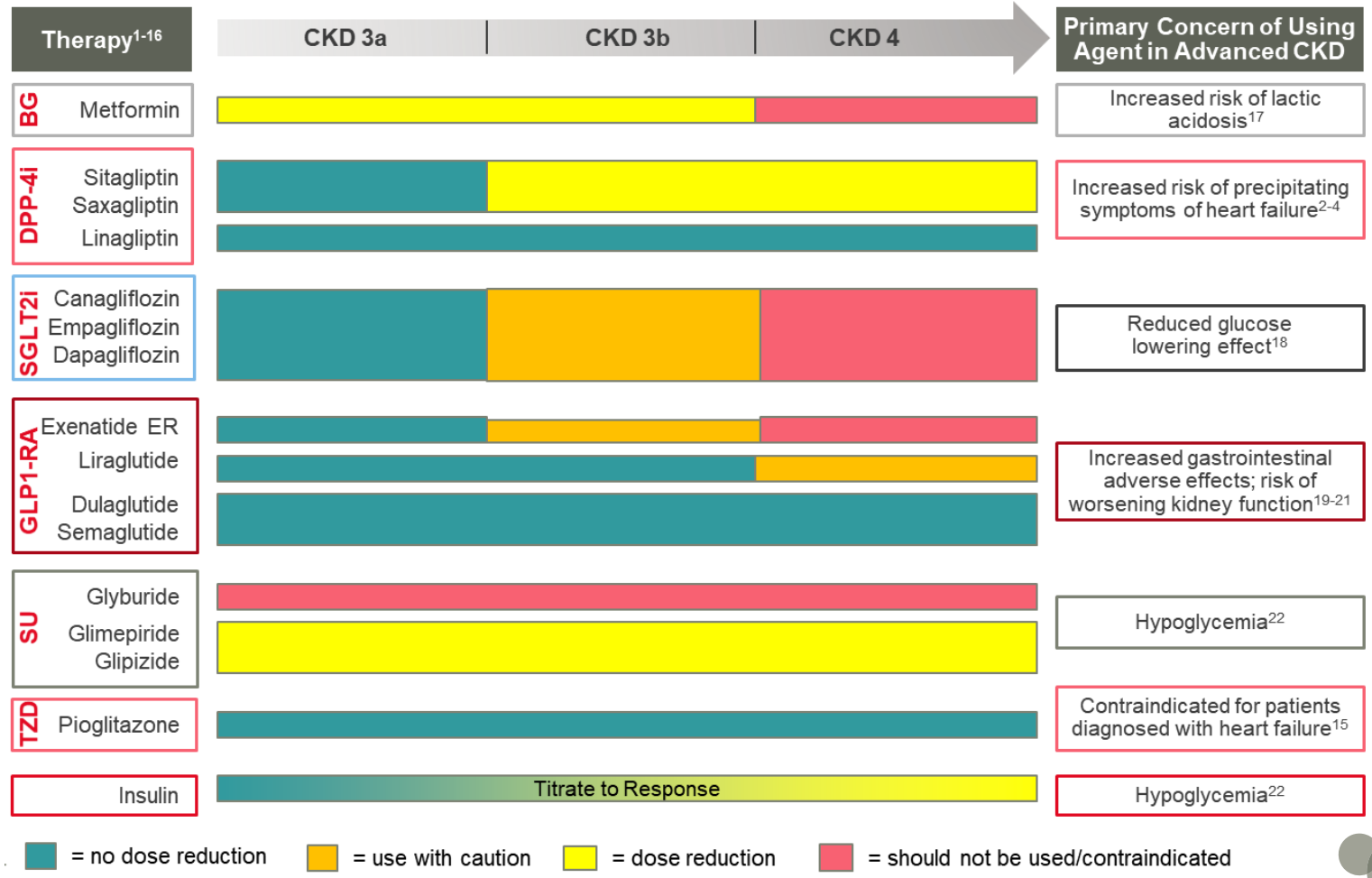
- Data, materials, information, IP, and FDA regulatory filings transferred from Metavant[2] to Poxel
- Exploring options to pursue for **T2D patients with chronic kidney disease stages 3b/4** (CKD 3b/4); **Ph3 ready product**, incl. **efficacy & safety readout in target population** & **FDA development guidance**

T2D with CKD stages 3b/4

- Diabetes is the most common cause of CKD
- ≈2.4 million adults in U.S.[3]
- Increased CV risk and challenging glucose management

Underserved patient population

- Many therapies require dose reduction or not recommended
- Insulin and sulphonylureas most commonly used at suboptimal doses to avoid hypoglycemia
- New therapy(ies) are needed: robust efficacy and safety; no hypoglycemia risk



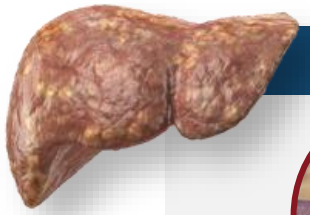
1. Not covered by the Sumitomo Dainippon Pharma agreement. 2. A subsidiary of Roivant Sciences. 3. Centers for Disease Control and Prevention (CDC).NHANES; 2015-2016; 4-22 – see Appendix.

NASH Programs

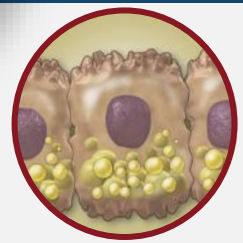
PXL770 - Direct AMPK Activator

PXL065 – Deuterium-stabilized *R*-pioglitazone

PXL770 and PXL065: Novel, First-in-Class Product Candidates



HALLMARKS OF NASH

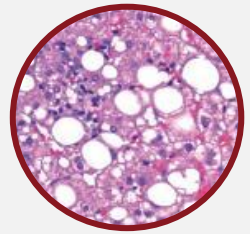


Lipid accumulation in hepatocytes

Steatosis

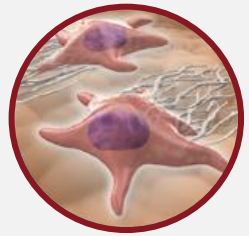
Immune cells (macrophages - MΦ)

Inflammation



Cellular damage-death

Ballooning



Hepatic stellate cell activation

Fibrosis

- **First-in-Class - Novel Mechanisms**
  - ability to target multiple hallmarks of NASH
- **Clinical validation**
  - positive Phase 2A results (‘770)
  - derived from pioglitazone – proven NASH benefits (‘065)
- **Daily oral administration**
  - combinable with other approaches
- **Innovative development approaches**
  - focus on patients with co-existing diabetes (‘770)
  - 505(b)(2) regulatory path (‘065)

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NASH

PXL770

Proprietary Program

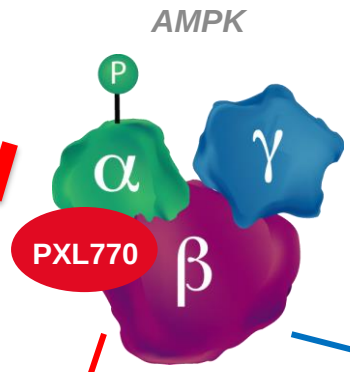
Direct AMPK Activator for the Treatment of NASH

PXL770 is a Direct AMP Kinase Activator

Mechanism, Preclinical Profile, Phase I Summary

Overnutrition (metabolic syndrome, NASH, Type 2 Diabetes)

Caloric Restriction, Exercise



***Activates* catabolic pathways**

↑ fatty acid oxidation
↑ glucose uptake

***Inhibits* anabolic pathways**

↓ de novo lipogenesis (DNL)
↓ adipose tissue lipolysis

***Other* benefits**

- Reduces inflammation
  - ↓ macrophage and dendritic cell activation
  - ↓ pro-inflammatory cytokines
- Blocks hepatic stellate cell activation

Phase I Clinical Summary:

- 132 healthy subjects; good tolerability, low incidence of AE's; acceptable PK
- Ph1b NAFLD study (n=20; 4 weeks): evidence of target engagement (suppression of DNL); improved glucose tolerance; insulin sensitization

AMPK - potential to target core drivers of NASH and to improve key cardiometabolic risk factors

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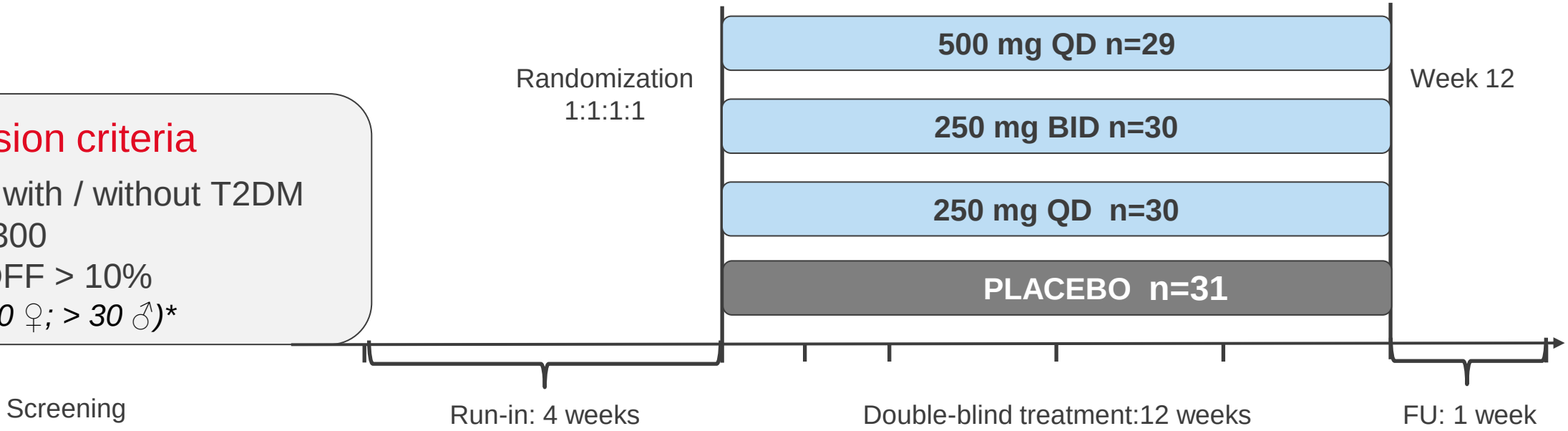
PXL770 Phase 2a Design & Baseline Characteristics

Key inclusion criteria

- NAFLD with / without T2DM
- CAP > 300
- MRI-PDFF > 10%
- *(ALT > 20 ♀; > 30 ♂)**



- **Primary Endpoint: Liver Fat Content (LFC)**
- **Baseline features:**
  - 41-47% Type 2 diabetes (T2D) in each cohort [HbA1c 6.6-7.1%]
  - LFC – 16-22%
  - ALT 37-41 IU/L

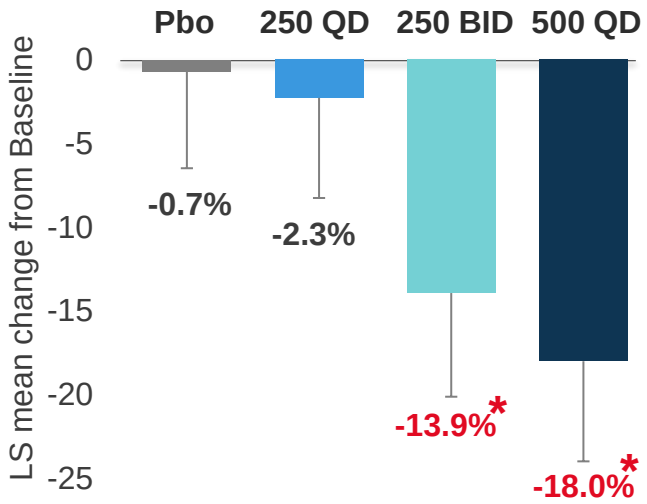
** ALT inclusion criteria has been removed during the course of the study to facilitate patients' recruitment.*

PXL770 Successful Phase 2a Results

Statistically Significant Results and Greater Efficacy in Patients with Diabetes

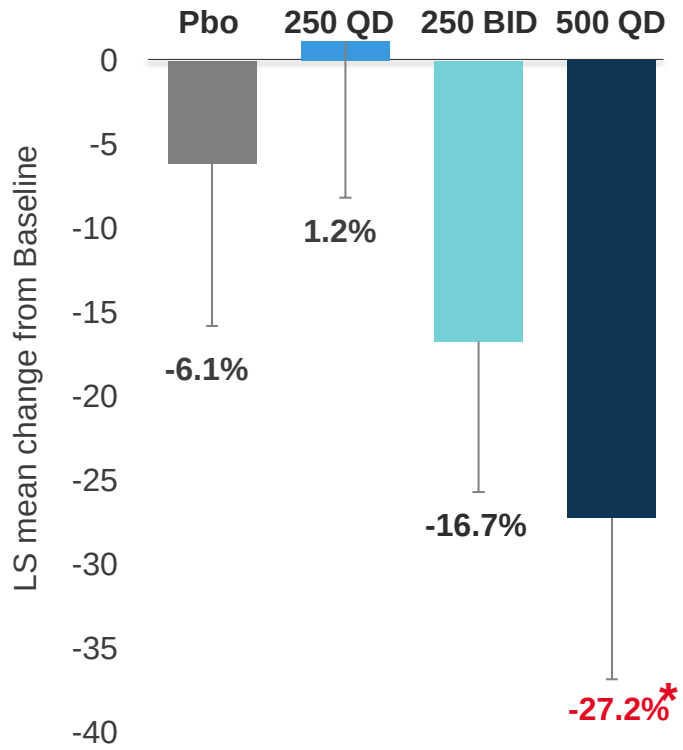
Liver Fat Content *(% Change from baseline)*

NAFLD with / without T2DM



500 mg: significant ALT reduction **(p = 0.04)**

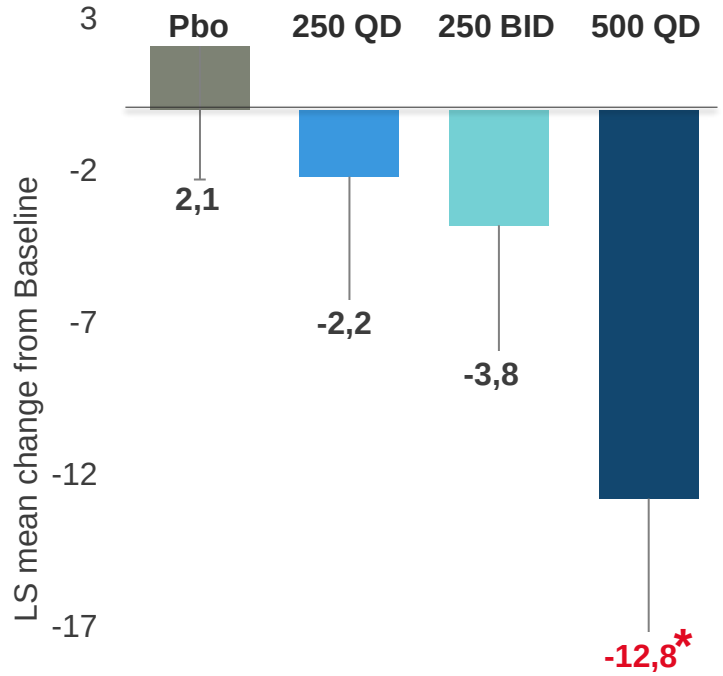
T2D subgroup



500 mg: 58% Responders (≥30%) vs. 7% Placebo **(p = 0.034)**

ALT *(IU/L Change from baseline)*

T2D subgroup



500 mg: significant AST reduction **(p = 0.02)**

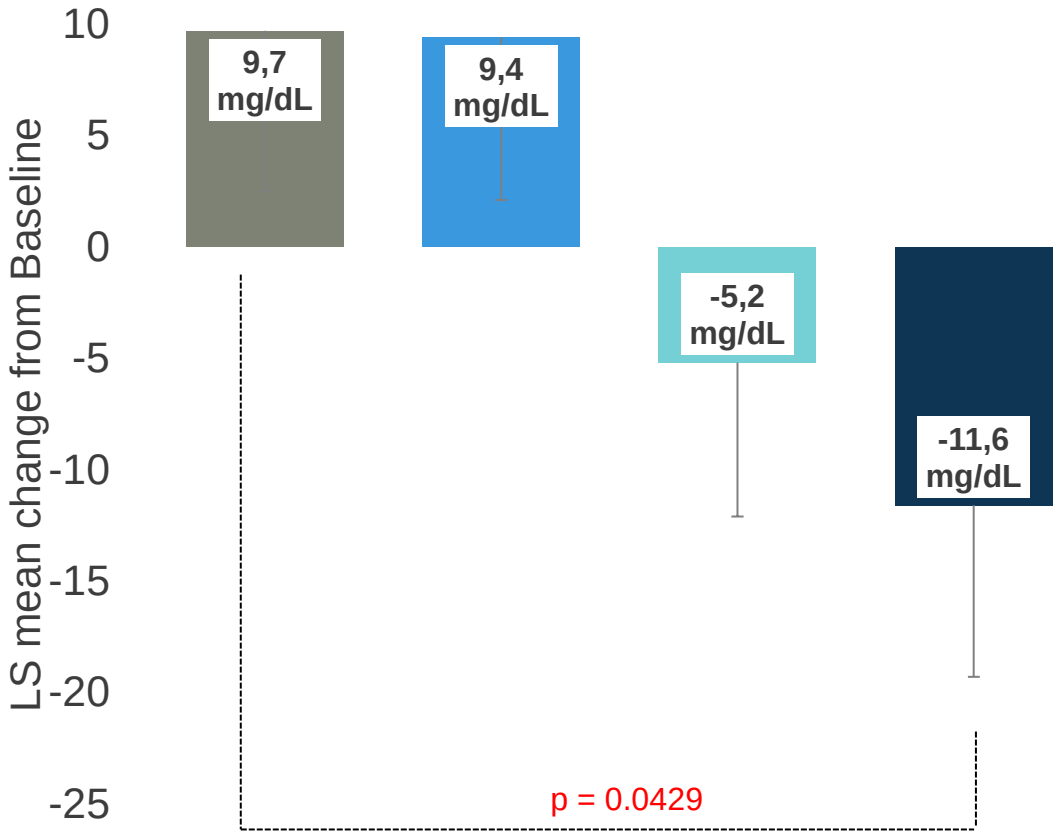
*p values 0.027-0.0036

T2D Subgroup - Improved Fasting Glucose & HbA1c

Despite Low Baseline Values

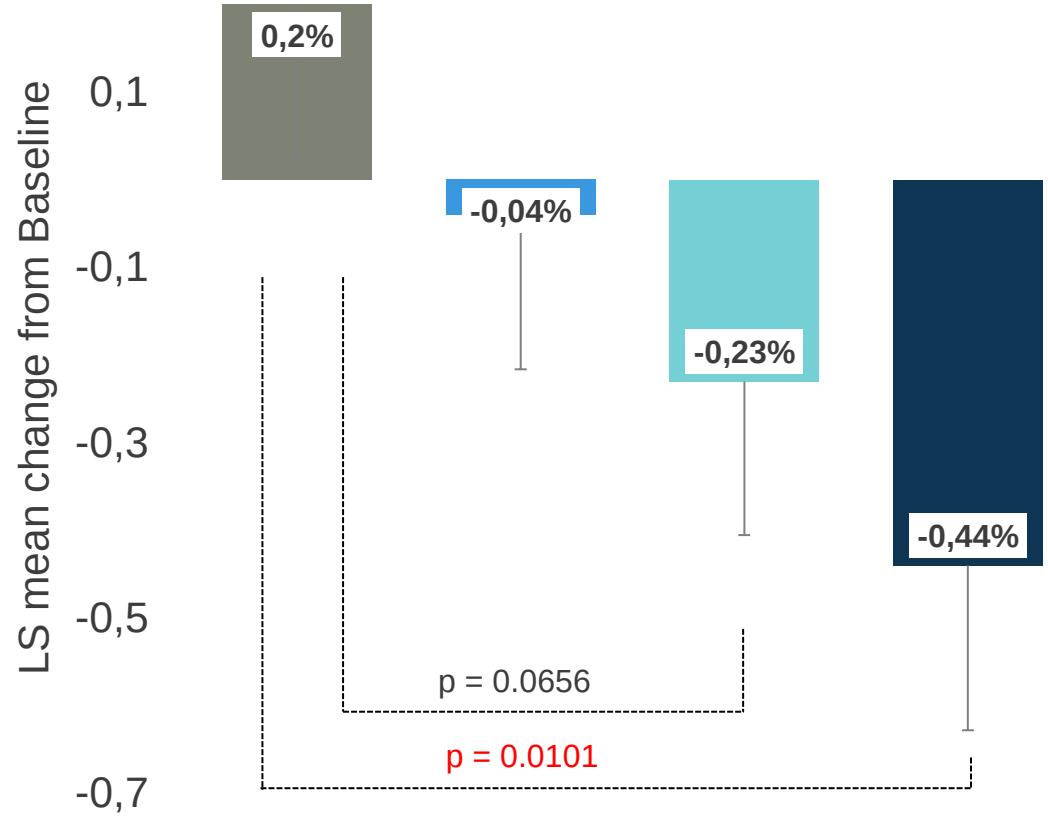
Fasting Glucose

Baseline	144.0 mg/dL	143.7 mg/dL	134.8 mg/dL	121.5 mg/dL
	Pbo	250 QD	250 BID	500 QD



HbA1c

Baseline	6.69 %	7.15 %	6.73 %	6.57 %
	Pbo	250 QD	250 BID	500 QD



Additional evidence of insulin sensitization – HOMA-IR (p=0.082) and QUICKI (p=0.022)

PXL770 Profile

Phase 2A Efficacy Results (in T2D Subgroup) vs. Selected Oral Competitors#

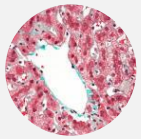
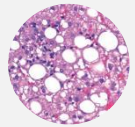
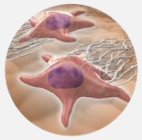
	PXL770◊ T2DM	Galmed Aramchol[1]	Madrigal Resmetirom[2]	Viking VK2809[3]	Intercept OCA [4,5]	Enanta EDP-305[6]	Metacrine MET409[7]
	AMPK	SCD1	THR-β	TR	FXR	FXR	FXR
Relative % LFC decrease vs. baseline	**-27.2**	**-12.6**	**-32.9**	**-53-60**	**-**	**-30.5**	**-37-55**
Relative % LFC decrease vs. placebo	**-21.1**	**-20**	**-22.5**	**-40-50**	**-17[3]**	**-18.6**	**-31-49**
Decrease in ALT (IU/L) vs. placebo	**-14. 9**	**-8.6***	**-3.0***	**-6.2***	**No change[4]**	**-12.5**	**-**
Decrease in HbA1c (%) vs. placebo	**-0.64**	**No effect**	**No effect**	**?**	**?**	**?**	**?**
Potential liabilities	**Mild GI**		**Mild GI**	**Potential QOD Dosing**	**Pruritus ↑LDL BBW for liver failure**	**Pruritus ↑LDL**	**Pruritus ↑LDL CYP3A4 inhibition**

1. Safadi R et al Clin Gastro & Hep 2014 (12 week Ph2a)
2. 12 week results; Tables 2,4 – Harrison SA et al. Lancet 2019 https://doi.org/10.1016/S0140-6736(19)32517-6;
3. Viking Corporate Presentation AASLD 2019 [12 week results]
4. Intercept presentation & Gastroenterology 2019;156:88–95. ALT in FLINT trial at 12 wks; MRI-PDFF results in smaller cohort from FLINT trial (40 pts treated with OCA)
5. Mudaliar S et al. Gastroenterology 2013;145:574–582 [6 week Ph2 study *in NAFLD pts with T2DM*]
6. Enanta presentation – 21% discontinuation due to "pruritus generalized" at 2.5 mg dose
7. Metacrine 2020 EASL poster presentation – 50/80 mg 12 wk results; net increase ALT with 50 mg at 12 wks vs decrease ALT with 80 mg; 16-40% pruritus; 24% increase LDL at 80 mg

◊ 500 mg QD group
 # Competitor data for 12 week treatment time points (except where noted if not available)
*** Not stat significant or stats not reported**

PXL770 - Translation of AMPK Activation Approach

Remaining Hypotheses to be Addressed in Phase 2b

	Rodent (*in vivo*)	Human Cells (*in vitro*)	NASH / NAFLD Patient
 **Steatosis**	✓ ↓ steatosis score; ↓ liver lipids; ↓ de novo lipogenesis	✓ ↓ de novo lipogenesis	✓ ↓ de novo lipogenesis; ↓ liver fat mass
 **Inflammation**	✓ ↓ inflammation score; ↓ liver leukocytes; MCP1 (+ other)	✓ ↓ cytokine secretion (macrophage)	*Pending Phase 2b*
 **Ballooning**	✓ ↓ ballooning score	no model	✓ ↓ ALT / AST *Pending Phase 2b*
 **Fibrosis**	✓ ↓ fibrogenesis	✓ ↓ stellate cell activation	*Pending Phase 2b*
↓ Insulin Resistance	✓ improved OGTT; ↑ glucose infusion rate (clamp) ↓ HbA1c	✓ ↑ glucose uptake (muscle cells)	✓ improved OGTT, HOMA-IR, Matsuda; ✓ ↓ HbA1c

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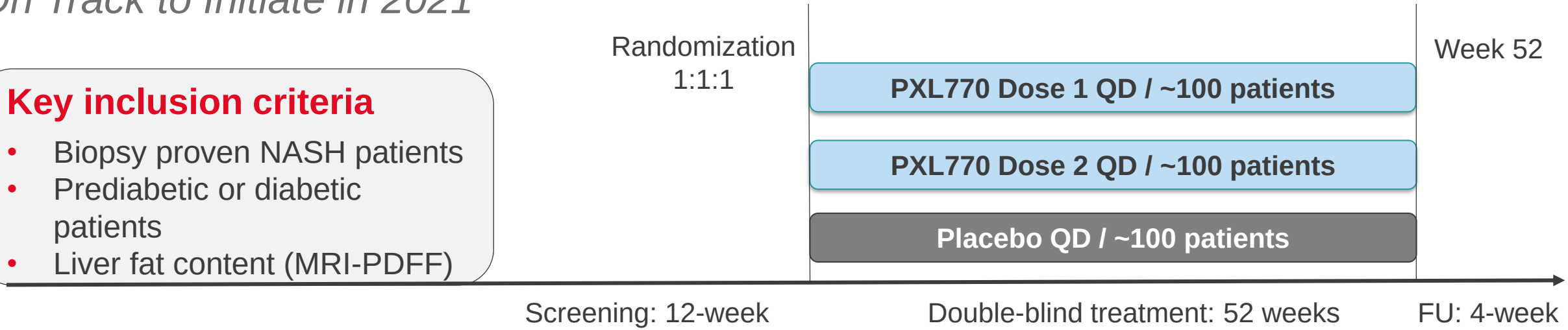
PXL770 Phase 2b Trial Design

On Track to Initiate in 2021

Key inclusion criteria

- Biopsy proven NASH patients
- Prediabetic or diabetic patients
- Liver fat content (MRI-PDFF)



Primary Endpoint

- Liver histology: NASH resolution without worsening of fibrosis

Secondary Endpoints

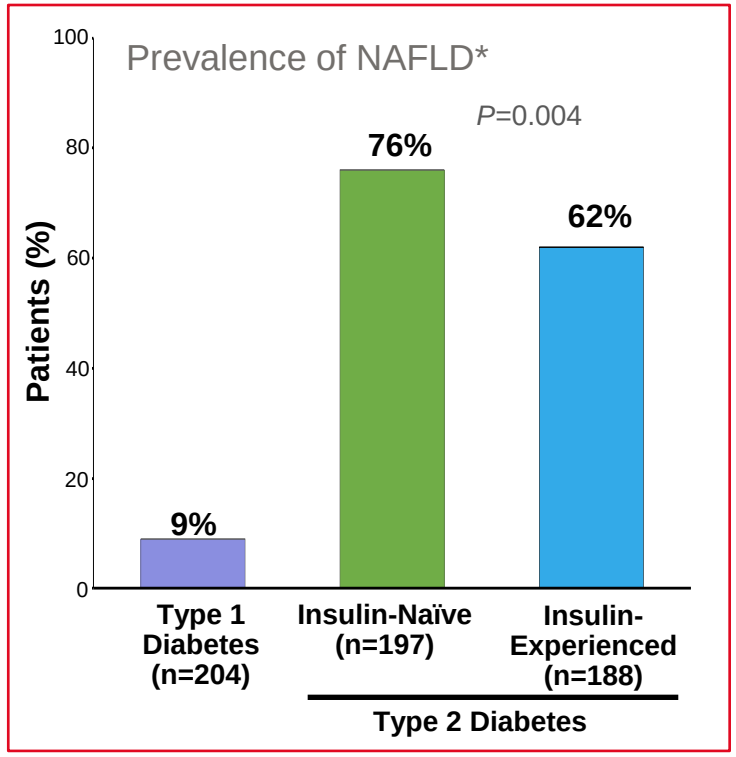
- Other histologic endpoints (fibrosis)
- Relative and absolute change in liver fat content (MRI-PDFF)
- Liver enzymes and other non-invasive biomarkers
- Metabolic parameters (FPG, HbA1c, insulin sensitivity indices, lipids, etc.)
- Safety, PK

Planning for Additional "Metabolic Benefits" T2D Trial Ongoing (24 week; 1-2 doses; 80-100 pts)

NASH and Type 2 Diabetes – Strong Clinical Overlap

NASH with T2D - High Prevalence and Greater Unmet Medical Need

- Approximately 40-50% of NASH patients have coexisting T2D[1]
- High prevalence of NAFLD (>60-70%) and NASH (26%) in T2D patients[2,3]



*NAFLD ≥ 6% hepatic fat fraction by MRI; data based on post-hoc analysis from 4 Phase III trials (n=589)

- Insulin resistance greater in patients with both NASH and T2D vs. either alone[4-6]
- 15% of patients with T2D have undiagnosed clinically significant fibrosis (F2-F4)[7]
- Clinical burden of NASH in patients with T2D greater than broader NASH population[1,6,8]
  - Progression of fibrosis
  - Worse CVD morbidity and mortality
- Economic burden for the group with prevalent NASH and T2D estimated $642 billion[8]

1. Younossi ZM et al; *Hepatology* 2016.
2. Cusi et al, *Diabetes Obes Metab.* 2017.
3. Portillo/Cusi et al, *J Clin Endocrinol Metab 2015.*
4. Cusi K, *Diabetes Care* 2020.
5. Bril/Cusi et al, *Hepatology* 2017.
6. Gastaldelli A & Cusi K, *JHEP Reports* 2019.
7. Lomonaco/Cusi, *Diabetes Care* (in press, 2021).
8. Younossi ZM et al, *Diabetes Care* 2020.

PXL770 - Safety & Conclusions

- Well tolerated, with acceptable safety profile
- Target engagement established (reduced DNL)
- Significant improvements in multiple NASH-related parameters
- Greater response in patients with T2D
  - consistent with lower endogenous AMPK “tone” hypothesis
  - additional glycemic benefits with improved insulin sensitivity
  - opportunity to target a large (45-50%) subpopulation of higher risk - patients with NASH *and* diabetes

⇨ PXL770 – first direct AMPK activator studied in human disease

⇨ Results support progression to later stage development

NASH

PXL065

Proprietary Program

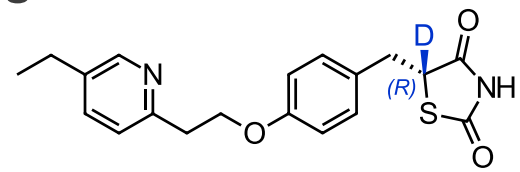
MPC Inhibitor for the Treatment of NASH

Utilizing the 505(b)(2) Regulatory Pathway

PXL065: Leveraging the Benefits of Pioglitazone

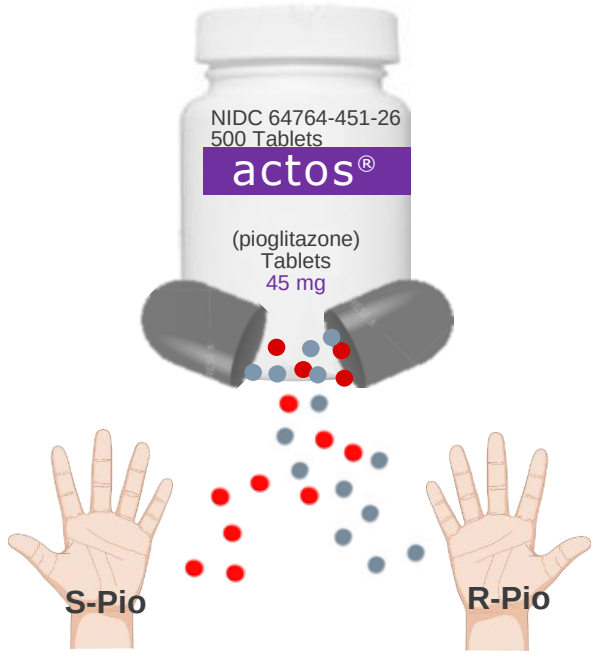
With Reduced PPARγ Activity

- Pioglitazone used in T2D[1,2] – most extensively studied molecule in NASH – multiple trials[3]
  - Recommended for NASH by AASLD & EASL Practice Guidelines[4]
  - Currently prescribed by ~14% of physicians for biopsy-proven NASH patients[5]
  - Limited use due to PPARγ-related side effects: weight gain, fluid retention, bone loss
- Pioglitazone is a mixture of 2 stereoisomers with dramatically different properties
- PXL065 is the deuterium-stabilized R-stereoisomer



S-Pioglitazone (stabilized)

- Strong PPARγ agonist
- Undesired side effects:
  - Weight gain
  - Fluid retention



PXL065 (stabilized R-pio)

- Very weak PPARγ agonism
- Operates via non-genomic pathways*
- Retains NASH activity in models

Composition of Matter IP

505(b)(2) Regulatory Path

1. Takeda 2014. https://www.takeda.com/newsroom/newsreleases/2014.
2. Diab Vasc Dis Res. 2019, 16(2), 133-143.
3. Ann Intern Med. 2016, 165(5), 305-315.
4. J Hepatol. 2016, 64(6),1388-402; Hepatology 2018, 67, 328-357.
5. Therap Adv Gastroenterol. 2016, 9(1), 4-12.

* Including inhibition of MPC – mitochondrial pyruvate carrier.

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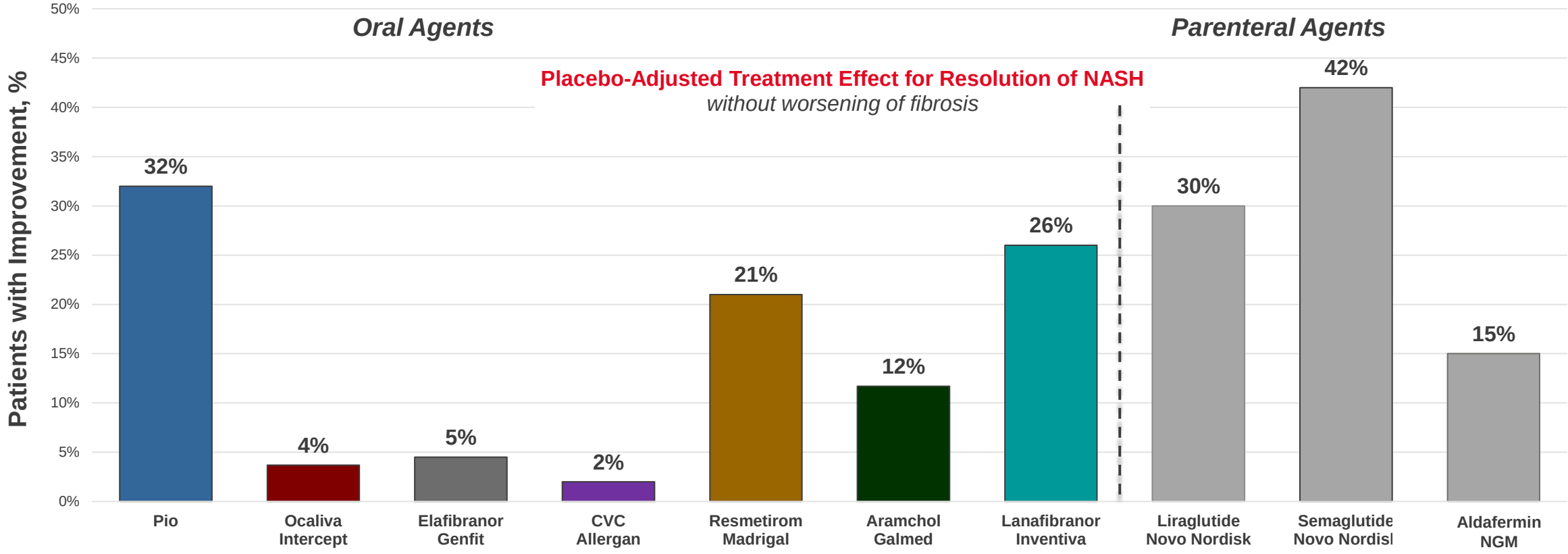
Pioglitazone Demonstrated Strong Efficacy in NASH Trials

Comparison vs. Other Agents in Development



NOTE: No head-to-head trials conducted.
Pio Cusi Phase 4 trial (30➝45 mg, 18 mos) - Ann Intern Med. 2016, 165, 305-315.
Ocaliva REGENERATE Phase 3 trial (25 mg, 18 mos) - Lancet. 2019, 394, 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
Resmetirom (MGL-3196) Phase 2 trial (80 mg +/- 20 mg, 36 wks) – Lancet 2019 394:2012-24.

.
Aramchol Phase 2 trial (600 mg, 52 wks) – press release June 12, 2018. .
Lanafibranor Phase 2 trial (1200 mg, 24 wks, ITT population) – Press release Jun 15, 2020
Liraglutide Phase 2 trial - The Lancet, 2016, 387(10019), 679–690
Semaglutide Phase 2 trial (0.4 mg, 72 wks) – Newsome et al NEJM Nov 19, 2020
Aldafermin (NGM282) Phase 2 trial (1 mg, 24 wks, cohort 4) - Press release Feb 25, 2020.

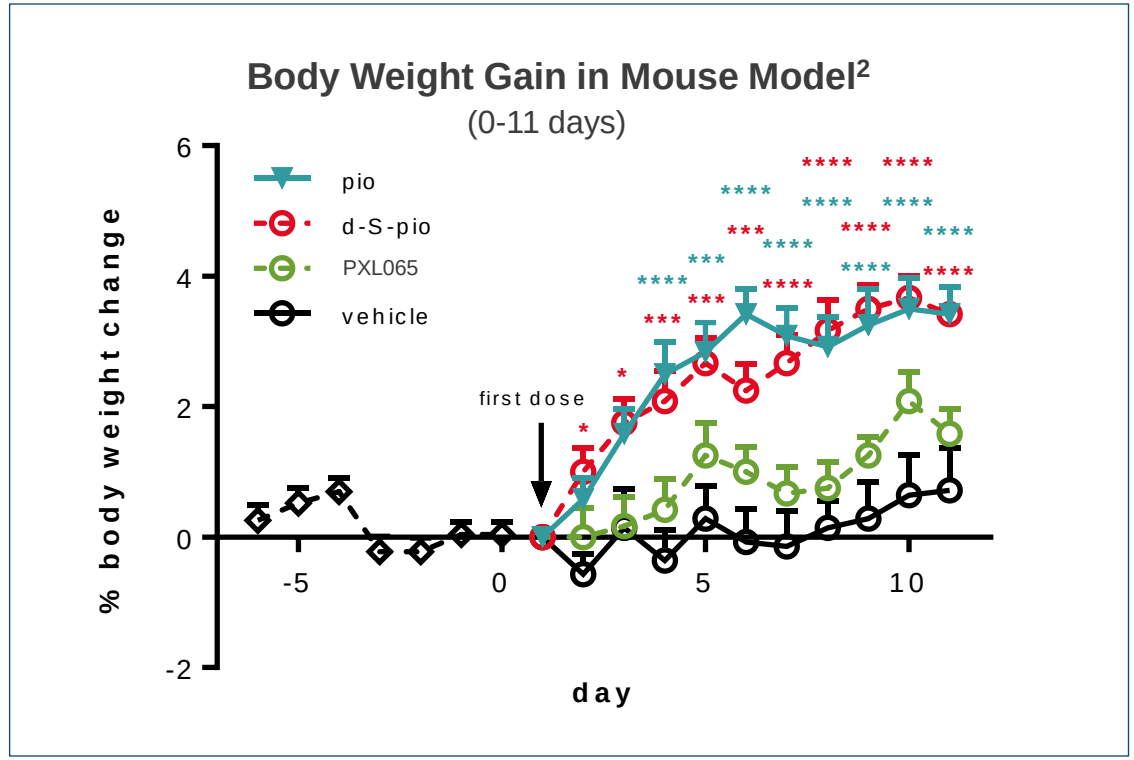
Meta-analysis OR >10 for improvement in advanced fibrosis[1]

1. Musso et al. Hepatology 65:1051-68, 2017.

PXL065 Profile in NASH Preclinical Models

PXL065 (R-Pio) Retains Benefits of Pio; S-Pio Drives Weight Gain and Fluid Retention

NASH Rodent Models[1] Functional Parameters	Pio	PXL-065
↓ Hepatic Triglycerides	✓	✓
↓ Hepatic Free Fatty Acids	✓	✓
↓ Hepatic Cholesterol	✓	✓
↓ Hepatic Steatosis	✓	✓
↓ Hepatic Inflammation	✓	✓
↓ Hepatic Ballooning	✓	✓
↓ Hepatic Fibrosis	✓	✓
↑ Weight Gain	✓	-
↑ Fluid Retention	✓	-

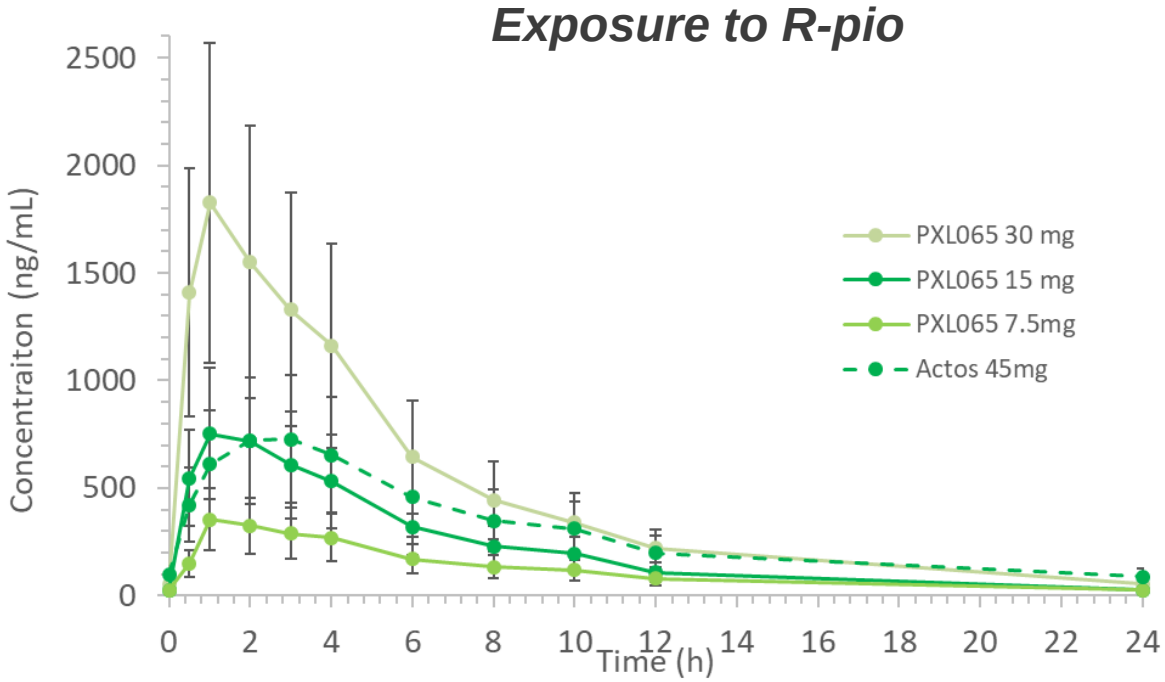


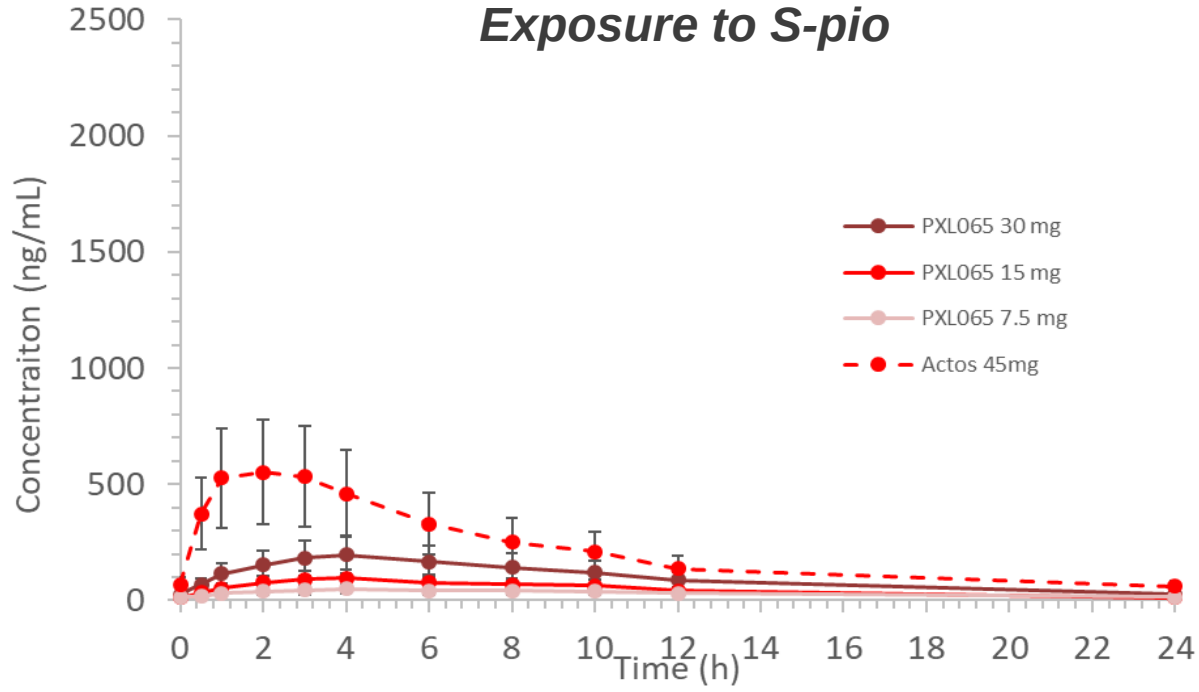
1. NASH rodent models selected based on literature: *C57BL/6J mouse model of weight gain & edema* (Nat Med 2005, 11, 861-866) and methionine-choline deficient (MCD) model of NASH (Lab Investig. 2007, 87, 56-65). Additional choline deficient (CD) model of NASH was validated with RenaSci. In MCD model 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-test average ± SEM; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $P < 0.0001$.

PXL065 Ph1 Study Results

15 mg vs. 45 mg Actos®[1]: Similar R-Pio Exposure; S-Pio Exposure Decreased ~5-fold





- Single (SAD) and repeated (Phase 1b) 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 Phase 1b study
- Well tolerated at all doses tested

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

1. Actos is the branded version of pioglitazone and a registered trademark of Takeda Chemical Industries, Ltd.

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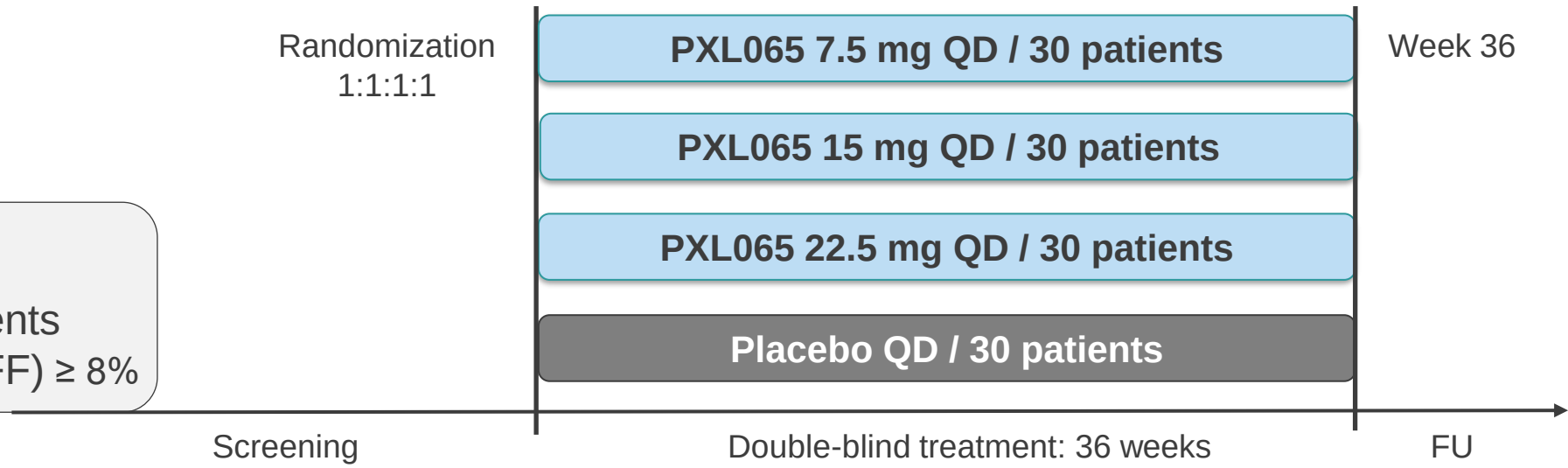
PXL065 Ongoing Phase 2 in Biopsy-Proven NASH Patients

Single Streamlined Study - 505(b)(2) Pathway; Designed to Select Ph3 Dose(s)

DESTINY 1

Key inclusion criteria

- Biopsy-proven NASH patients
- Liver fat content (MRI-PDFF) ≥ 8%



Primary Endpoint

- Relative change in liver fat content (MRI-PDFF)

Secondary Endpoints

- Liver histology: NASH resolution without worsening of fibrosis
- Liver enzymes
- Metabolic parameters
- Biomarkers, Safety, PK

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PXL770 and PXL065: NASH Value Proposition

- Two **oral**, **first-in-class Phase 2** programs addressing an **unmet medical need** with large market opportunity
- **Differentiated approaches** to control key pathways that lead to liver injury with **innovative development** strategies
- **PXL770** - **differentiated Phase 2b plan** focusing on coexisting high-risk T2DM patients, which represent approximately **50% of NASH patients**
- **PXL065 - streamlined Phase 2 development** approach leveraging 505(b)(2) pathway and extensive knowledge of pioglitazone
- Mechanisms support **potential for combination use**
- Favorable safety profiles to-date

Additional Opportunities

Pipeline Expansion

Chronic and Rare Metabolic Indications

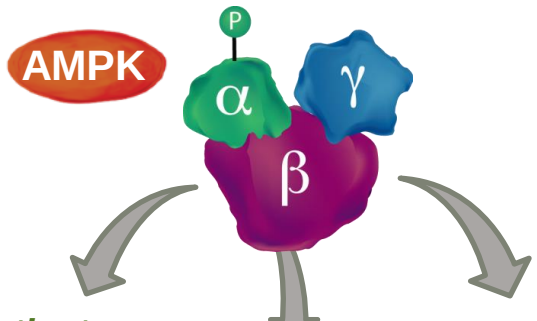
Next Generation AMPK Activators

Next Generation D-TZD's*

*Deuterium-modified thiazolidinediones.

Harnessing AMPK and D-TZD Platforms to Address Diseases with Metabolic Pathophysiology

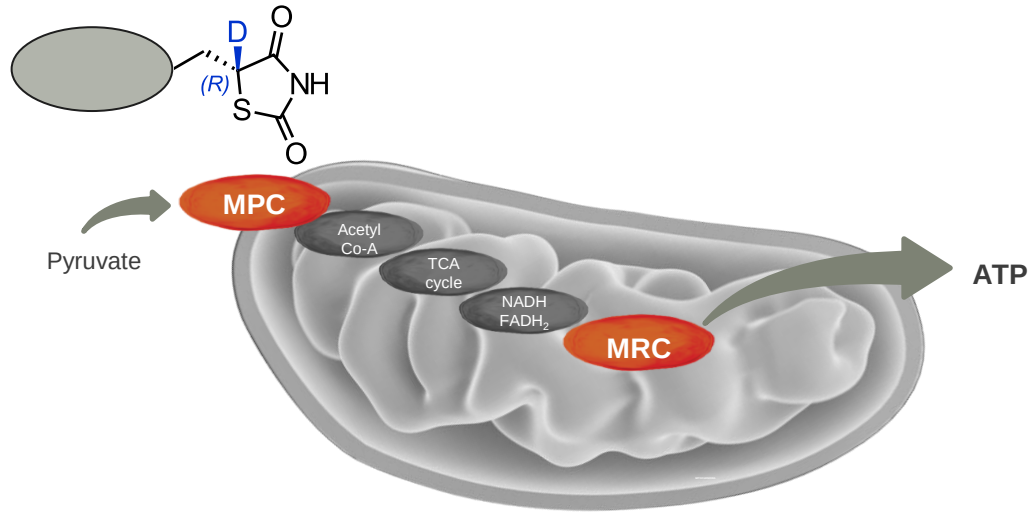
Next Generation Programs Approaching Clinical Candidate Selection (Both Platforms)



Activates ***catabolic pathways***

Inhibits ***anabolic pathways***

Inhibits ***inflammation apoptosis***



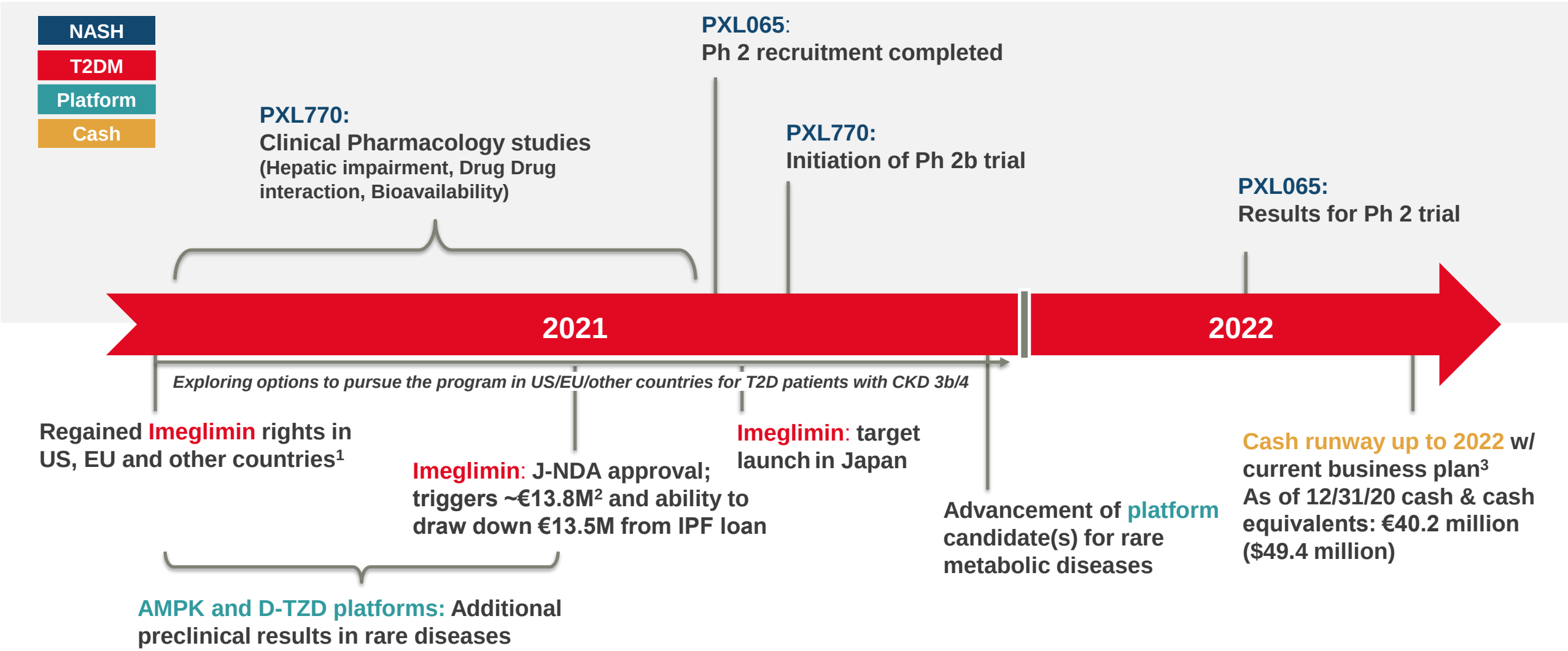
Renal
Diabetic kidney disease
Polycystic kidney disease

Endocrine
Type 2 diabetes
Polycystic ovary syndrome

Rare Metabolic
Adrenoleukodystrophy (ALD; AMN)
Mitochondrial disorders

Upcoming Milestones

Near-Term Milestones to Drive Poxel's Growth



For countries not part of the DSP agreement. 2. Based on the JPY/€ exchange rate at December 31, 2020. 3. Taking into account ~€13.8M milestone payment by Sumitomo Dainippon Pharma, and €13.5M from IPF loan, which are both subject to the marketing approval of Imeglimin in Japan, expected in 2021 (Sumitomo Dainippon Pharma's fiscal year), and not including the financing of the Ph.2b study for PXL770.

Thank You

Contacts

Aurélie Bozza
Investor Relations and Communication Director
aurelie.bozza@poxelpharma.com
+33 6 99 81 08 36

Catherine David
Investor Relations & Communication Manager
catherine.david@poxelpharma.com
+33 7 64 57 61 78

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