



Full Year 2022 Financial and Corporate Update

March 23, 2023



Agenda

1. 2022 Summary & Early 2023 Corporate Update
2. Extended cash runway based on debt restructuring and new equity-linked financing (announced today)
3. Commercial Update - TWYMEEG
4. Financial Update – FY 2022 results
5. Clinical Update
 - Rare Metabolic Disease Programs
 - NASH
6. Conclusion & Q&A

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.

2022 Summary & Early 2023 Corporate Update (1/2)

Financing Update

- Extension of the cash runway through Q2 2025 based upon:
 - A debt restructuring agreement, which postpones initiation of repayments until Q1 2025 at the latest, to be repaid with positive net royalty¹ flow to Poxel anticipated to start in Sumitomo Pharma's FY2024² based on the strong growth trajectory of TWYMEEG[®] (Imeglimin) sales
 - New equity-linked financing facility³, assuming full drawdown, with IRIS (initial drawdown of €3.5 million⁴)
 - As of December 31, 2022, cash and cash equivalents were €13.1 million
- Actively pursuing various additional financing options to fund Phase 2 proof-of-concept (POC) studies in ALD, the next chapter of Poxel's strategic focus in rare metabolic diseases

Commercial update

- TWYMEEG sales for Type-2-Diabetes in Japan grew 90% over the prior quarter
- Strong growth trajectory leading to a 20% increase of the Sumitomo Pharma fiscal year 2022 forecast

1. First 8% of royalties on net sales of Imeglimin are paid to Merck Serono. Net royalties above 8% retained by Poxel.

2. Sumitomo Pharma fiscal year 2024 ends March 31, 2025.

3. Assuming full drawdown of EUR 15 million, subject to the conditions described in the paragraph "operation arrangements" in the press release dated March 22, 2023

4. Based on the initial drawdown of EUR 3.5 million only, the Company expects that its resources will be sufficient to fund its operations and capital expenditure requirements through November 2023.

2022 Summary & Early 2023 Corporate Update (2/2)

Clinical update

- Rare disease:
 - Adrenoleukodystrophy (ALD): Phase 2 POC studies prepared to initiate, pending additional financing
 - Additional regulatory designations: Orphan (EU & US); Fast Track (US) for ALD for both PXL770 & PXL065
 - Autosomal-dominant polycystic kidney disease (ADPKD): PXL770 is Phase 2 ready asset
 - Orphan designation (US) for PXL770
 - Publication in *Kidney International*
- NASH: Positive Phase 2 Trial (DESTINY-1) for PXL065
 - Primary efficacy endpoint met & strong improvement in fibrosis without worsening of NASH (FDA approval endpoint)
 - Presented at AASLD (November 2022) and published in *Journal of Hepatology* (February 2023)

Organizational Update

- Ongoing savings plan initiated in 2022
- Board of Directors resized to 4 members
 - Other existing Board members transitioning to a new Board Advisory Committee

Today's announcement

*Debt Restructuring Agreements and
New Equity-linked financing*



Cash Runway Extended through Q2 2025

Based on Debt Restructuring Agreements and New Equity-linked financing¹

- **Debt Restructuring**

- Agreements with lenders to postpone initiation of repayments to be repaid with positive net TWYMEEG royalties², expected Q1 2025 at latest, under conservative forecast
 - Before the end of Sumitomo fiscal year 2024 (ending March 31, 2025), Poxel expects TWYMEEG net sales in Japan to reach JPY 5 billion, entitling Poxel to receive 10% royalties on all TWYMEEG net sales and a sales-based payment of JPY 500 million (EUR 3.6 million³)
- Full repayment to PGE banks expected by Q2 2028 and to IPF by Q2 2029
 - After this time, subsequent net royalties and sales-based payments will revert back to Poxel

- **New Equity-linked financing facility**

- Initial drawdown of EUR 3.5 million⁴
- Future tranches at the sole discretion of Poxel, up to a total of EUR 15 million¹
- Total outstanding held by IRIS not to exceed EUR 7 million at any time

- **Ongoing savings plan**

- **Pursuing additional financing, including partnership discussions, to launch ALD Phase 2 POC studies**

1. Assuming full drawdown of EUR 15 million, subject to the conditions described in the paragraph "operation arrangements" in the press release dated March 22, 2023

2. First 8% of royalties on net sales of Imeglimin are paid to Merck Serono. Net royalties above 8% retained by Poxel.

3. Currency exchange rate at December 31, 2022.

4. Based on the initial drawdown of EUR 3.5 million only, the Company expects that its resources will be sufficient to fund its operations and capital expenditure requirements through November 2023.

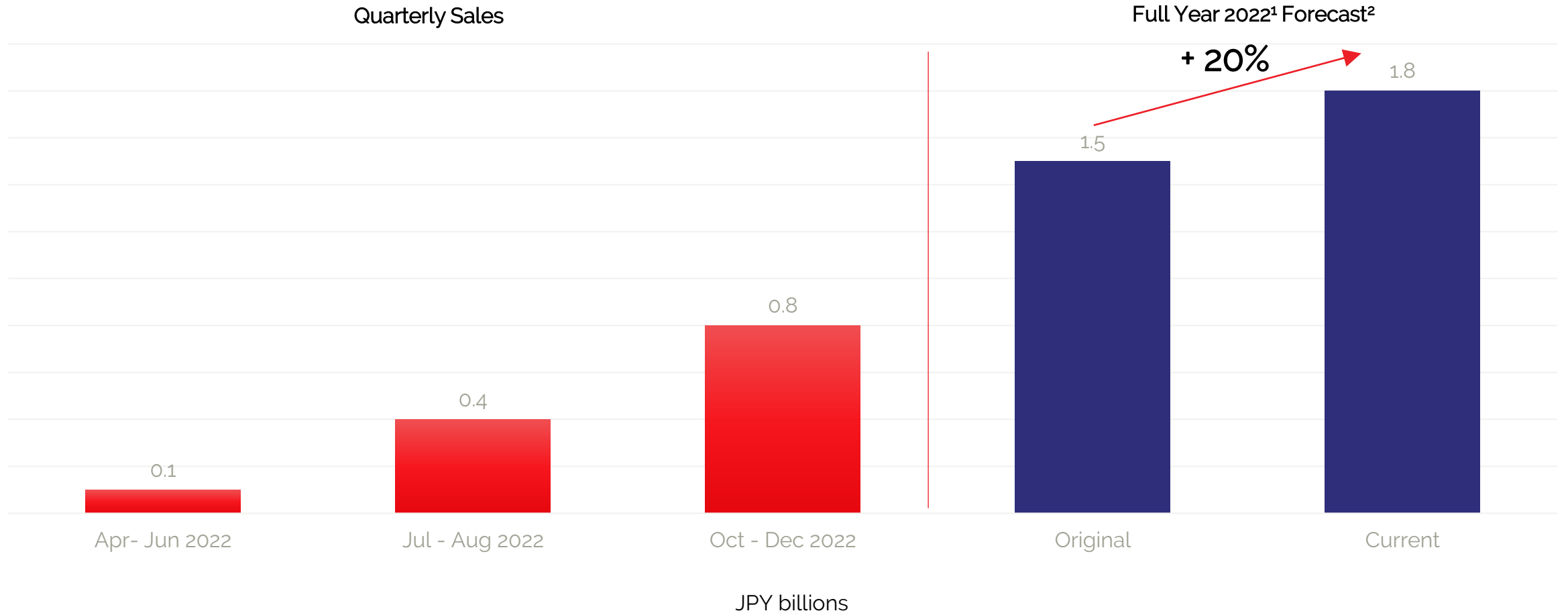
Commercial Update

TWYMEEG[®] (Imeglimin) Sales in Japan



TWYMEEG Sales in Japan

Strong Growth Leading to 20% Increase of Sumitomo FY2022¹ Forecast²



1. Sumitomo Pharma fiscal year April-March.
2. Gross Sales and FY2022 forecast of JPY 1.8 billion published on January 31, 2023 by Sumitomo Pharma.

TWYMEEG® (Imeglimin): Strong Growth Trajectory

Partnered in Asia¹ with Diabetes Market Leader, Sumitomo Pharma



Commercial Strategy

- Sumitomo #1 diabetes franchise; FY21² JPY 79B;
- Positioning: TWYMEEG can be prescribed as add-on to any therapy and as monotherapy; **Increasing combination use** with DPP4 (prescribed to 80% T2D patients³) and also SGLT2 inhibitors
- Extensive medical affairs & clinical activities
- Patent estate extends to 2036 (incl. potential 5-year patent term extension), with other applications ongoing

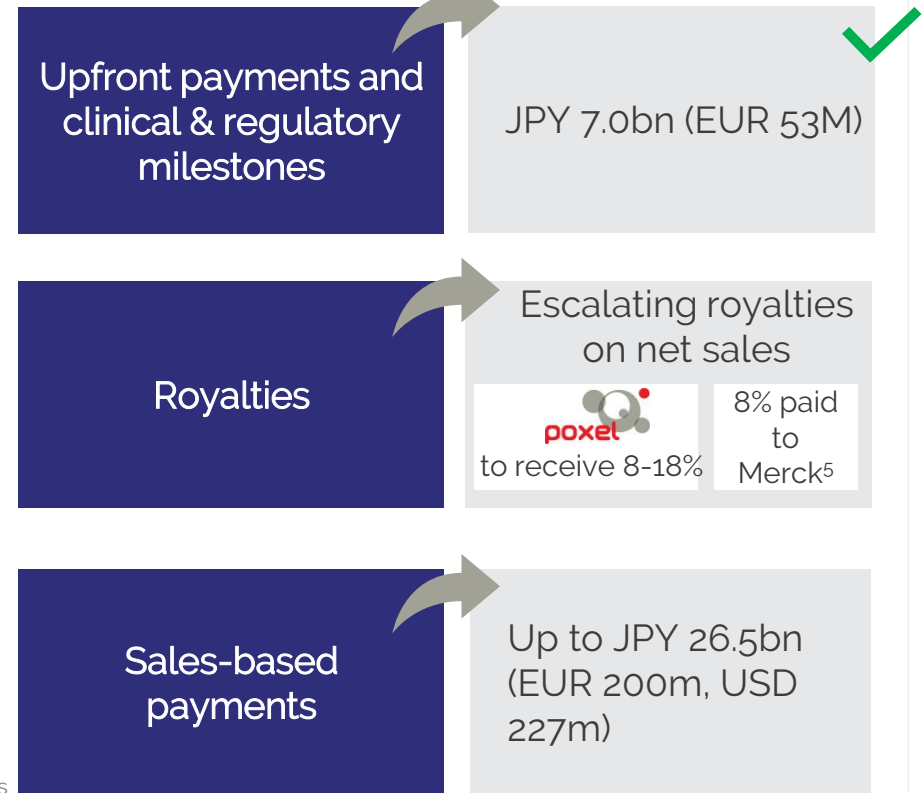
TWYMEEG Revenue Trends

- Sales in Japan for October-December 2022 **+90% over prior quarter**
- **Sumitomo FY2022² forecast increased 20% to JPY 1.8B (EUR 12.8 million)⁴**
- For Sumitomo FY2023, Poxel expects 8% royalty on net sales⁵
- Before the end of Sumitomo FY2024², Poxel expects net sales in Japan to reach JPY 5 billion (EUR 35.6 million)⁴, entitling Poxel to receive 10% royalties on net sales and a sales-based payment of JPY 500 million (EUR 3.6 million)⁴

Potential additional partnerships in specific territories

Sumitomo Pharma

Collaboration Summary



1. Including: Japan, China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, the Philippines, Singapore, Myanmar, Cambodia, and Laos
2. Sumitomo Pharma fiscal year April-March.
3. IQVIA data FY2016 and NDB data FY2016.
4. Currency exchange as of December 31, 2022.
5. First 8% of royalties on net sales of Imeglimin paid to Merck Serono.

Corporate Update

Board of Directors – Changes in Organization

Board of Directors

- Resized to 4 current members
- Khoso Baluch as Chairman



Khoso Baluch
Chairman of the Board



Pascale Boissel
Independent Board member



Richard Kender
Independent Board member



Thomas Kuhn
Chief Executive Officer of Poxel

New Board Advisory Committee

- Creation of a new Board advisory committee composed of former Board members, who will continue to assist the Company in all its activities



Pierre Legault
President



Janice Bourque
Member



Kumi Sato
Member



John Kozarich
Member

Financial Update

Full Year 2022



2022 Revenue*

Mainly reflecting royalty revenue from Sumitomo Pharma

<i>EUR (in thousands)</i>	FY 2021 12 months	FY 2022 12 months
Sumitomo Agreement	13 377	673
Other	20	1
Total revenues	13 397	674

- Revenue for 2022 reflects of JPY 95 million (EUR 0.672 million) of **royalty revenue** from Sumitomo Pharma, which represents **8% of TWYMEEG net sales in Japan**

Statement of Comprehensive Income as of Dec. 31, 2022*

<i>EUR (in thousands)</i>	December 31, 2021	December 31, 2022
Revenue	13,397	674
Cost of sales	(59)	(672)
Gross margin	13,339	2
Research and development		
Research and development expenses	(27,479)	(13,940)
Tax credit & subsidies	2,305	1,491
General and administrative	(10,627)	(9,443)
Operating profit	(22,463)	(21,890)
Financial income/(expenses)	(2,082)	(9,738)
Foreign exchange gains/(losses)	785	229
Profit before tax	(23,760)	(31,396)
Income tax	(2)	(2)
Net income	(23,763)	(31,398)

Reflects mainly JPY 95 million (EUR 0.672 million) of royalty revenue from Sumitomo Pharma, which represents 8% of TWYMEEG net sales in Japan

Represents royalties paid to Merck on sales of Imeglimin in Japan (fixed 8%, independent of the level of sales)

Primarily reflects the clinical study costs incurred for the Phase 2 DESTINY study evaluating PXL065 in NASH

Includes interests and fees on IPF debt as well as non-cash accounting adjustments

Statements of Financial Position as of December 31, 2022*

Assets

<i>EUR (in thousands)</i>	December 31, 2021	December 31, 2022
Intangible assets	16,631	16,606
Property, plant and equipment	1,716	1,323
Other non-current financial assets	206	211
Deferred tax assets	-	0
Total non-current assets	18,552	18,140
Trade receivables and related accounts	50	394
Other receivables	3,999	3,122
Current tax receivables	-	-
Cash and cash equivalents	32,287	13,058
Total current assets	36,337	16,574
Total assets	54,889	34,714

Mostly reflects DeuteRx portfolio acquisition in 2018

Change in cash (-€19.2m) mainly reflects operating cash burn partially offset by the IRIS financing

Statements of Financial Position as of December 31, 2022*

Shareholders' Equity and Liabilities

EUR (in thousands)	December 31, 2021	December 31, 2022	
Total shareholders' equity	8,206	-18,241	Mostly reflects FY2022 net loss
Employee benefits	370	252	
Non-current financial liabilities	30,094	25,218	Reflects debt - IPF (€32m), PGE (€6m) & IRIS (€4.6m)
Provisions	318	67	
Non-current liabilities	30,782	25,537	
Current financial liabilities	5,046	19,042	
Derivative liabilities	153	1,533	
Trade payables and related accounts	8,417	4,406	
Other current liabilities	2,285	2,438	
Current liabilities	15,901	27,419	
Total liabilities	54,889	34,714	

Statements of Cash Flow as of Dec. 31, 2022*

<i>EUR (in thousands)</i>	December 31, 2021	December 31, 2022
Cash flows from operating activities before change in WC	(18,791)	(18,477)
(-) Changes in working capital requirements	1,898	(3,335)
Cash flows from operating activities	(16,893)	(21,813)
Acquisitions of intangible assets	(49)	23
Other	7	23
Cash flows from investing activities	(42)	0
Share capital increase	295	0
Other financing operations	8,730	2,585
Cash flows from financing activities	9,021	2,585
Increase (decrease) in cash and cash equivalents	(7,915)	(19,229)

Reflects operating loss net of non cash accounting adjustments

Reflects IRIS financing (€6m) partially offset by interests and repayment of IPF debt

As of December 31, 2022, total cash and cash equivalents were EUR 13.1 million (USD 14 million)

Cash runway extended through Q2 2025 with debt restructuring and equity-linked financing

Robust Mid-to-Late Stage Metabolic Pipeline

Focus on NASH and Rare Metabolic Diseases

	Indication	MOA	Discovery/ PC	PH 1	PH 2	PH 3	Approved/ Marketed	Recent & Upcoming Milestones	
NASH									
PXL065	NASH	Non-Genomic TZD ¹	[Progress bar from Discovery/PC to end of PH 2]						<ul style="list-style-type: none"> Positive Phase 2; Discussions for a potential pivotal program in NASH; leveraging 505(b)(2) pathway
Rare Metabolic Indications									
PXL770	ALD ³	AMPK Activator ²	[Progress bar from Discovery/PC to end of PH 1]						<ul style="list-style-type: none"> Fast Track & Orphan Drug Designations (2022) Phase 2a launch pending additional financing
PXL770	ADPKD ⁴	AMPK Activator ²	[Progress bar from Discovery/PC to end of PH 1]						<ul style="list-style-type: none"> Orphan Drug Designation (2022) Completed preclinical Phase 2 ready, developing clinical strategy
D-TZD (PXL065)	ALD ³	Non-Genomic TZD	[Progress bar from Discovery/PC to end of PH 1]						<ul style="list-style-type: none"> Fast Track & Orphan Drug Designations (2022) Phase 2a launch pending additional financing
Type 2 Diabetes (T2D)									
TWYMEEG® Japan / Asia ⁵ Sumitomo Pharma	T2D	MRC ⁶ Modulator	[Progress bar from Discovery/PC to end of PH 2]						<ul style="list-style-type: none"> TWYMEEG approved for T2D in Japan (June 2021) Product launched September 2021 Poxel entitled to receive 8-18% royalty on net sales
Imeglimin US / EU / Other	T2D	MRC Modulator	[Progress bar from Discovery/PC to end of PH 1]						<ul style="list-style-type: none"> Considering specific territories partnerships

1. Deuterium-modified thiazolidinedione
 2. AMP-kinase
 3. X-linked Adrenoleukodystrophy
 4. Autosomal dominant polycystic kidney disease

5. Includes: China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, Philippines, Singapore, Myanmar, Cambodia, Laos
 6. Mitochondrial Respiratory Chain



Rare Metabolic Disease Programs

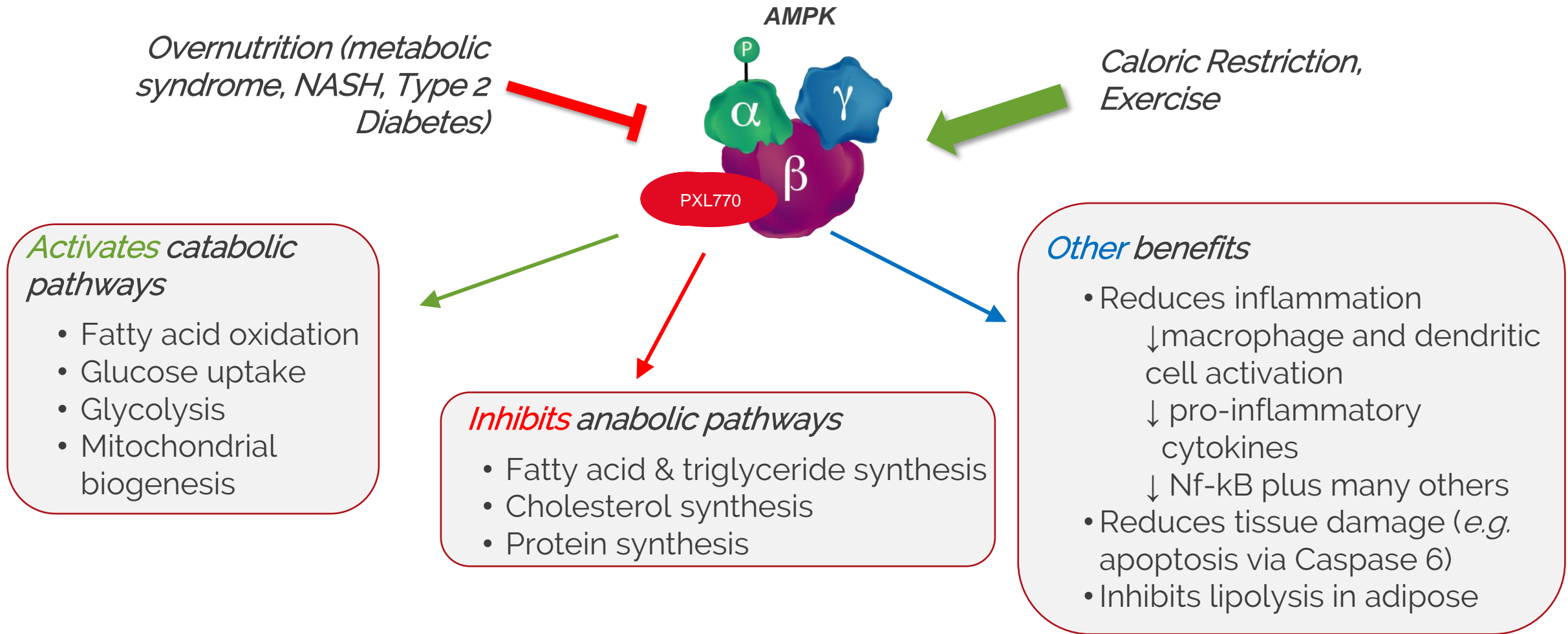
PXL770 - AMPK Activator

- Adrenoleukodystrophy (ALD) - Fast Track & Orphan Drug
- Autosomal Dominant Polycystic Kidney Disease (ADPKD)



AMP Kinase Activation

PXL770 and Next Generation Molecules



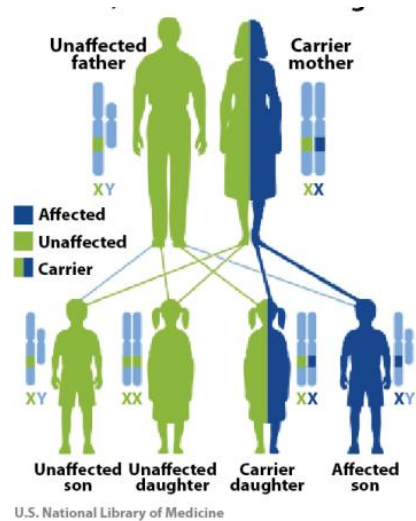
Potential to Target a Broad Range of Diseases with Metabolic Pathophysiology

Adrenoleukodystrophy

A Not-so-Rare Orphan Neurometabolic Disease

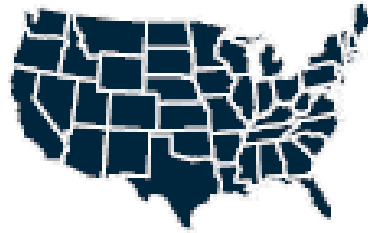
Genetics

- Monogenic, X-linked mutations in ABCD1 gene
- Gene encodes a transporter present in peroxisomes required for metabolism of very long chain fatty acids (VLCFA)
- *Males more severely affected*



Prevalence

Estimated US Prevalence¹
20,000 – 29,000



Estimated Global Prevalence¹
444,000 – 644,000



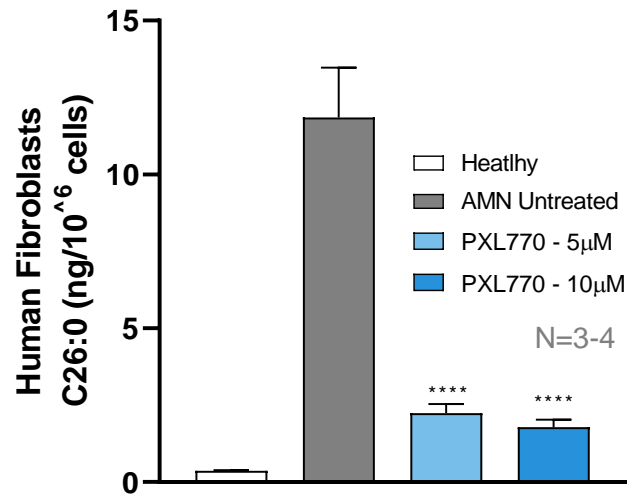
Diagnosis & Clinical Features

- Diagnosis –
 - newborn screening – increasingly common (now >60% of newborns in US)
 - clinical presentation followed by measurement of VLCFA and genotyping
- Clinical –
 - spinal cord degeneration (adrenomyeloneuropathy – AMN) in ≈100% of males with adult onset
 - cerebral lesions – up to ≈60% lifetime risk – both children and adults
 - adrenal insufficiency

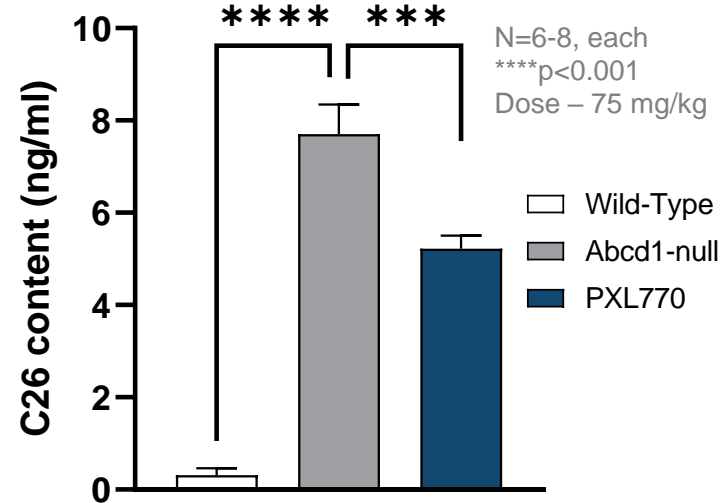
ALD: AMPK Rationale and Strong Preclinical Data

- Deletion of AMPK in disease cells → mitochondrial dysfunction¹ ; reduced AMPK in patient-derived cells and patient brain tissue^{2,3}
- AMPK activation evidence of efficacy in patient cells and animal model^{3,4}
- PXL770 is active in patient-derived cells and in the classical animal model⁵:

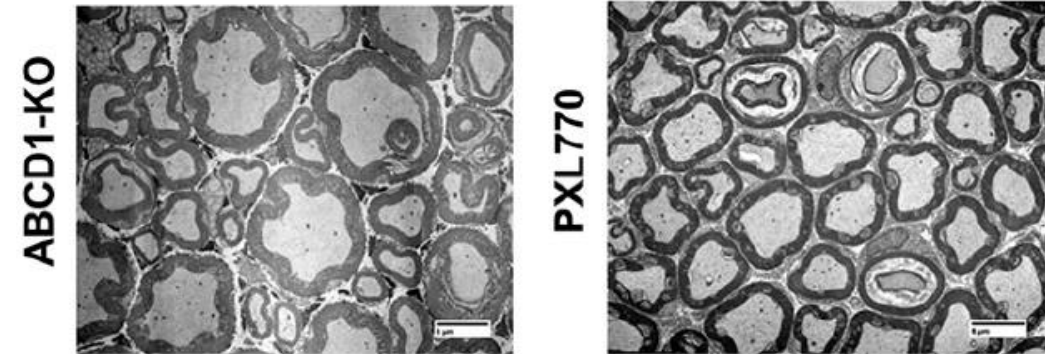
**AMN - Fibroblasts
Suppression of Elevated VLCFA**



**ABCD1 null Mouse
Spinal Cord Suppression
of Elevated VLCFA (C26:0)**



**Improved Neural Histology (& Locomotor Function)
In ABCD1 null Mice**



Beneficial Effects of the Direct AMP-Kinase Activator PXL770 in In Vitro and In Vivo Models of X-Linked Adrenoleukodystrophy⁵

[dx.doi.org/10.1124/jpet.122.001208](https://doi.org/10.1124/jpet.122.001208)
J Pharmacol Exp Ther 382:208–222, August 2022

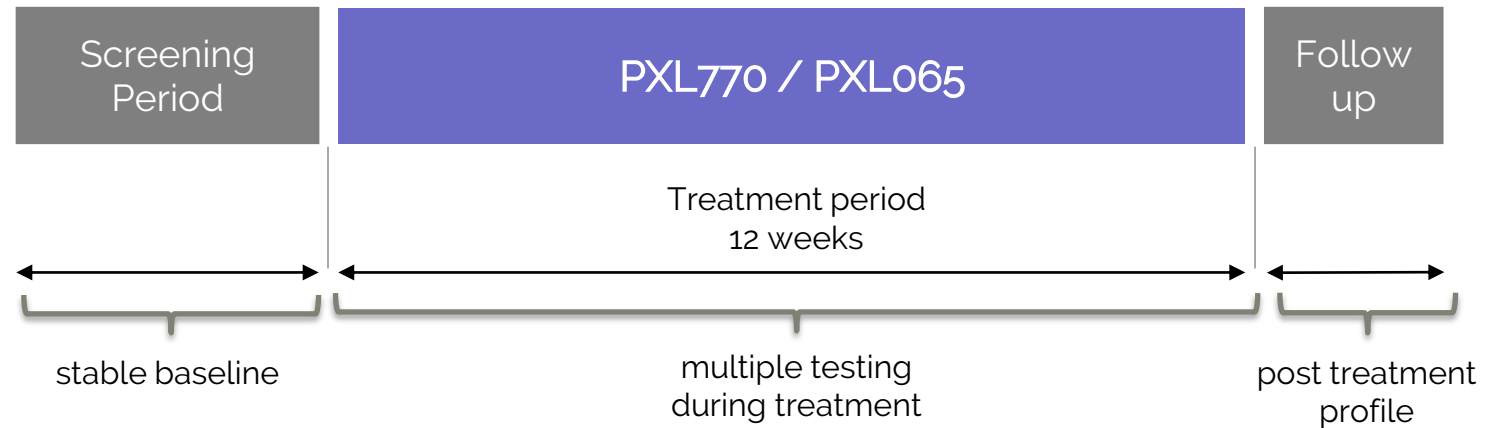
Additional Strong Rationale and Preclinical Efficacy with D-TZD Platform (PXL065)
Phase 2a Studies Planned

Planned Phase 2a Studies in ALD/AMN

Fast Track & Orphan Designation for PXL770 & PXL065; Two Identical Studies

Key inclusion criteria

- Males with AMN
- Age 18-65
- No active cerebral disease
- 12-24 patients each



Endpoints

- VLCFA – biomarker and hallmark of disease – drives pathology
- Neurofilament light chain – validated biomarker of neuronal damage
- Other / exploratory biomarkers
- PK
- Safety

Subject to financing, Phase 2a planned to initiate as soon as possible

ALD Opportunity Summary

High Unmet Needs, Blockbuster Market Potential

- **Blockbuster market opportunity**

- US prevalence of 20,000-29,000; Global prevalence of 444,000 – 644,000
- Ability for premium pricing based upon other orphan drugs with similar prevalence
- Potential Regulatory designations:
 - US: Orphan (7 years exclusivity), Fast Track, Breakthrough, Priority Review
 - EU: Orphan (10 years exclusivity), PRIME

- **Expedited Clinical Development**

- Established safety profiles of PXL770 and PXL065 (with 505b2) mitigate risk & may reduce clinical development timelines
- Data from ALD preclinical models suggest potential for significant impact on key biomarkers (VLCFA, neurofilament light chain)
- Fast Track Designation for PXL770 and PXL065; potential for accelerated approval based upon biomarkers

- **Community Engagement**

- Established relationships with Key Opinion Leaders
- Collaborations with important patient advocacy groups



ADPKD and Rationale for AMPK & PXL770

ADPKD

- Autosomal-dominant genetic form of CKD
- 140,000 patients in US; fourth leading cause of CKD
- >50% develop renal failure by age 50 → dialysis, transplant
- 1 drug approved - tolvaptan - used to attenuate progression; severe liver AE's and poor tolerability (polyuria)

Why AMPK?

- AMPK activity lower in kidney of rodents & humans with CKD¹
- Metabolic status influences clinical disease progression²⁻⁴
- Food restriction attenuates/reverses PKD in animals³⁻⁵; AMPK activation mimics effects of food restriction^{2,5}
- mTOR*, CFTR** & cAMP drive PKD pathology; AMPK: inhibits mTOR, suppresses CFTR, lowers cAMP^{3,7}
- Inflammation, fibrosis increased in ADPKD; AMPK suppresses^{3,8}
- Indirect AMPK activation (metformin; high concentration) suppresses cyst growth *in vitro* & *in vivo*⁹
- *In vivo* (mouse) efficacy with direct AMPK activation (salsalate)¹⁰



Normal Kidney

Polycystic Kidney

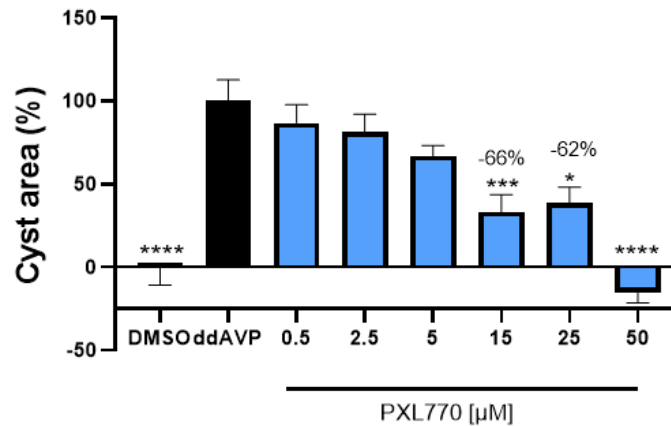
1. *Am J Physiol Renal Physiol* 309: F414-, 2015; *J Clin Invest* 123: 4888-, 2013
2. *Nat Rev Nephrol* 14: 678-687, 2018; *Nat Rev Nephrol* 15: 735- 749, 2019
3. *Front Med* 2022 doi: 10.3389/fmed.2022.753418
4. *CJASN* 2020 doi: 10.2215/CJN.13291019
5. *J Am Soc Nephrol* 27:1437- 1447, 2016
6. *Nature* 493: 346-55, 2013; *Cell* 178:1102-14, 2019
7. *Nephrol Dial Trans* 21:598-604, 2006. *PNAS* 108: 2462-2467, 2011; *J Clin Invest* 105:1711-1721, 2000
8. *HepatoL Commun*, 2022. 6: 101-119.
9. *J Clin Invest* 108:1167-74, 2001; *PNAS* 108: 2462-2467, 2011; *Sci Rep* 7: 7161, 2017; *Am J Renal Physiol* 322: F27-, 2022
10. *EBioMedicine* 47:436-445, 2019

PXL770 Opportunity in ADPKD

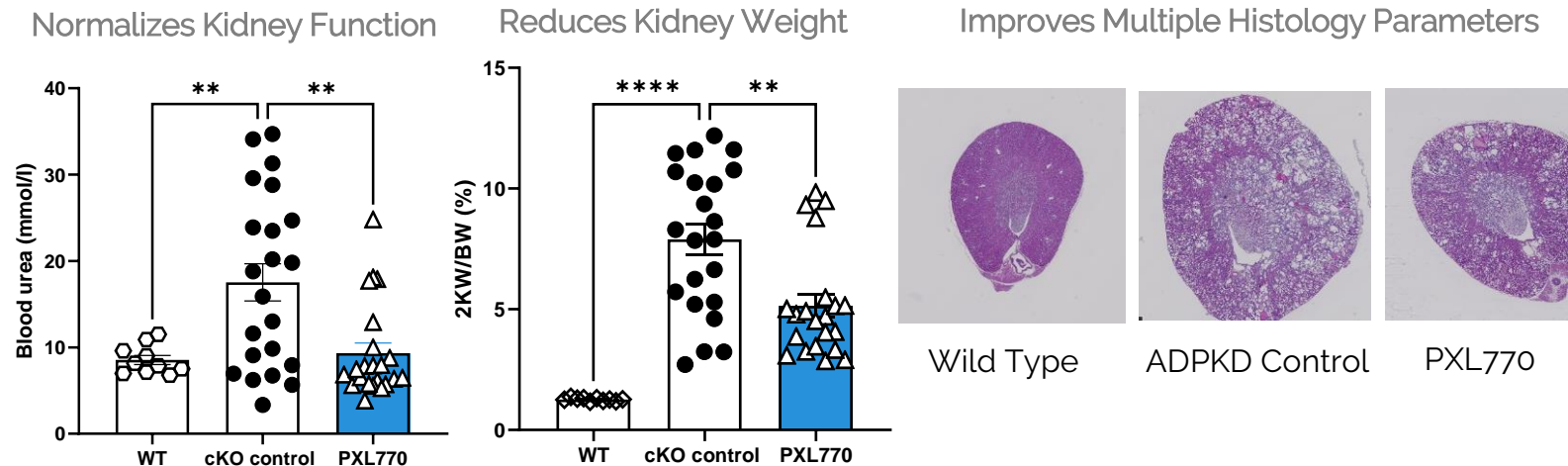
Phase 2-Ready Asset with Orphan Drug Designation

- Robust efficacy profile with target engagement in established ADPKD model systems:
 - reduced cyst growth in human and canine assays
 - in inducible kidney epithelium-specific Pkd1 knockout mouse: normalized kidney function (urea), improved kidney weight (2KW/BW) and histology – immunohistochemistry (cyst index, proliferation, inflammation, fibrosis)
- Additional efficacy also demonstrated in diabetic kidney disease model

Reduced Human Cyst Growth



Efficacy Profile in ADPKD Mouse Model (62 Days)



Preclinical Results Now Published - <https://doi.org/10.1016/j.kint.2023.01.026>
Development Program Prepared - Regulatory Interactions Ongoing

Clinical Update

PXLo65 in NASH, results of Phase 2
NASH Trial (DESTINY-1)

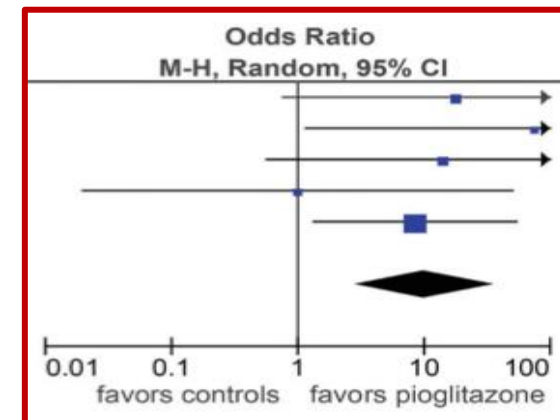
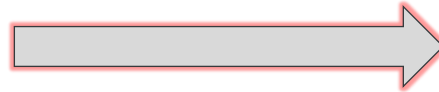


Pioglitazone Extensively Studied and Effective in NASH

Recommended Use by AASLD-EASL - not Prescribed due to Common AE's

	Study	N	Duration	Improvements in NASH			
				ALT/AST	Steatosis	Inflammation	Fibrosis
6 Biopsy Trials	Promrat 2004 ¹	18	48 wks	✓	✓	✓	✓
	Belfort 2006 ² , Gastaldelli 2021 ³	55	6 mos	✓	✓	✓	✓
	Aithal 2008 ⁴	74	12 mos	✓			✓
	Sanyal 2010 ⁵ (PIVENS)	247	96 wks	✓	✓	✓	
	Cusi 2016 ⁶	101	18 mos		✓	✓	✓
	Huang 2021 ⁷	90	24 wks	✓	✓	✓	
	<i>Meta-analysis</i> (Musso 2017 ⁸)	392	6-24 mos	-	-	-	✓
	<i>Meta-analysis</i> (Boettcher 2012 ⁹)	271	6-24 mos	-	✓	✓	✓

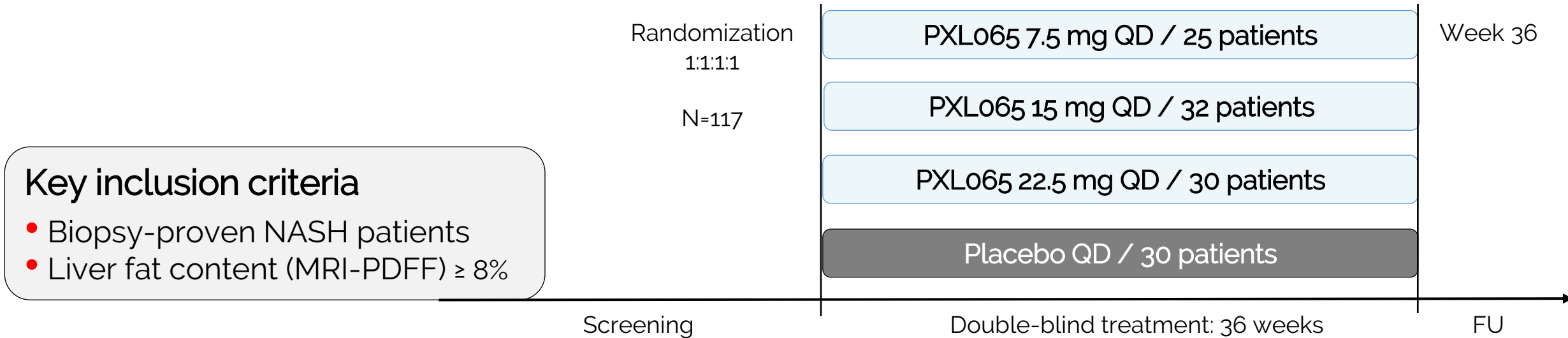
- Fibrosis meta-analysis⁷: OR for improvement in advanced (F3-F4) fibrosis in NASH patients
- Network *meta-analysis* of 48 NASH trials (data through 2019) - pioglitazone is a highly effective therapeutic agent¹⁰



1. Promrat 2004 - Hepatology 39: 188-196. 2. Belfort 2006 - N Engl J Med 355: 2297-2307 3. Gastaldelli A 2021 Liver Internatl DOI: 10.1111/liv.15005; 4. Aithal 2008 - Gastroenterology 135: 1176-1184 5. Sanyal 2010 - NEJM 362, 1675-1685 (post hoc analysis of in Therapeutic Advances in Gastroenterology 2011, 4, 249-263) 6. Cusi 2016 - Ann Intern Med. 165, 305-315 (also Resolution of NASH). 7. Huang J-F 2021 Hepatol Internatl doi/10.1007/s12072-021-10242-2 (also Resolution of NASH) 8. Musso 2017 - Hepatology 2017, epub. (efficacy in advanced fibrosis). 9. Boettcher 2012 - Aliment Pharmacol Ther 35, 66-75 (includes reanalysis of PIVENS data) 10. Panunzi S 2021 Diabetes Obes Metab doi/10.1111/dom.14304

PXL065 Phase 2 Trial Design:

Single Streamlined Study - 505(b)(2) Pathway



Key inclusion criteria

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

Primary Endpoint

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

Secondary Endpoints

- Liver histology
- Non-invasive NASH-related tests
- Metabolic parameters
- Safety, PK

Regulatory Requirements for Phase 3:

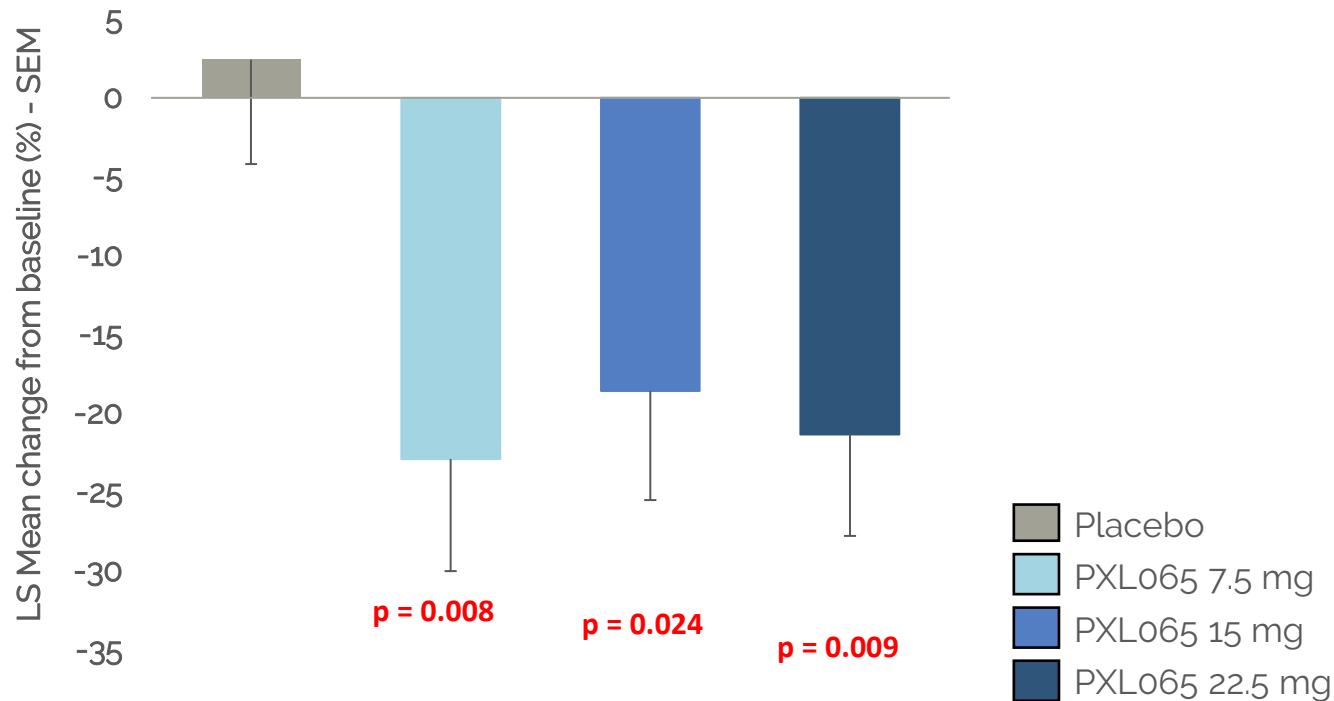
- FDA accepts 1 of 2 endpoints for Phase 3 registrational trials: (1) Fibrosis improvement \geq 1 stage & no worsening of NASH or (2) NASH resolution & no worsening of fibrosis¹
- EMA requires BOTH endpoints to be met for marketing approval²

Relative Change in LFC (%) from Baseline to Week 36

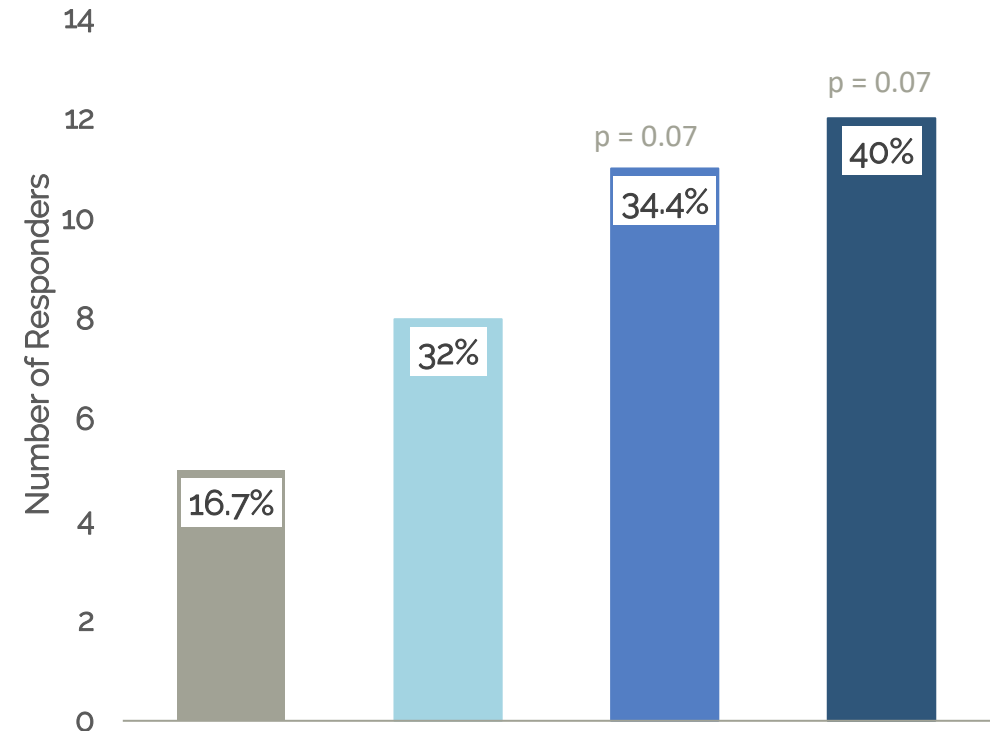
Primary Efficacy Endpoint - Primary Analysis - ITT Set



Relative Change in LFC (%) from Baseline to Week 36¹



Relative Reduction in LFC (%) ≥ 30% from Baseline to Week 36²



Improvement (21-25% vs. placebo) in LFC (primary endpoint) achieved in all PXL065 groups

¹ ANCOVA model adjusting for treatment and for randomization stratification factors and baseline LFC as a continuous covariate.

² Cochran-Mantel-Haenszel test stratified according to T2DM status and NASH CRN fibrosis scoring system. P-value obtained from Cochran-Mantel-Haenszel test of general association. Missing Week 36 assessments were imputed using a multivariate imputation approach by fully conditional specification regression method assuming missing at random mechanism. Results were combined across imputed sets of data using Rubin's rule.

p-values shown for comparisons versus placebo.

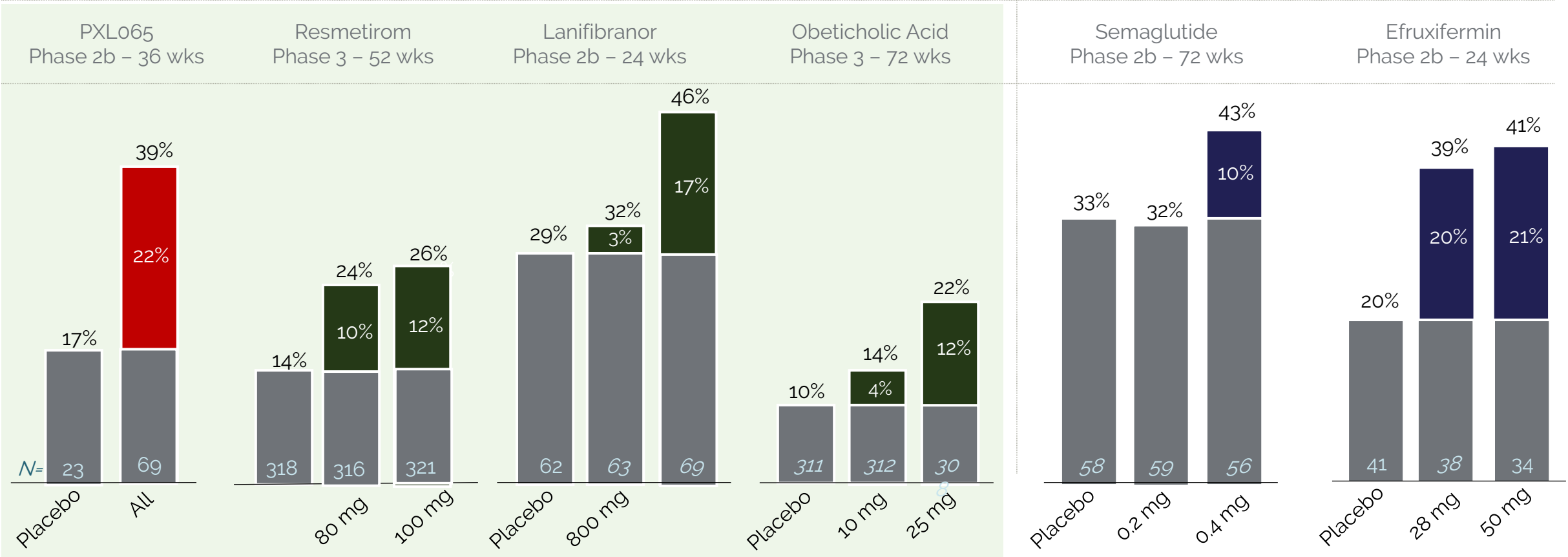
PXL065 Fibrosis Response Compared to Other Candidates

≥1 Stage Fibrosis Improvement with no Worsening of NASH (FDA Approval Endpoint)



Orals

Injectables



Effect on fibrosis well positioned compared to competitors



Safety Summary



- Good safety-tolerability
- No dose dependent weight gain
- No increase in edema
- **Summary of Treatment Emergent Adverse Events (TEAEs)**
 - No relevant difference in the incidence of subjects presenting with TEAE (60 to 80%), mainly from grade 1 or grade 2 severity
 - Low incidence in subjects presenting with related TEAE (12 to 27%)
 - One death (placebo); only one TEAE leading to discontinuation at the dose of 22.5 mg*
 - Similar incidence in Serious TEAE (3 to 9%) , all considered non-related to the drug (no SUSAR)
- **No other AE of specific interest**
 - Except one case of increase liver enzyme in the placebo group

Results Published in Journal of Hepatology

Nature Review: "Safer pioglitazone alternative is effective"

Browser tabs: Evaluation of PXL065 – Deuterium

Address bar: [https://www.journal-of-hepatology.eu/article/S0168-8278\(23\)00091-0/fulltext](https://www.journal-of-hepatology.eu/article/S0168-8278(23)00091-0/fulltext)

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NASH Patients: a Phase 2 randomized placebo-controlled trial (DESTINY-1)

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[Open Access](#) • Published: February 17, 2023 • DOI: <https://doi.org/10.1016/j.jhep.2023.02.004>

- Highlights
- Abstract
- Graphical abstract
- Keywords
- Impact and implications
- Introduction
- Patients

Highlights

- Pioglitazone is used in NASH but has side effects
- PXL065 is a novel stabilized R-Pioglitazone enantiomer which lacks PPAR γ activity
- PXL065 reduced liver fat; improved - non-invasive tests, histology, glycemia-insulin sensitivity
- PXL065 reduced potential PPAR γ -driven side effects of weight gain and oedema
- PXL065 is a new oral approach to NASH which merits further study in a pivotal trial

Abstract

Research highlights

NASH

Safer pioglitazone alternative is effective

A deuterium-stabilized enantiomer of pioglitazone known as PXL065 has greater clinical potential than pioglitazone itself for the treatment of nonalcoholic steatohepatitis (NASH), results of a phase II trial suggest. Previous evidence indicates that pioglitazone is effective in NASH but has adverse effects owing to its activation of peroxisome proliferator-activated receptor- γ (PPAR γ). The placebo-controlled trial of PXL065 indicated that it has a similar efficacy profile to pioglitazone, but this molecule does not activate PPAR γ so is potentially safer. The investigators conclude that a pivotal clinical trial of PXL065 is justified.

Ian Fyfe

Original article: Harrison, S. A. et al. Evaluation of PXL065 – deuterium-stabilized (R)-pioglitazone in NASH patients: a phase 2 randomized placebo-controlled trial (DESTINY-1). *J. Hepatol.* <https://doi.org/10.1016/j.jhep.2023.02.004> (2023)

Phase 2 PXL065 Summary & Next Steps



- Primary efficacy endpoint met
- Strong improvement in fibrosis observed (FDA approval endpoint) - effect size as good or better than leading competitors' results
 - PXL065 has potential for better fibrosis benefit than Resmetirom (Phase 2 vs Phase 3 data), which remains the key unmet need in NASH
- Metabolic benefits – significant HbA1c and insulin sensitivity effect
- Safe and well tolerated without PPAR γ – driven AE's
- PXL065 is a differentiated NASH development candidate
 - Results confirm potential to retain beneficial hepatic and metabolic effects of pioglitazone with reduced PPAR γ -driven side effects; consistent PK profile
 - Strong potential of PXL065 in combination with Resmetirom as the MOA's and profiles are highly complementary (NASH resolution / Fibrosis and Glycemic plus Lipid benefits)

- ✓ Phase 2 results oral presentation at AASLD (Nov 2022)
- ✓ Publication in Journal of Hepatology (Feb 2023)
- ✓ Ongoing discussions with potential partners for a pivotal program in NASH

NEXT STEPS

- Regulatory interactions leading to end of Phase 2 meeting

Conclusion

Summary & Upcoming milestones



Summary Highlights

- **TWYMEEG in Japan – strong growth trajectory confirmed**
 - Sales grew 90% over prior quarter; Sumitomo FY2022 forecast increased 20%
 - Confidence in increasing royalties facilitated debt restructuring
- **Significant extension of our cash runway through Q2 2025**
 - Based upon debt restructuring and new equity-linked financing facility, assuming full drawdown
 - Pursuing additional financing initiatives, including ongoing active partnership discussions, to launch ALD
- **Building the value of our assets, focus on rare diseases and NASH**
 - **ALD:** Phase 2 POC for PXL770 & PXL065 to start subject to financing
 - Orphan Drug & Fast Track Designations
 - **ADPKD:** PXL770 is Phase 2 ready program
 - Orphan Drug
 - **PXL065: NASH Positive Phase 2 results**
 - New PXL065 US patent provides additional protection through 2041

Strategic Focus on NASH and Rare Diseases

Targeting Indications with High Unmet Needs - Differentiated Molecules Can Make The Difference

Next steps

NASH

- PXL065 prioritized to advance in NASH as a partnered program
 - Discussions for a potential pivotal program in NASH initiated

RARE DISEASES

- PXL770 development focus on rare diseases:
 - Subject to additional financing, launch of a Phase 2a biomarker POC clinical trial in ALD
 - Potential to advance PXL770 into Phase 2 for ADPKD; significant opportunity addressing underlying pathology
- D-TZD platform potential in rare diseases to be assessed
 - through Phase 2a biomarker POC clinical trial in AMN-ALD with PXL065



Question & Answer Session

Participants can submit questions in the chat

