



Half Year 2022 Financial and Corporate Update

September 21, 2022



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.

Agenda

- **Recent developments and Corporate highlights**

- Thomas Kuhn, CEO



- **H1 2022 Financials**

- Anne Renevot, EVP, CFO



- **Clinical Update in Rare Diseases & Focus on PXL065 Phase 2 DESTINY-1 results**

- Pascale Fouqueray, MD, PhD, EVP, Clinical Development & Regulatory Affairs

- Vlad Ratziu, Prof. of Hepatology at Sorbonne Université and Pitié-Salpêtrière Hospital



- **Conclusions** - Thomas Kuhn, CEO



Poxel Recent Strategic Developments



- **Positive results from Phase 2 NASH Trial (DESTINY-1) for PXL065**
 - Primary efficacy endpoint met: statistically significant improvements in the relative decrease in liver fat content at 36-weeks for all doses.
 - PXL065 was observed to be safe and well tolerated with no dose-dependent increase in body weight and low incidence of edema, similar to placebo.
 - Consistent histology findings: strong improvement in fibrosis observed – effect size comparable to best competitors results; improvement seen in other NASH histology components.
- **Confirmation of strategic focus on NASH and rare metabolic indications**
 - PXL065 will be prioritized for further development in NASH. Discussions for a potential pivotal program in NASH will be initiated.
 - PXL770 development will exclusively focus on rare diseases based on stronger potential in multiple rare metabolic indications.
 - Validated hypothesis: d-TZD platform reduces PPAR γ side-effects while retaining efficacy benefits, and warrants exploration in other rare diseases, such as ALD.

Year to date 2022 Highlights

- **Strengthening the value of PXL065 and PXL770**
 - PXL065: New US patent provides additional protection through 2041 and could expand protection worldwide, with the potential for an additional 5 years through patent term extension
 - PXL065 & PXL770: FDA Fast Track and Orphan Drug Designations in ALD attained
 - PXL770: Phase 2 ready in polycystic kidney disease (ADPKD) with strong preclinical data.
- **Debt restructuring agreement with IPF Partners (IPF) and equity-linked financing facility with Iris Capital Investment (IRIS):**
 - Cash runway extended through at least February 2023
 - Cash & cash equivalents: EUR 16.1 million (USD 16.8 million) as of 6/30/2022
- **TWYMEEG® (Imeglimin) royalties progressing in Japan**
 - As of Sept 1, 2022, first year prescribing restrictions lifted
 - Considering selected regional partnerships outside Sumitomo Pharma territories

Robust Mid-to-Late Stage Metabolic Pipeline

Focus on Rare Metabolic Diseases and NASH

	Indication	MOA	Discovery/ PC	PH 1	PH 2	PH 3	Approved/ Marketed	Upcoming Milestones	
NASH									
PXL065	NASH	Non-Genomic TZD ¹	[Progress bar: Discovery/PC to PH 2]						<ul style="list-style-type: none"> Positive Phase 2; Initiation of discussions for a potential pivotal program in NASH; leveraging 505(b)(2) pathway
Rare Metabolic Indications									
PXL770	ALD ³	AMPK Activator ²	[Progress bar: Discovery/PC to PH 1]						<ul style="list-style-type: none"> Fast Track and Orphan Drug Designations granted in 2022 Initiate Phase 2a as soon as possible⁷
PXL770	ADPKD ⁴	AMPK Activator ²	[Progress bar: Discovery/PC to PH 1]						<ul style="list-style-type: none"> Completed preclinical; Phase 2 ready, developing clinical strategy
Next-Gen D-TZD (PXL065)	ALD ³	Non-Genomic TZD	[Progress bar: Discovery/PC to PH 1]						<ul style="list-style-type: none"> Fast Track and Orphan Drug Designations granted in 2022 Initiate Phase 2a as soon as possible⁷
Type 2 Diabetes (T2D)									
TWYMEEG® Japan / Asia ⁵ Sumitomo Pharma	T2D	MRC ⁶ Modulator	[Progress bar: Discovery/PC to PH 2]						<ul style="list-style-type: none"> TWYMEEG approved for T2D in Japan in 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: Discovery/PC to PH 2]						<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
 7. Subject to additional financing.

Financial Update

First Half 2022



H1 2022 Revenue*

Mainly reflecting royalty revenue from Sumitomo Pharma

<i>EUR (in thousands)</i>	H1 2021 6 months	H1 2022 6 months
Sumitomo Pharma Agreement	13,274	83
Other	-	-
Total revenues	13,274	83

- Revenue for the first half of 2022 reflects JPY 11 million (EUR 81 thousand) of **royalty revenue** from Sumitomo Pharma which represents 8% of TWYMEEG net sales in Japan

Statement of Comprehensive Income as of June 30, 2022*

<i>EUR (in thousands)</i>	June 30, 2021 Adjusted**	June 30, 2022
Revenue	13,274	83
Cost of sales		(83)
Gross margin	13,274	
Research and development expenses	(16,243)	(8,818)
Tax credit & subsidies	1,570	936
General and administrative	(5,434)	(4,295)
Operating profit	(6,851)	12,178
Financial income/(expenses)	(1,465)	(1,383)
Foreign exchange gains/(losses)	287	160
Profit before tax	-8,011	(13,401)
Income tax	-	-
Net income	-8,011	(13,401)

Reflects JPY 11 million (EUR 81 thousand) 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.

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

Includes interest on IPF debt.

Statements of Financial Position as of June 30, 2022*

Assets

<i>EUR (in thousands)</i>	December 31, 2021	June 30, 2022
Intangible assets	16,631	16,615
Property, plant and equipment	1,716	1,572
Other non-current financial assets	206	143
Total non-current assets	18,552	18,330
Trade receivables and related accounts	50	51
Other receivables	3,999	4,501
Cash and cash equivalents	32,287	16,143
Total current assets	36,337	20,694
Total assets	54,889	39,024

Mostly reflects DeuteRx portfolio acquisition in 2018

Statements of Financial Position as of June 30, 2022*

Shareholders' Equity and Liabilities

<i>EUR (in thousands)</i>	December 31, 2021	June 30, 2022
Total shareholders' equity	8,206	-3,594
Employee benefits	370	237
Non-current financial liabilities	30,094	26,155
Provisions	318	74
Non-current liabilities	30,782	26,466
Current financial liabilities	5,046	7,842
Derivative liabilities	153	0
Trade payables and related accounts	10,687	8,201
Other current liabilities	15	19
Current liabilities	15,901	16,152
Total liabilities	54,889	39,024

Statements of Cash Flow as of June 30, 2022*

<i>EUR (in thousands)</i>	June 30, 2021 Adjusted**	June 30, 2022
Cash & cash equivalent as of the opening date	40,203	32,287
Cash flows from operating activities	(16,067)	(13,301)
Cash flows from investing activities	10	(70)
Cash flows from financing activities	12,775	(2,774)
Cash & cash equivalent as of the closing date	36,921	16,143

- Interest and repayment of IPF debt.

- Cash runway extended through February 2023 with the IPF debt restructuring and IRIS financing announced in August

Key Financial & Shareholder Information

Market data



Ticker: POXEL

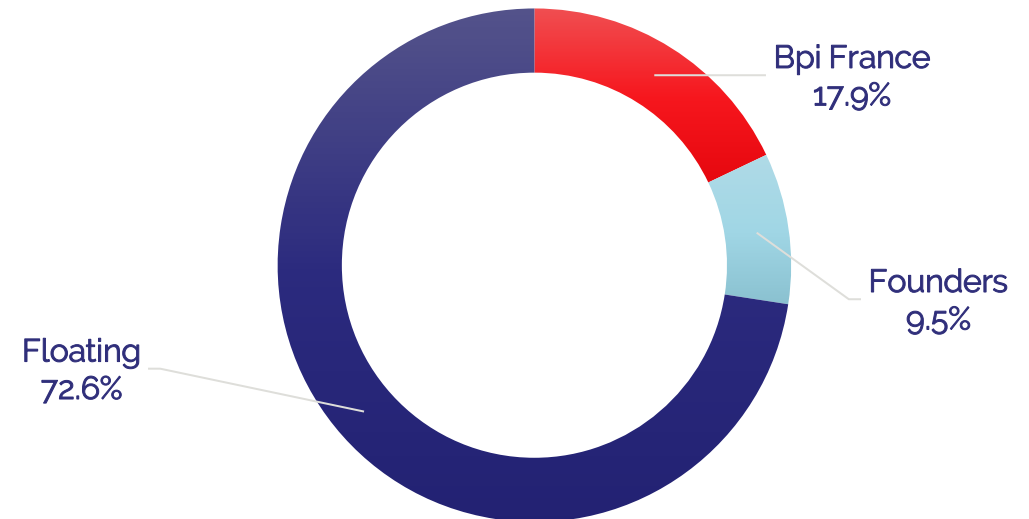
ISIN: FR0012432516

Number of shares: 29 242 251¹

Key financials

- As of 6/30/22 cash & cash equivalents: EUR 16.1 million (USD 16.8 million)

Shareholder ownership²



Analyst coverage

Bryan Garnier	Alex Cogut
Degroof Petercam	David Seynnaeve
Jefferies	Lucy Codrington
JMP Securities	Jason Butler
Oddo	Martial Descoutures

Additional Opportunities in Rare Diseases

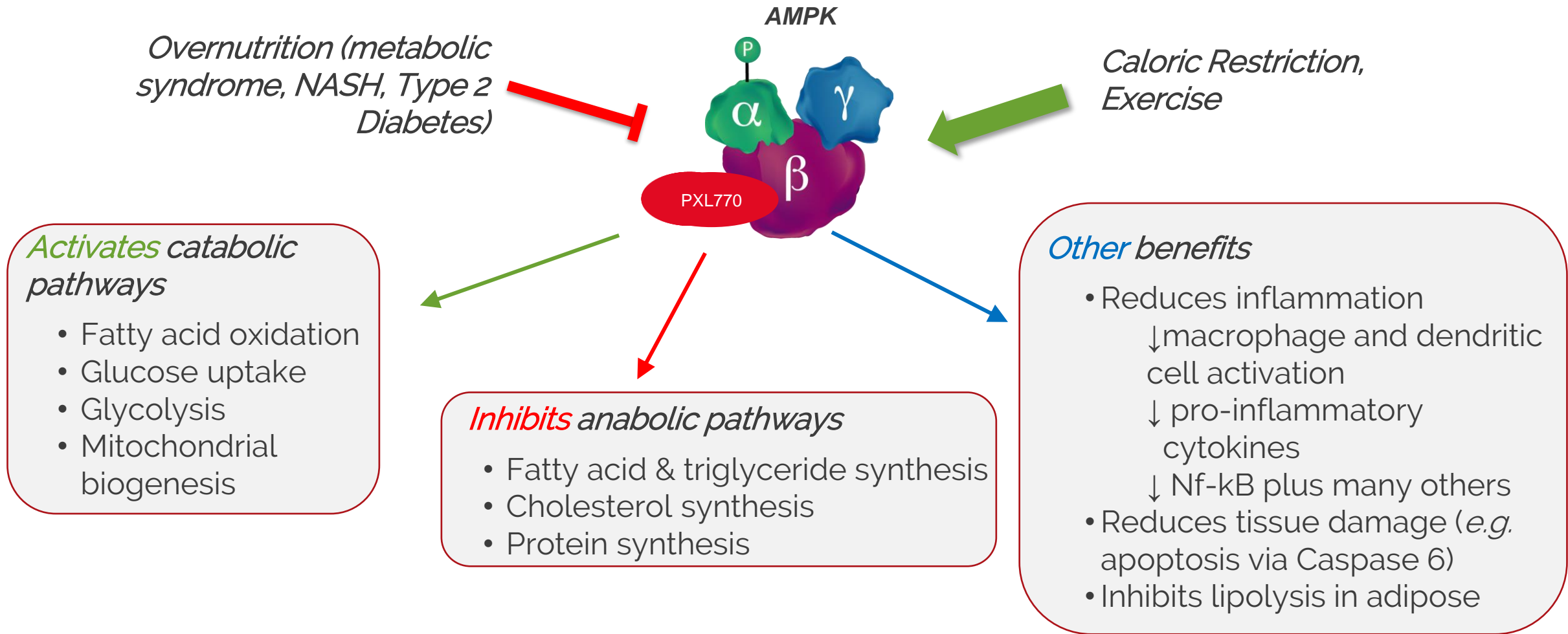
Adrenoleukodystrophy (ALD)

Autosomal Dominant Polycystic
Kidney Disease (ADPKD)



AMP Kinase Activation

PXL770 and Next Generation Molecules

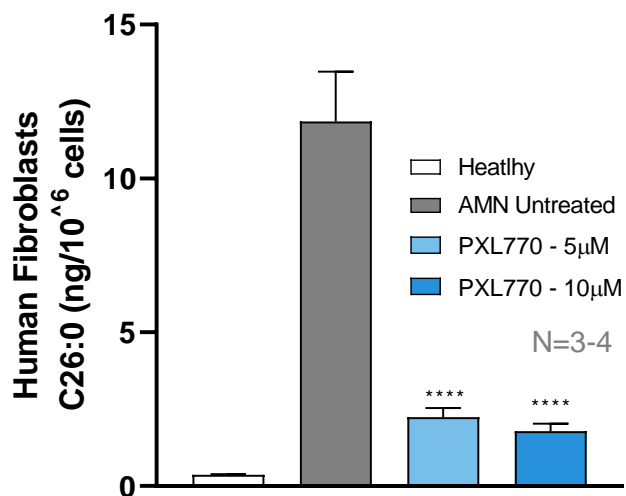


Potential to Target a Broad Range of Diseases with Metabolic Pathophysiology

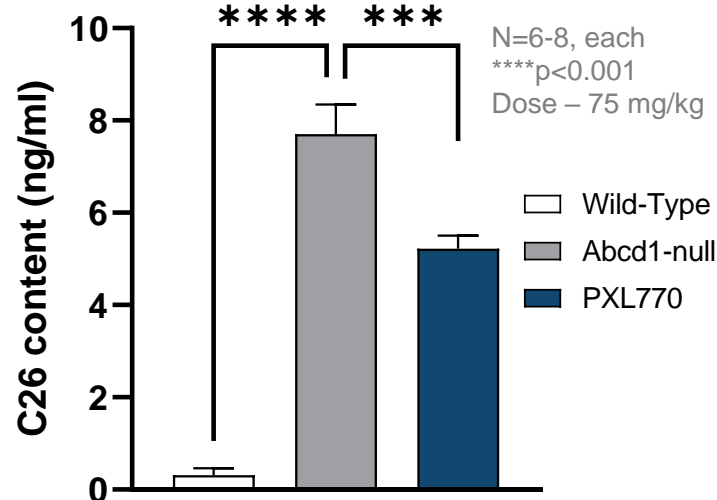
ALD: AMPK Rationale and Strong Preclinical Data

- 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:

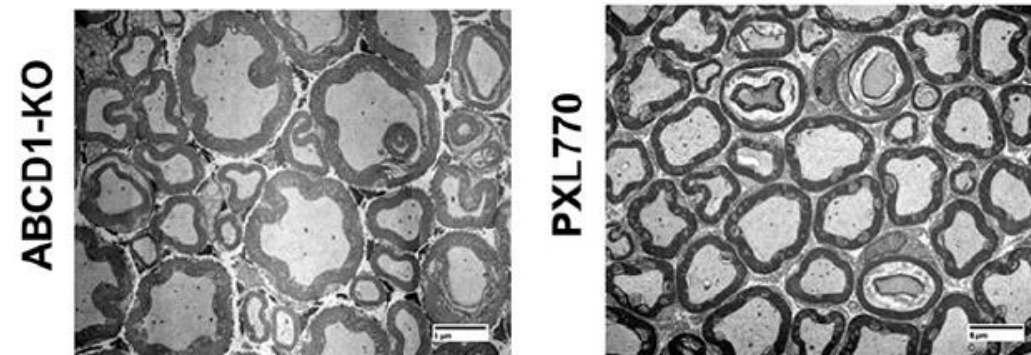
**AMN - Fibroblasts
Suppression of Elevated VLCFA**



**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

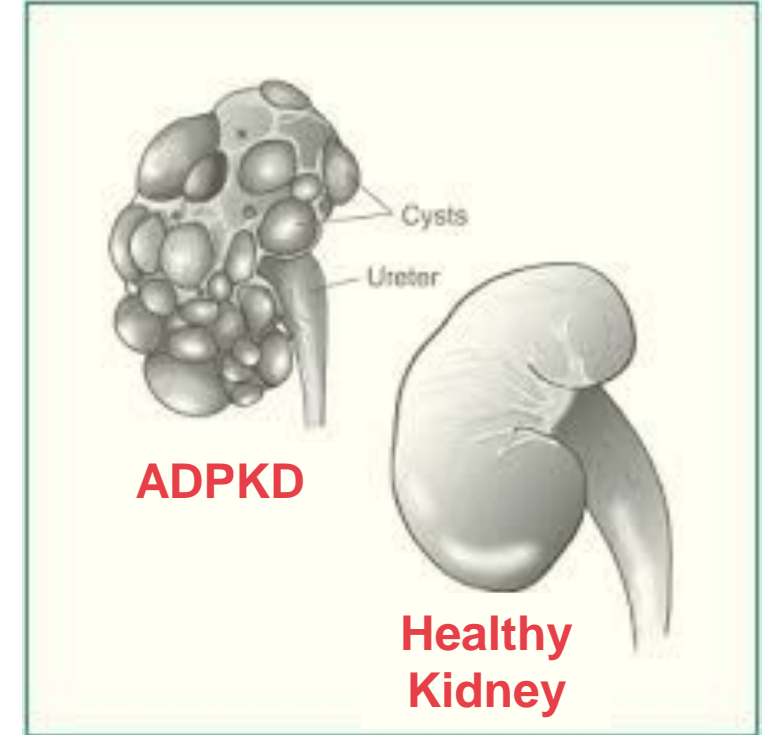
Additional Strong Rationale and Preclinical Efficacy with D-TZD Platform (PXL065)
Phase 2a Studies Planned

ADPKD and AMPK

- 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



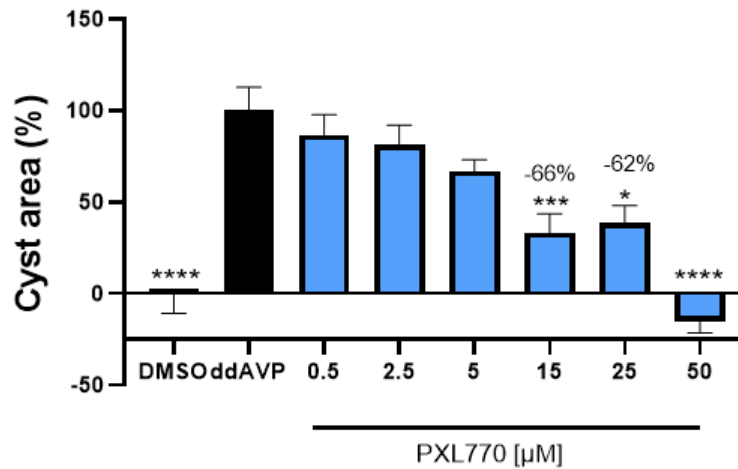
1. *Am J Physiol Renal Physiol* 309: F414-, 2015; *J Clin Invest* 123: 4888-, 2013
2. *Nat Rev Nephrol* 14: 678-687, 2018; *Nat Rev Nephrol* 15: 735- 749, 2019
3. *Front Med* 2022 doi: 10.3389/fmed.2022.753418
4. *CJASN* 2020 doi: 10.2215/CJN.13291019
5. *J Am Soc Nephrol* 27:1437- 1447, 2016
6. *Nature* 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

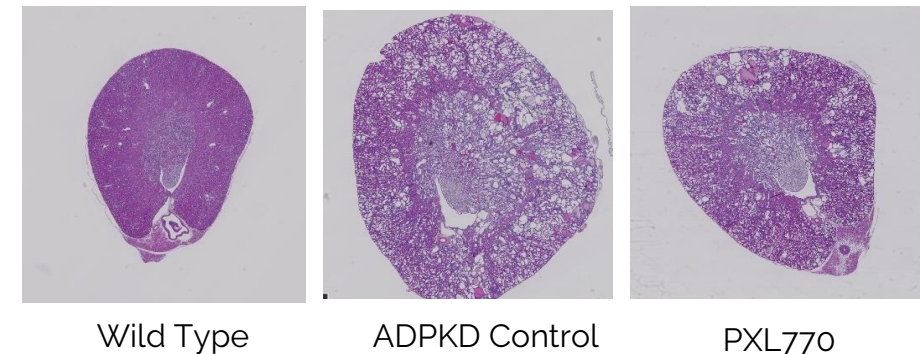
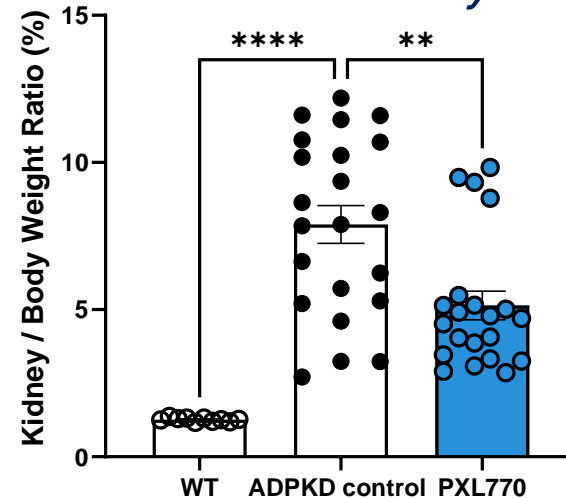
AMPK - Compelling Target; Phase 2-Ready Asset

- Pathophysiology - altered kidney metabolism, activation of growth pathways that AMPK inhibits; AMPK activation shown to attenuate disease in preclinical models¹⁻⁴
- PXL770 - robust efficacy profile in established model systems:

Reduced Human Cyst Formation



Efficacy Profile in ADPKD Mouse Model (62 Day)



Development Program Planning and Regulatory Interactions Ongoing

1. Nat Rev Nephrol 15: 735- 749, 2019
2. J Clin Invest 108:1167-74, 2001
3. PNAS 108: 2462-2467, 2011
4. EBioMedicine 47:436-445, 2019

DESTINY-1 results

Phase 2 NASH Trial for PXL065

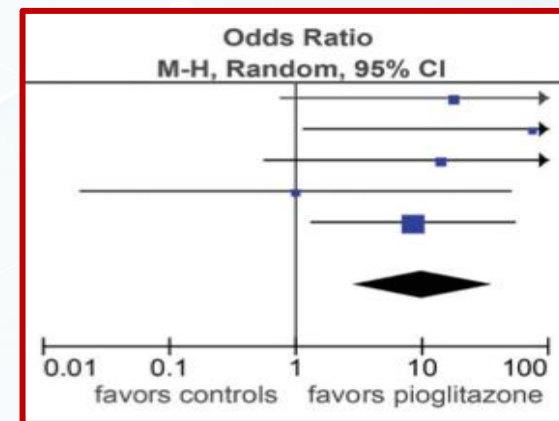
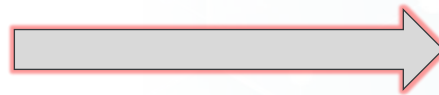


Pioglitazone Extensively Studied and Effective in NASH

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

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

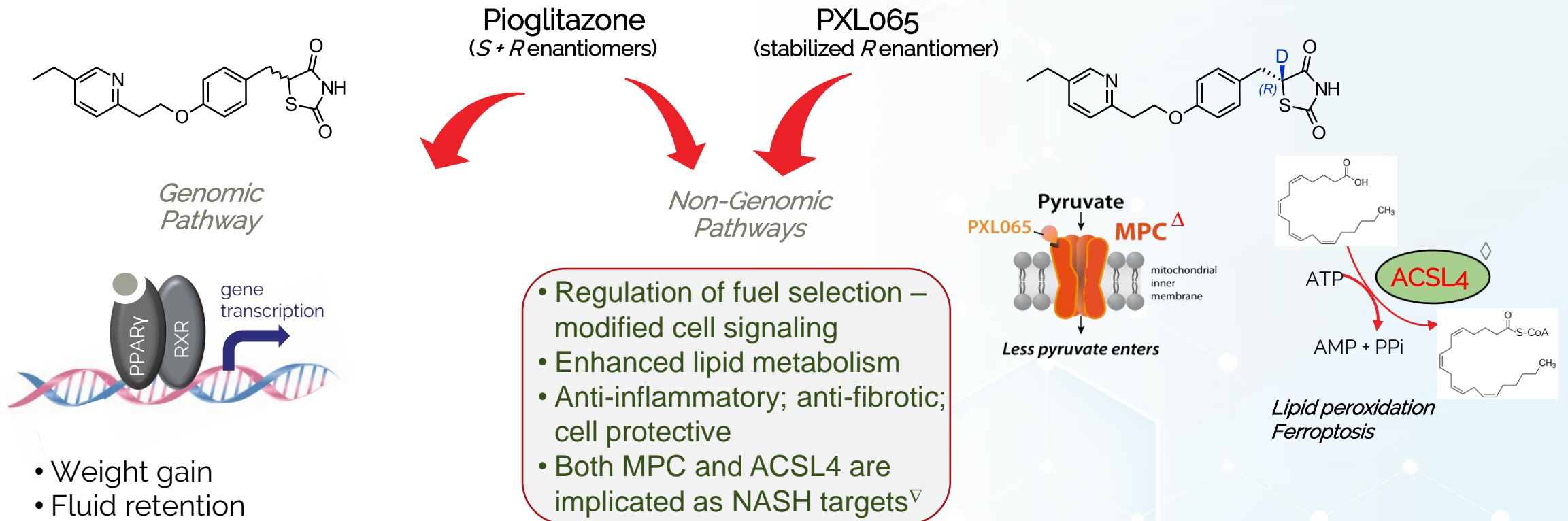
- Fibrosis meta-analysis⁷: OR for improvement in advanced (F3-F4) fibrosis in NASH patients
- Network *meta-analysis* of 48 NASH trials (data through 2019) - pioglitazone was the most effective therapeutic agent⁹



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

PXL065: Oral NCE Derived from Pioglitazone

- Pioglitazone, TZDs*: 2 enantiomers that rapidly interconvert; both genomic (PPAR γ) and non-genomic mechanisms
- PXL065 is deuterium-stabilized single stereoisomer (NCE); selectively mediates non-PPAR γ effects of pioglitazone – retains efficacy in preclinical NASH models with no significant weight gain-fluid retention



∇ Cell Metab 2015; 22:682-94; Hepatology 2017; 65:1543-56; Mol Metab 2017; 6:1468-79; Nat Chem Biol 2017; 13:91-98; Mol Metab 2018; 9:43-56; Diabetes 2007; 56:2759-65; Am J Physiol 2016; 310:G117-27; Cell Death Dis 2019; 10:449; Am J Pathol 2020; 190:68-81; Int J Mol Sci 2019; 20:4968

Phase 2 Trial Design

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



Randomization
1:1:1:1

Key inclusion criteria

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

PXLo65 7.5 mg QD / 30 patients

PXLo65 15 mg QD / 30 patients

PXLo65 22.5 mg QD / 30 patients

Placebo QD / 30 patients

Week 36

Screening

Double-blind treatment: 36 weeks

FU

Primary Endpoint

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

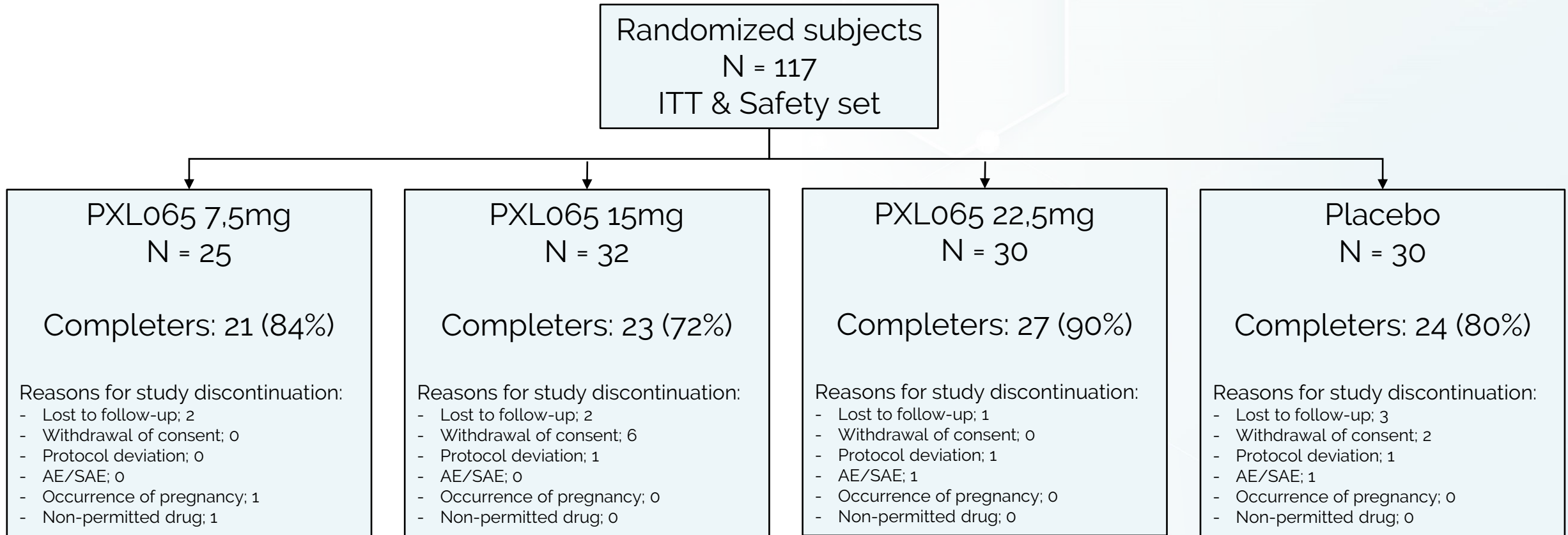
Secondary Endpoints

- 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 >1 stage & no worsening of NASH or (2) NASH resolution and no worsening of fibrosis¹
- EMA requires BOTH endpoints to be met for marketing approval²

Summary of Subject Disposition



Summary of Demographic and Baseline Characteristics

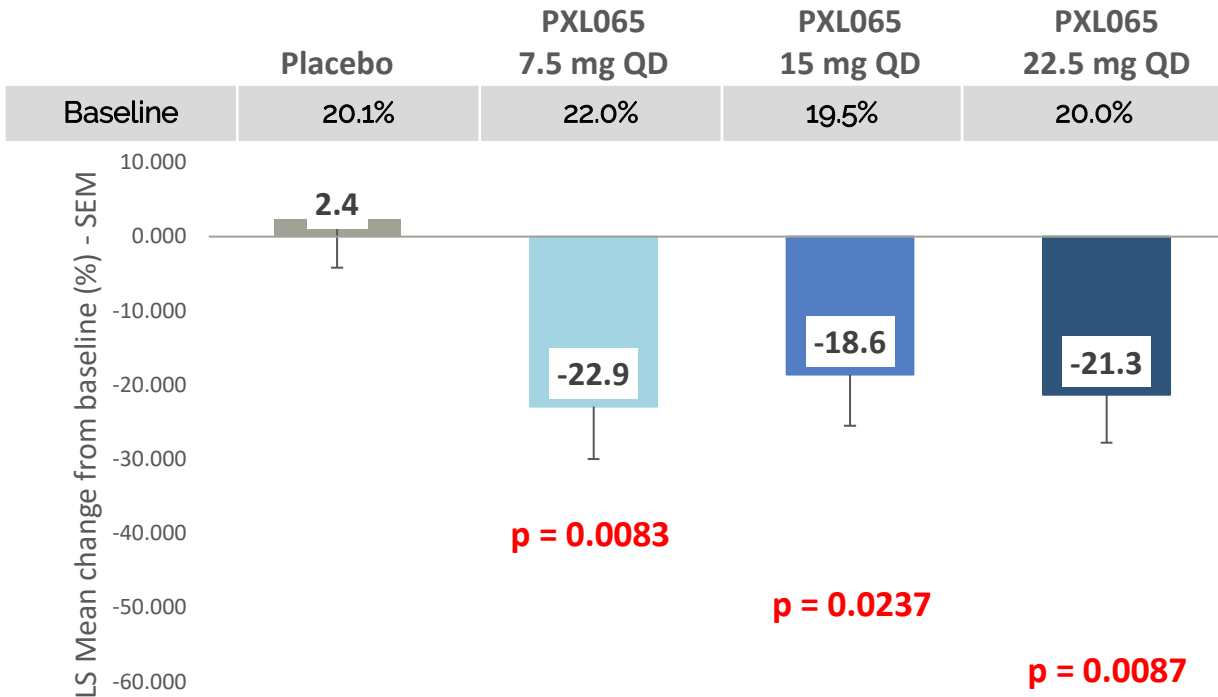
ITT Set

	PXL065 7.5mg QD (N = 25)	PXL065 15mg QD (N = 32)	PXL065 22.5mg QD (N = 30)	Placebo (N = 30)	Overall (N = 117)
Age (years), mean (SD)	50.7 (17.3)	54.1 (10.9)	53.4 (12.4)	54.8 (10.2)	53.4 (12.6)
Ethnicity, n (%)					
Hispanic or latino	11 (44.0)	8 (25.0)	13 (43.3)	9 (30.0)	41 (35.0)
BMI (kg/m ²), mean (SD)	33.9 (5.4)	37.7 (5.9)	36.4 (5.6)	36.1 (7.5)	36.1 (6.2)
NASH CRN score ^[1] , n (%)					
F1	9 (36.0)	11 (34.4)	11 (36.7)	10 (33.3)	41 (35.0)
F2/F3	16 (64.0)	21 (65.6)	19 (63.3)	20 (66.7)	76 (65.0)
LFC (%), mean (SD)	22. (10.5)	19.5 (7.7)	20 (7.0)	20.1 (7.0)	20.3 (8.0)
ALT (U/L), mean (SD)	71.6 (43.3)	58.7 (26.6)	61.0 (29.8)	54.2 (36.4)	60.9 (34.2)
T2DM ^[1] , n (%)					
T2DM Previously treated	10 (40.0) 8 (32.0)	13 (40.6) 11 (43.4)	12 (40.0) 11 (36.7)	13 (43.3) 11 (36.7)	48 (41.0) 41 (35)
HbA1c (%), mean (SD)	6.2 (0.9)	6.1 (0.8)	6.3 (1.1)	6.2 (0.7)	6.2 (0.9)

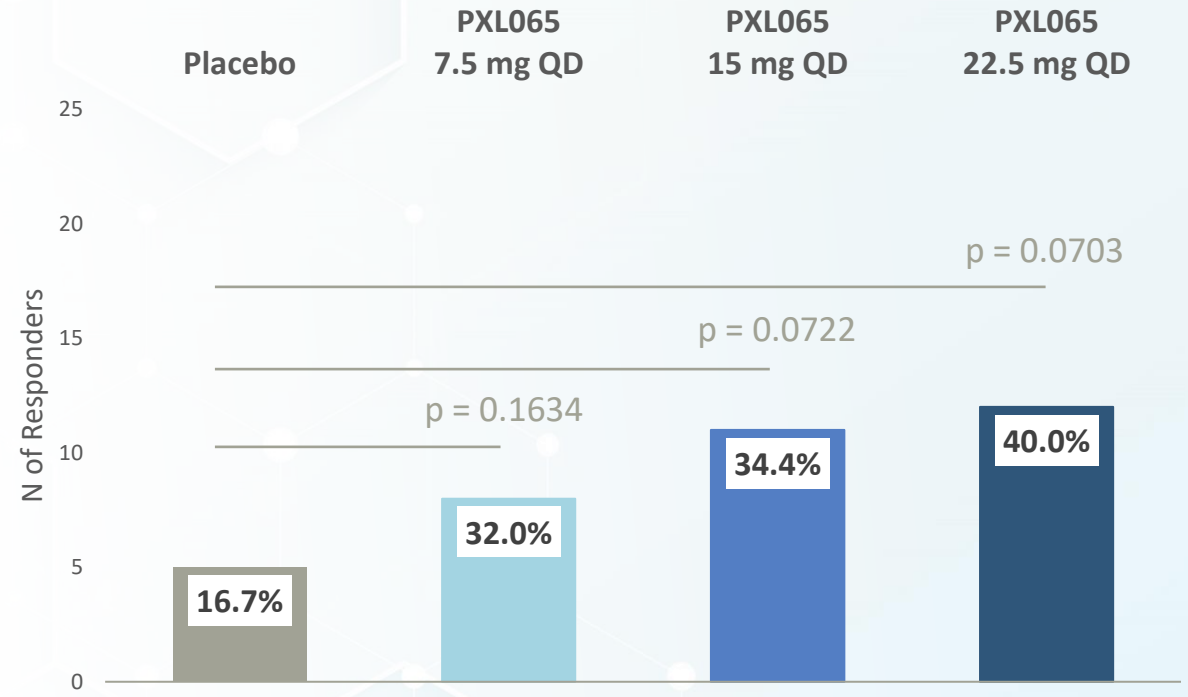
Relative Change in LFC (%) from Baseline to Week 36

Primary Efficacy Endpoint - Primary Analysis - ITT Set

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



Relative Reduction in LFC (%) $\geq 30\%$ from Baseline to Week 36²



Improvement in LFC (primary endpoint) is achieved in all the PXL065 groups

¹ ANCOVA model adjusting for treatment and for randomization stratification factors, i.e. T2DM status and NASH CRN fibrosis scoring system, 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.

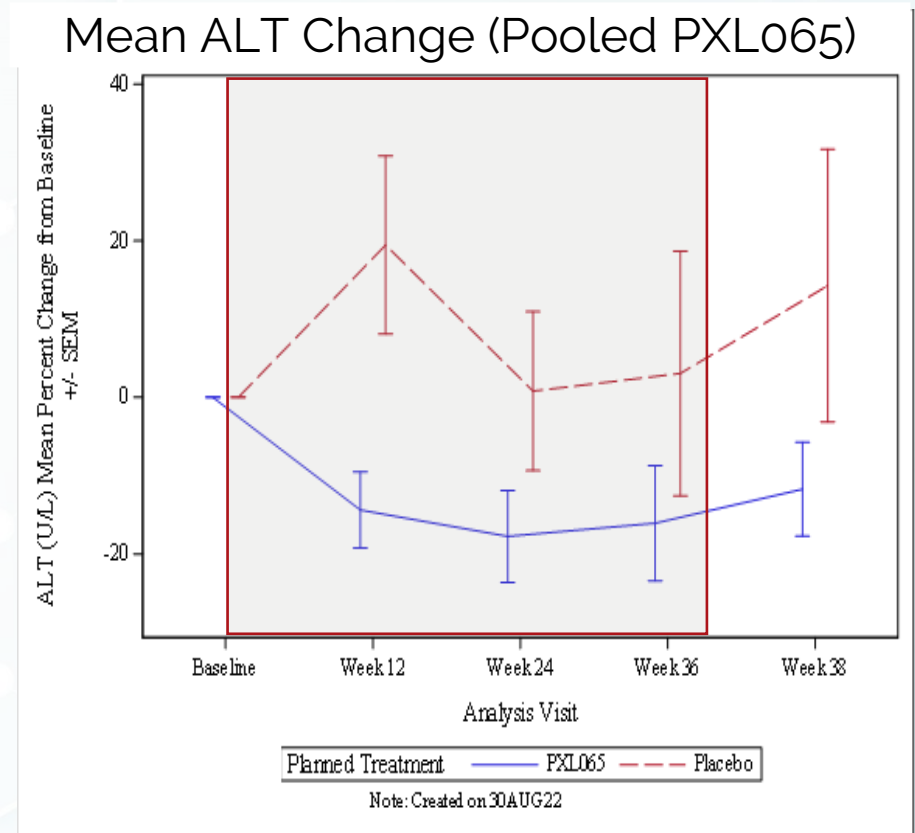
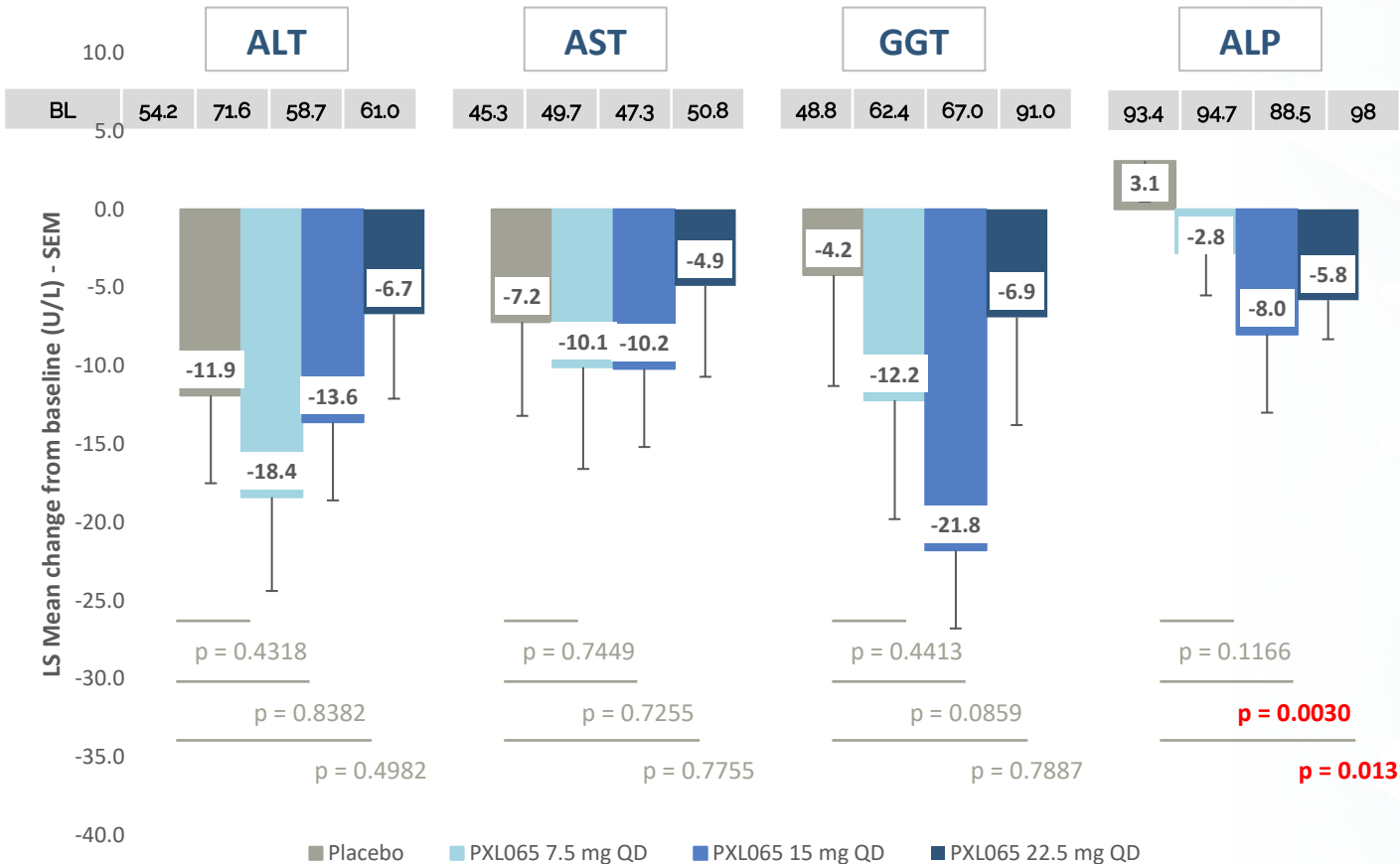
Missing Week 36 assessments were imputed using a multivariate imputation approach by fully conditional specification regression method assuming missing at random mechanism.

Results were combined across imputed sets of data using Rubin's rule.

p-values shown for comparisons versus placebo.

Change from Baseline to Week 36 in Liver Function Tests

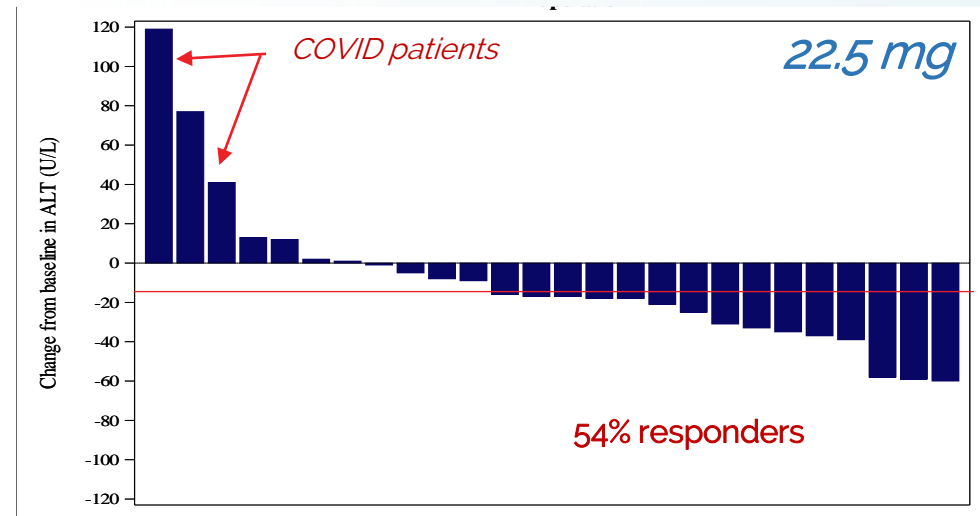
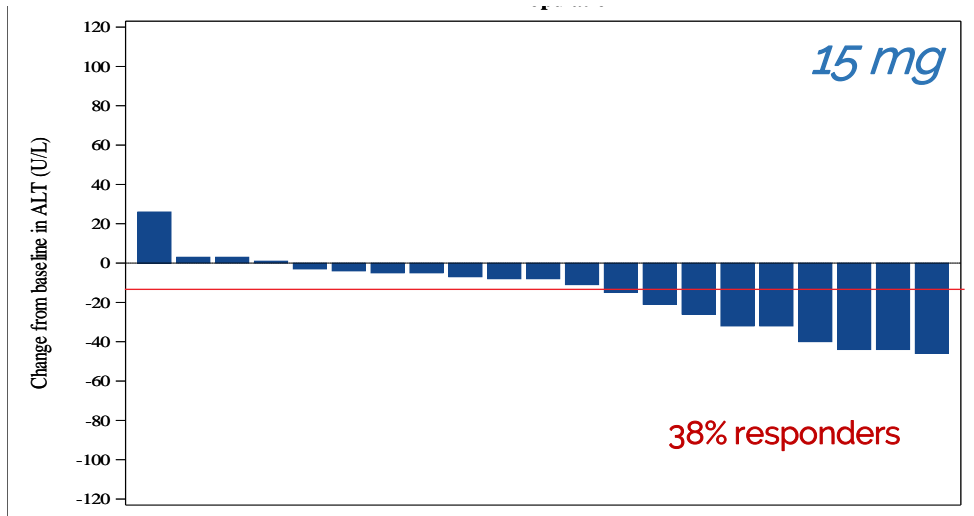
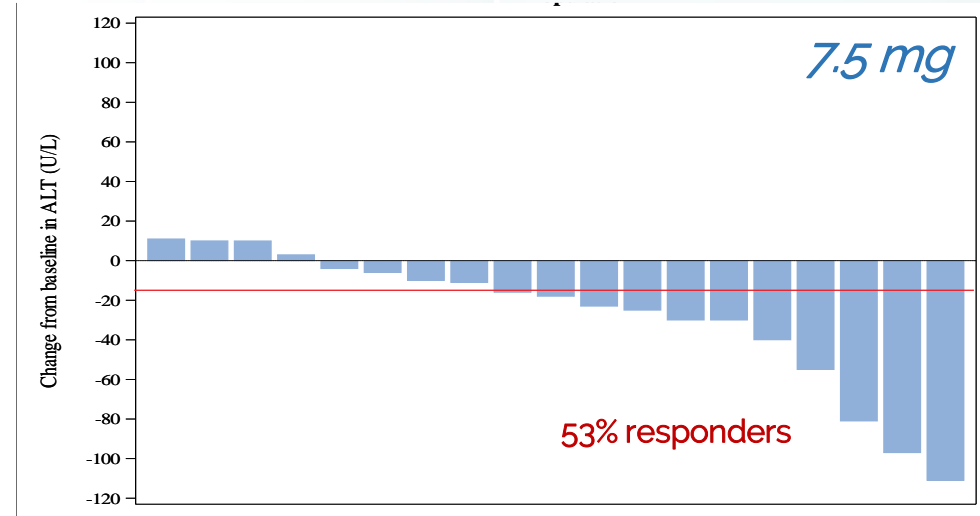
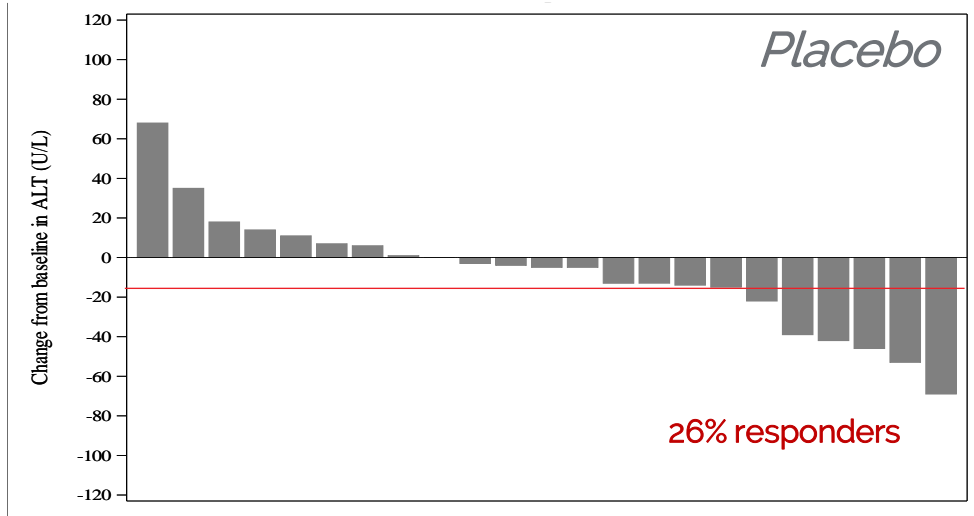
Secondary Efficacy Endpoints – ITT Set



Positive trend in liver enzyme decreases in PXL065 groups
 Strong placebo response and several Covid patients contributed to lesser apparent effects with PXL065 22.5mg

Individual Patient ALT Change from Baseline (IU/L)

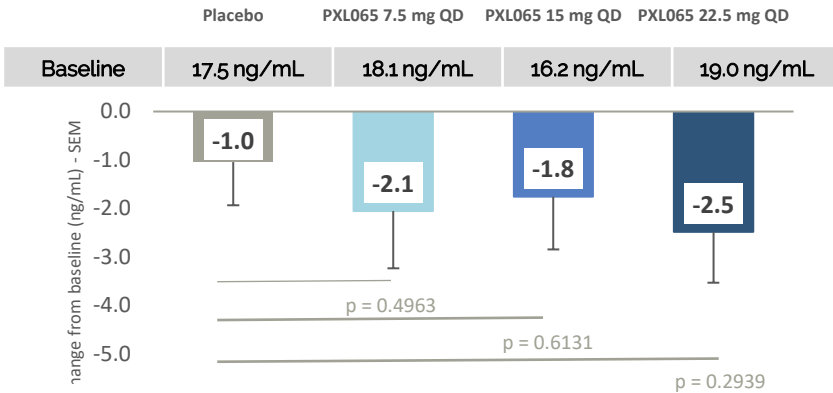
Positive Trends in all PXL065 Dose Groups



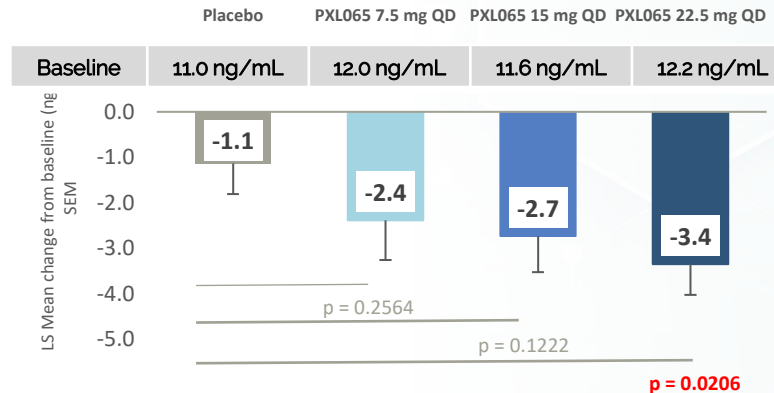
Improved Biomarkers of Fibrogenesis - Fibrosis Risk Scores

Exploratory Efficacy Endpoints - ITT Set

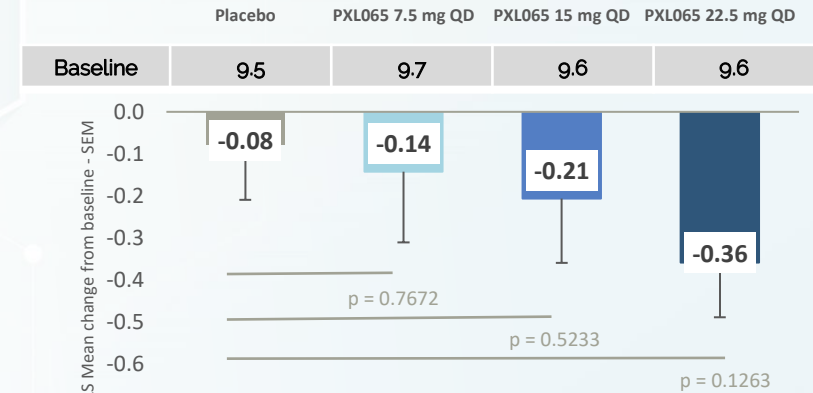
Pro-C3



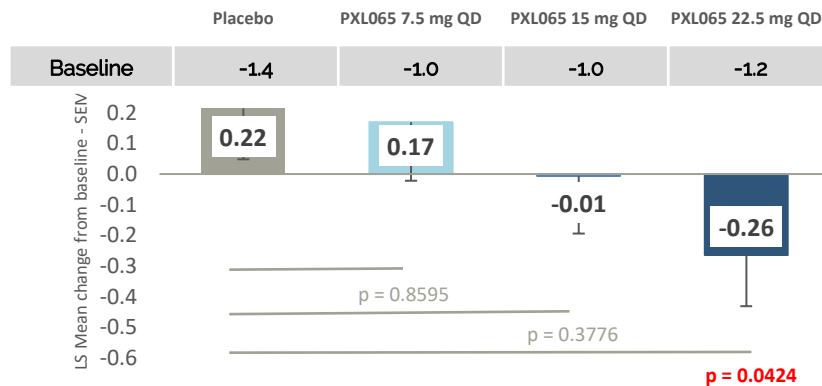
PIIINP



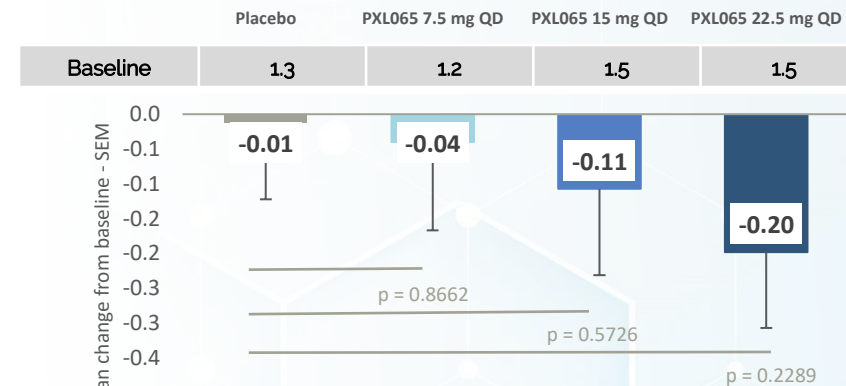
ELF



NFS



Fib-4

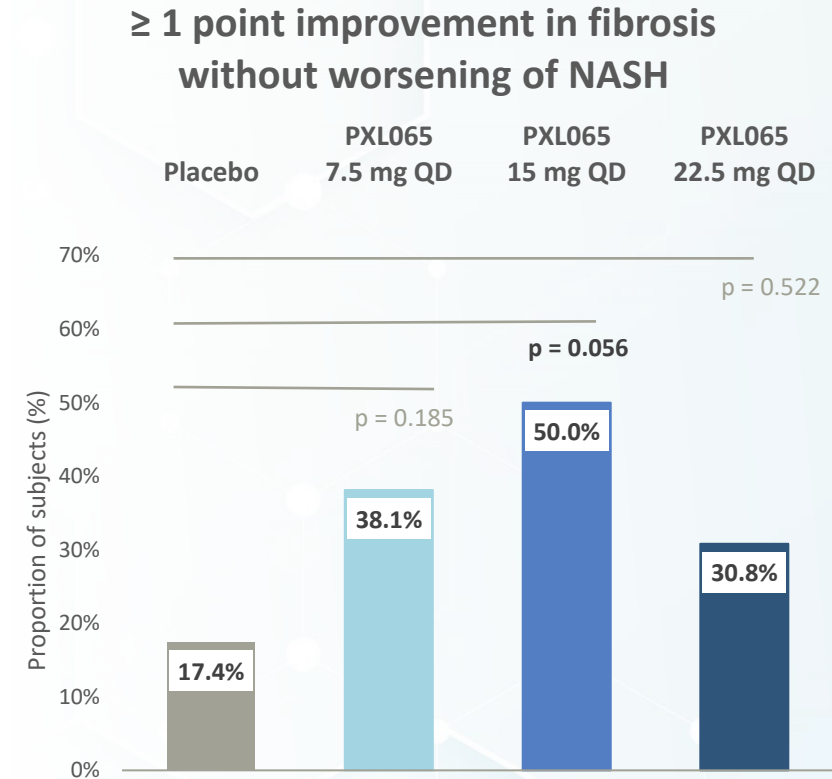
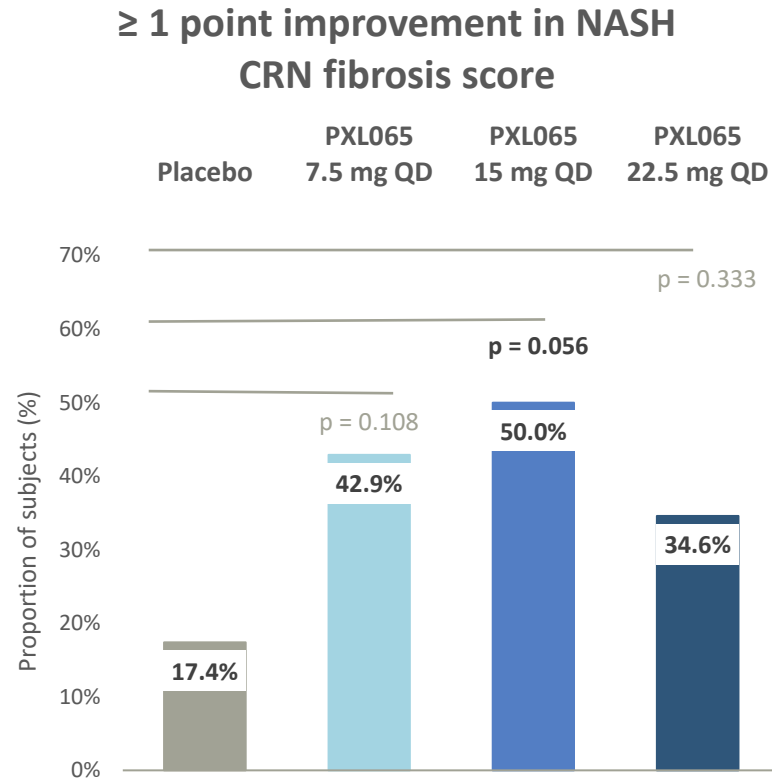


Positive Effects on All Measured Parameters



Responses in Liver Histology – Fibrosis

*Exploratory Efficacy Endpoint– Completers with Biopsy**



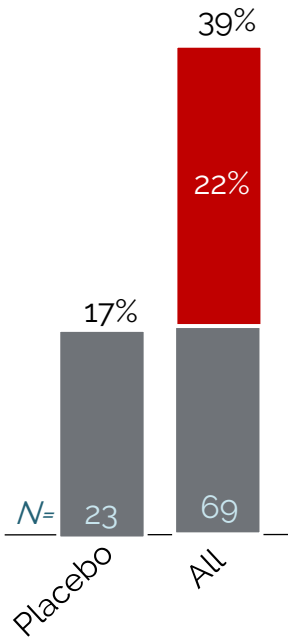
Dose dependent improvement in fibrosis and strong improvement in fibrosis without worsening of NASH achieved with PXL065 (close to significance)

PXL65 Fibrosis Response Comparison to Other Candidates

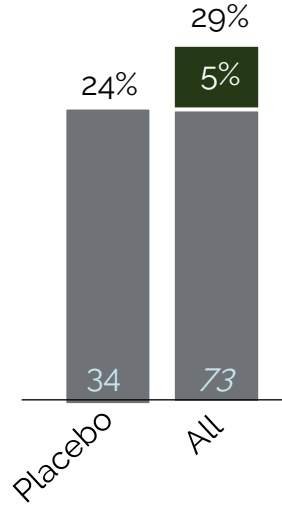
*≥1 Stage Fibrosis Improvement with no Worsening of NASH**



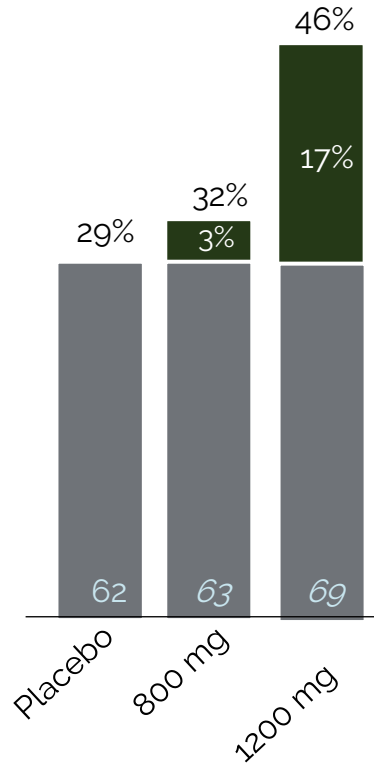
PXL065
Phase 2b – 36 wks



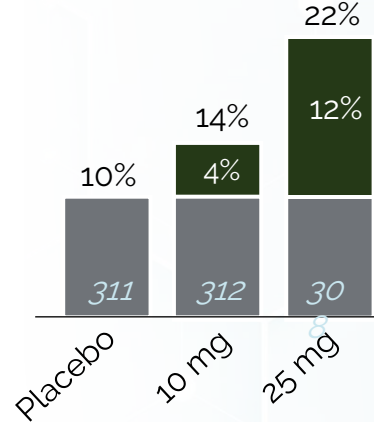
Resmetirom
Phase 2b – 36 wks



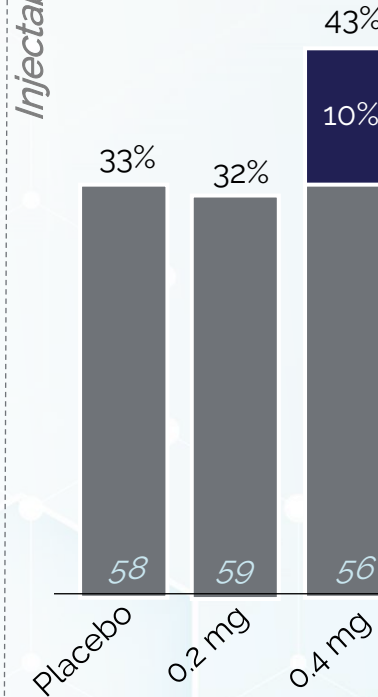
Lanifibranor
Phase 2b – 24 wks



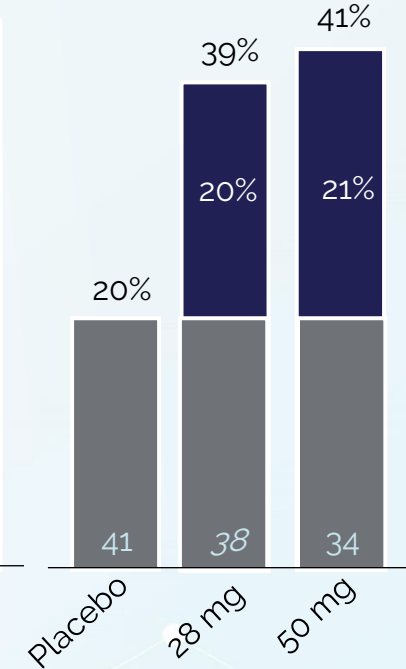
Obeticholic Acid
Phase 3 – 72 wks



Semaglutide
Phase 2b – 72 wks



Efruxifermin
Phase 2b – 24 wks



Orals
Injectables

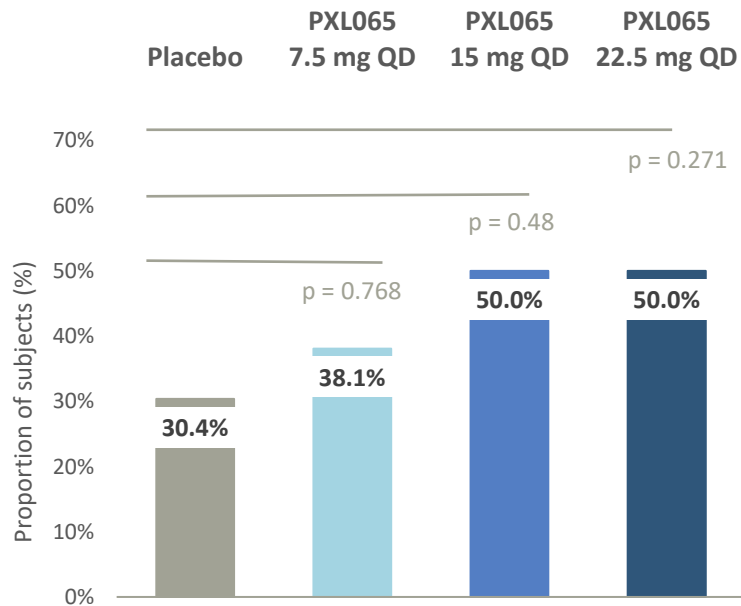
Effect on fibrosis well positioned compared to competitors
*FDA Approval Endpoint



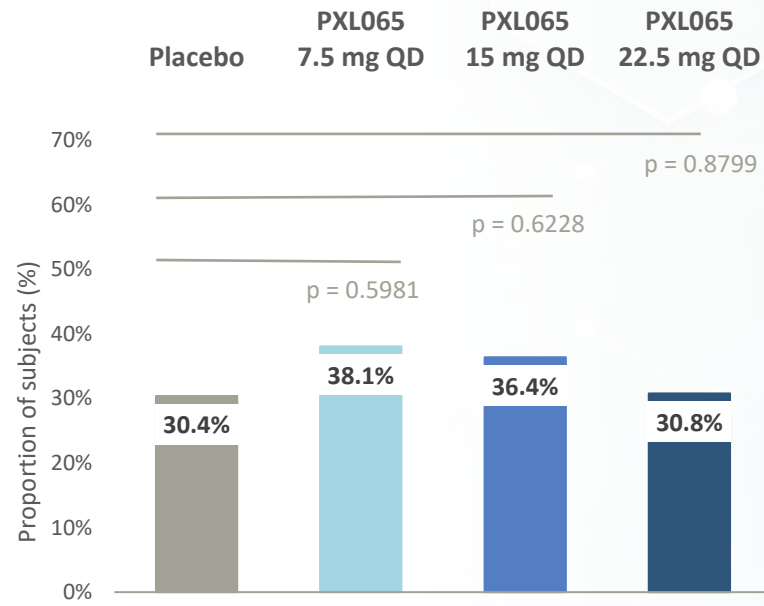
Responses in Liver Histology - NASH

Exploratory efficacy endpoint – Completers with Biopsy

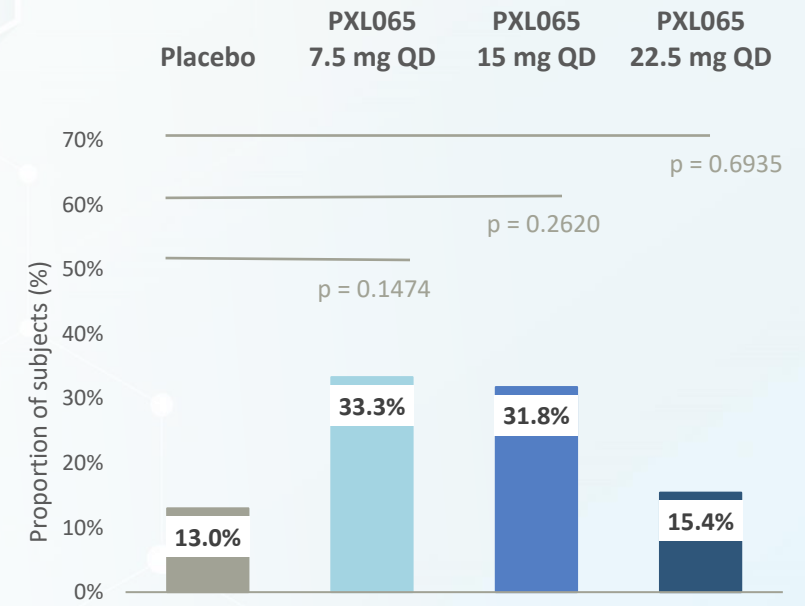
≥ 2-point improvement in NAS without worsening of fibrosis score



NASH Resolution with no worsening in Fibrosis score



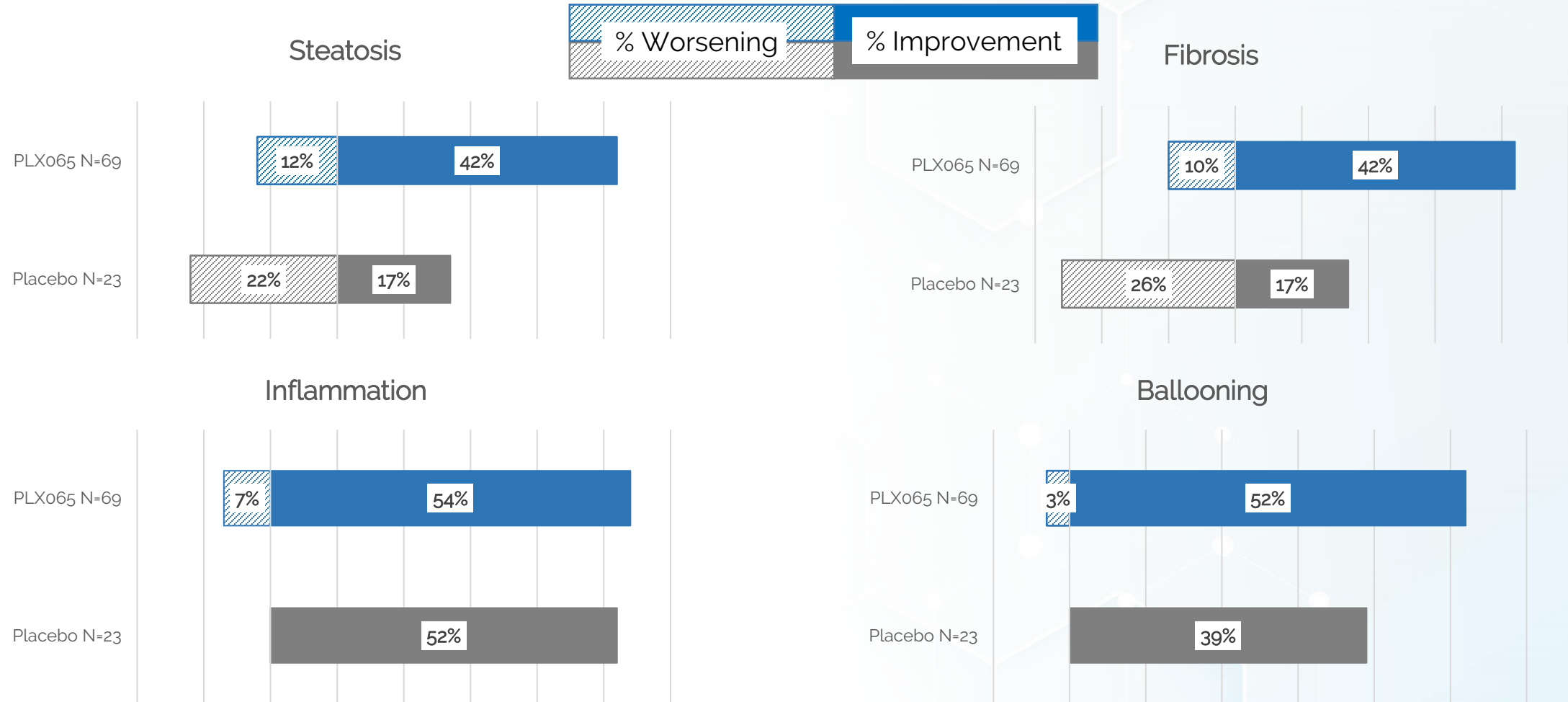
NASH Resolution with ≥ 1 point improvement in NASH CRN Fibrosis Score



Higher number of PXL065 patients improved NAS and reached NASH resolution AND improvement in fibrosis by at least 1 stage

Responses in Liver Histology – Pooled PXL065

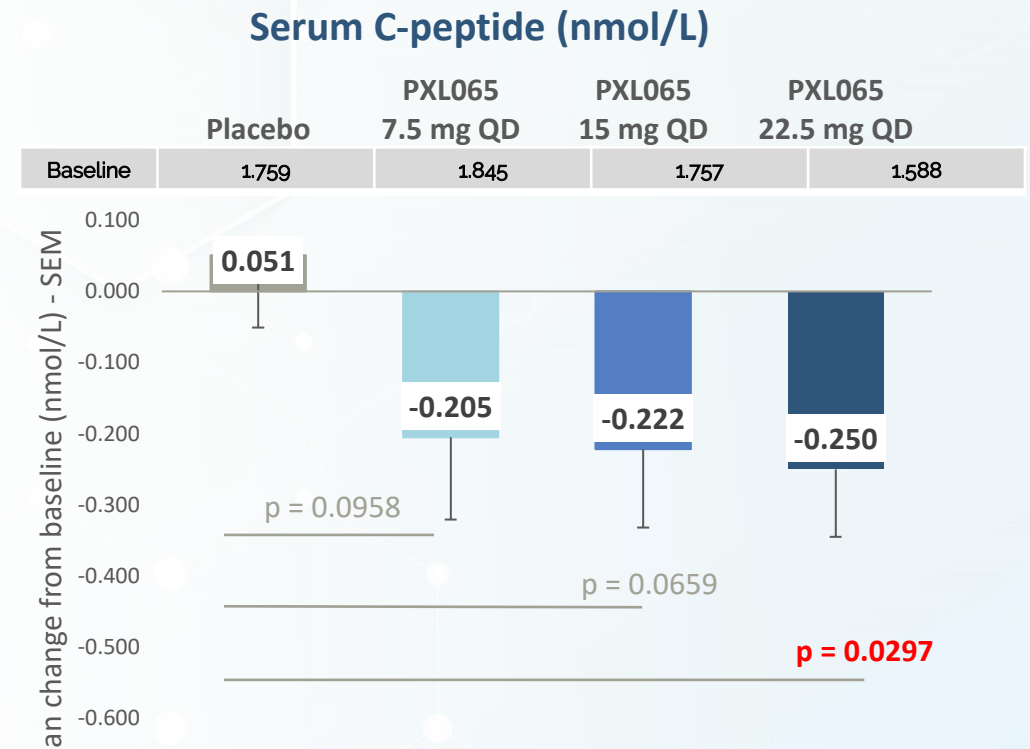
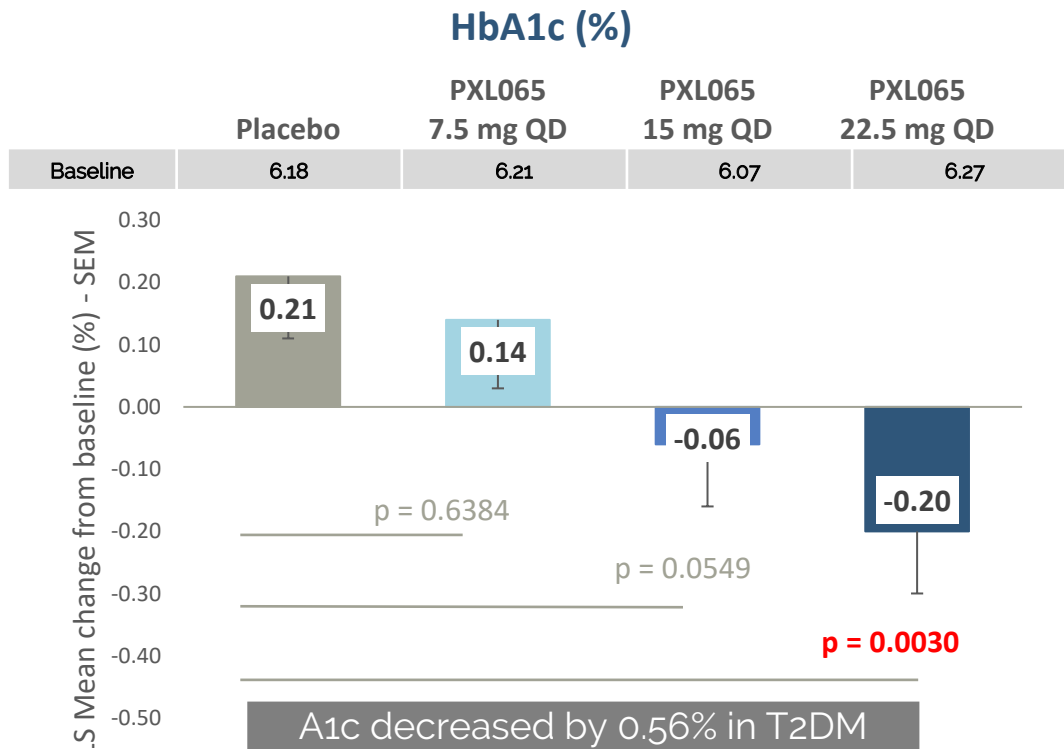
Post Hoc Analysis – Completers with Biopsy



PXL065 improves steatosis and fibrosis *and* prevents worsening in fibrosis
 ~50% improvement in inflammation and ballooning with PXL065 but unexpected high response in placebo

Metabolic Parameters - HbA1c and Insulin Sensitivity

Secondary Efficacy Endpoint - ITT Set



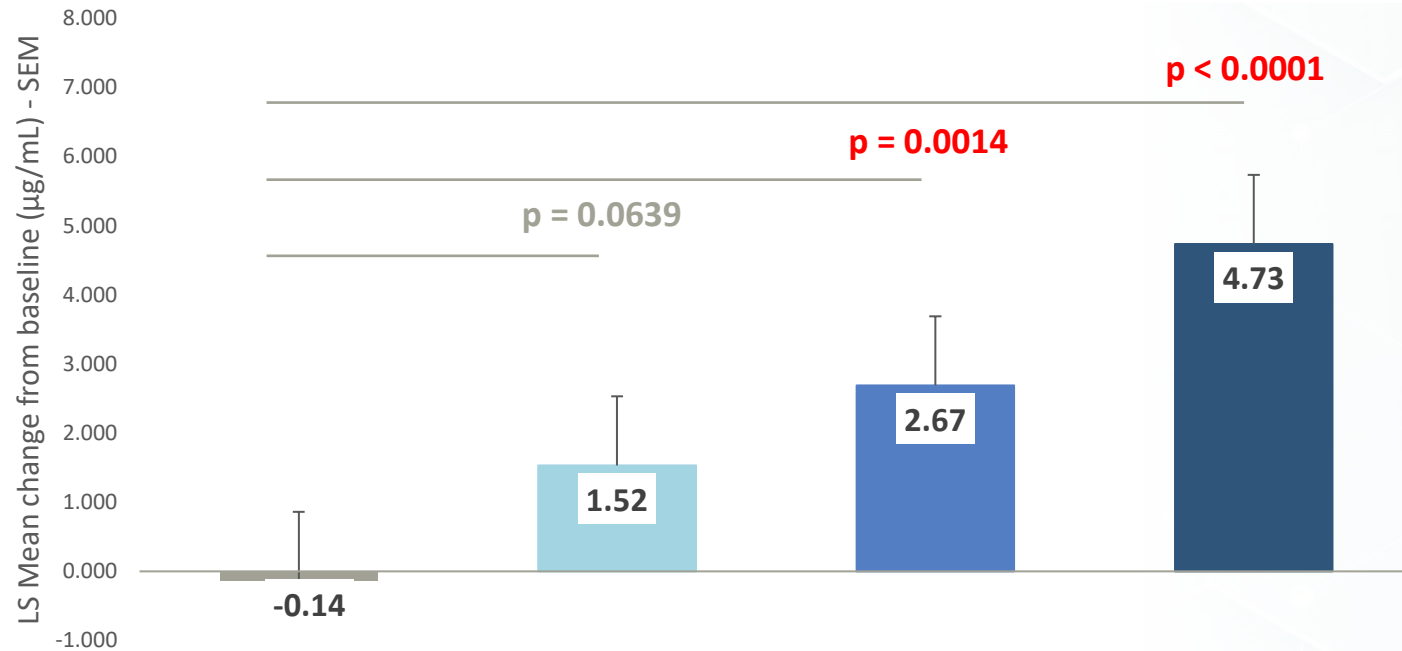
- Improved glycemic control in a well controlled diabetes population
- Decreased C-peptide
- Additional statistically significant improvements in insulin sensitivity indices (HOMA-IR and Adipo-IR)

MMRM model with fixed effects of treatment group, stratification factors, i.e. T2DM status and NASH CRN fibrosis scoring system, time point, and treatment by time point interaction, and baseline as a covariate. The Compound symmetry covariance structure is used in the analysis. p-values shown for comparisons versus placebo.

Metabolic Parameters - Adiponectin and Lipids

Exploratory Efficacy Endpoint - ITT Set

	Placebo	PXL065 7.5 mg QD	PXL065 15 mg QD	PXL065 22.5 mg QD
Baseline	4.02	3.67	3.44	4.28

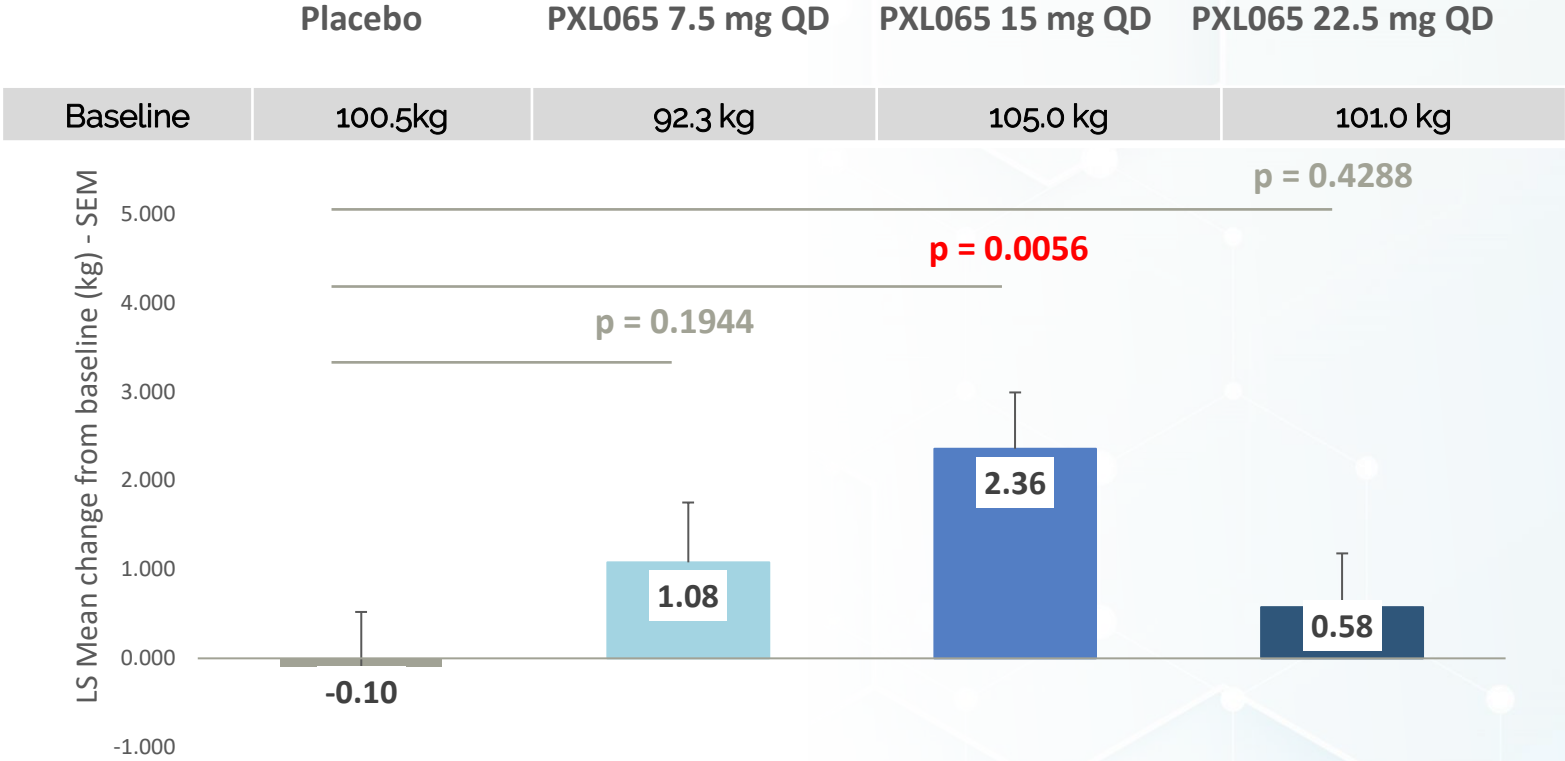


- No change in total / LDL cholesterol
- Increased HDL cholesterol (up to +7%)
- No change in triglycerides

Moderate increase in adiponectin, in line with limited residual PPAR γ activity

Change from Baseline in Body Weight (kg) to Week 36

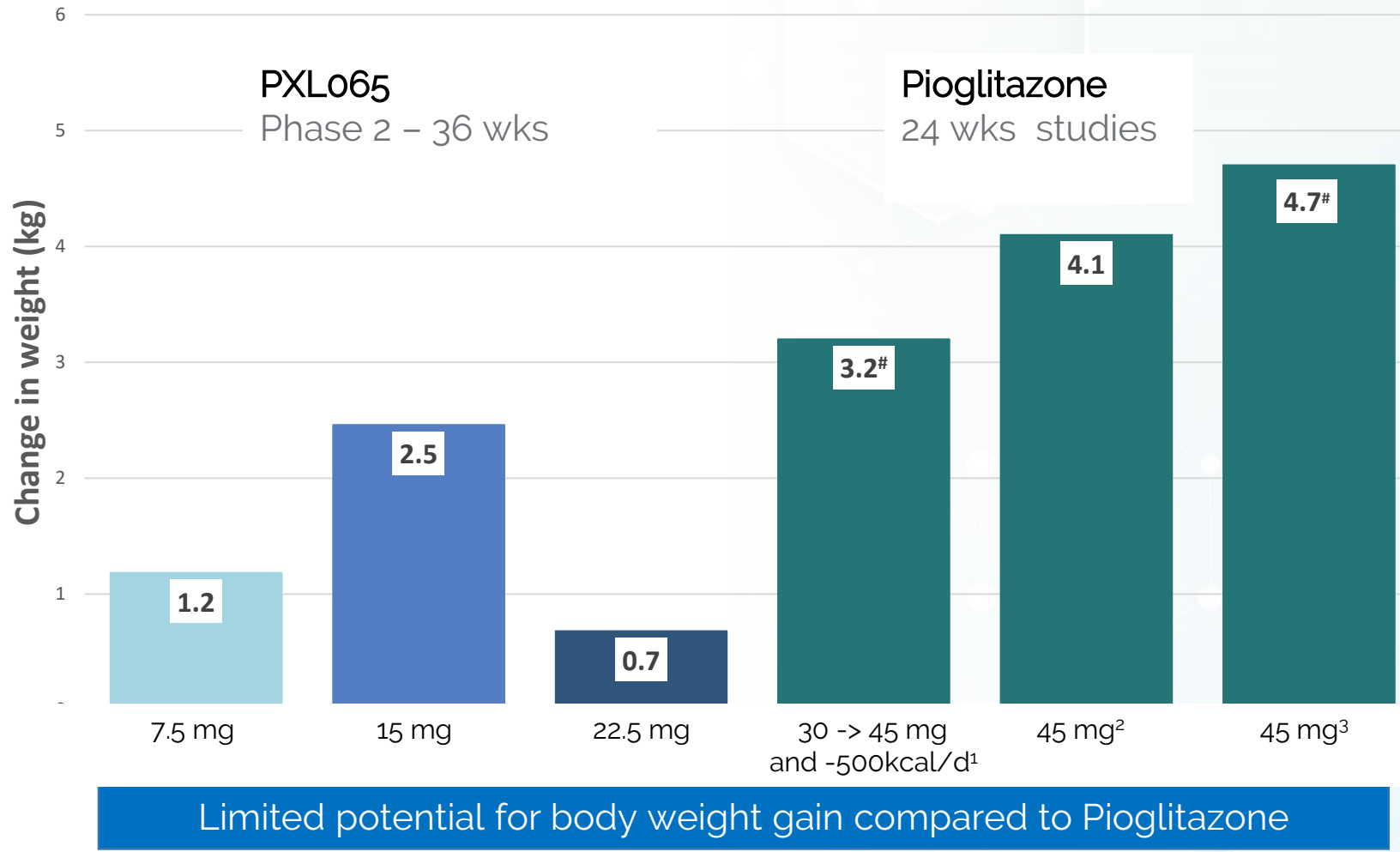
Safety Endpoint - Safety Set



No dose dependent body weight gain versus placebo, no weight gain at the top dose

Placebo Adjusted Change in Body Weight

Comparison to Published Pioglitazone Results



Placebo adjustment estimated using the mean differences

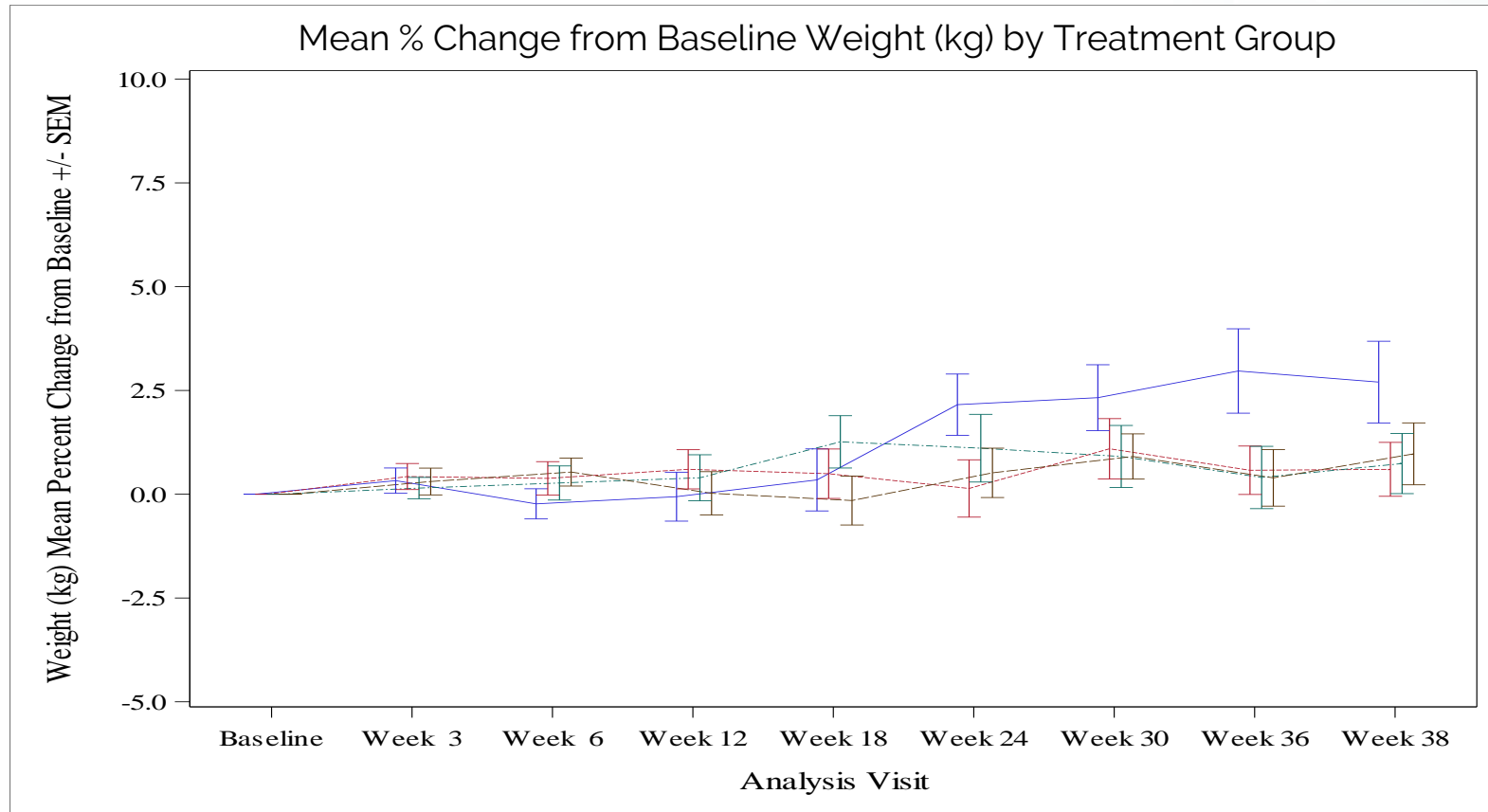
¹ Belfort et al., N Engl J Med 2006;355:2297-307 (55 patients with impaired glucose tolerance or T2DM and NASH, 30 -> 45 mg + caloric intake reduced by 500 kcal/day, 6 months)

² Aronoff et al., Diabetes Care 2000;23(11):1605-1611 (Phase 2, 408 T2DM patients, 7.5, 15, 30 and 45 mg, 6 months)

³ Smith et al., Metabolism Clin Exp 2005, 54, 24-32 (48 T2DM, 45 mg, 24 weeks)

Timecourse of Body Weight (kg) and Incidence of Edema

Safety Endpoint - Safety Set



	Pitting Edema N (%)	Peripheral Edema N (%)
Placebo (N = 30)	2 (7)	3 (10)
7,5mg (N = 25)	3 (12)	3 (12)
15mg (N = 32)	0	1 (3)
22,5mg (N = 30)	3 (10)	3 (10)

— Placebo - · - PXL065 7.5mg — PXL065 15mg - - - PXL065 22.5mg

No increased incidence of edema

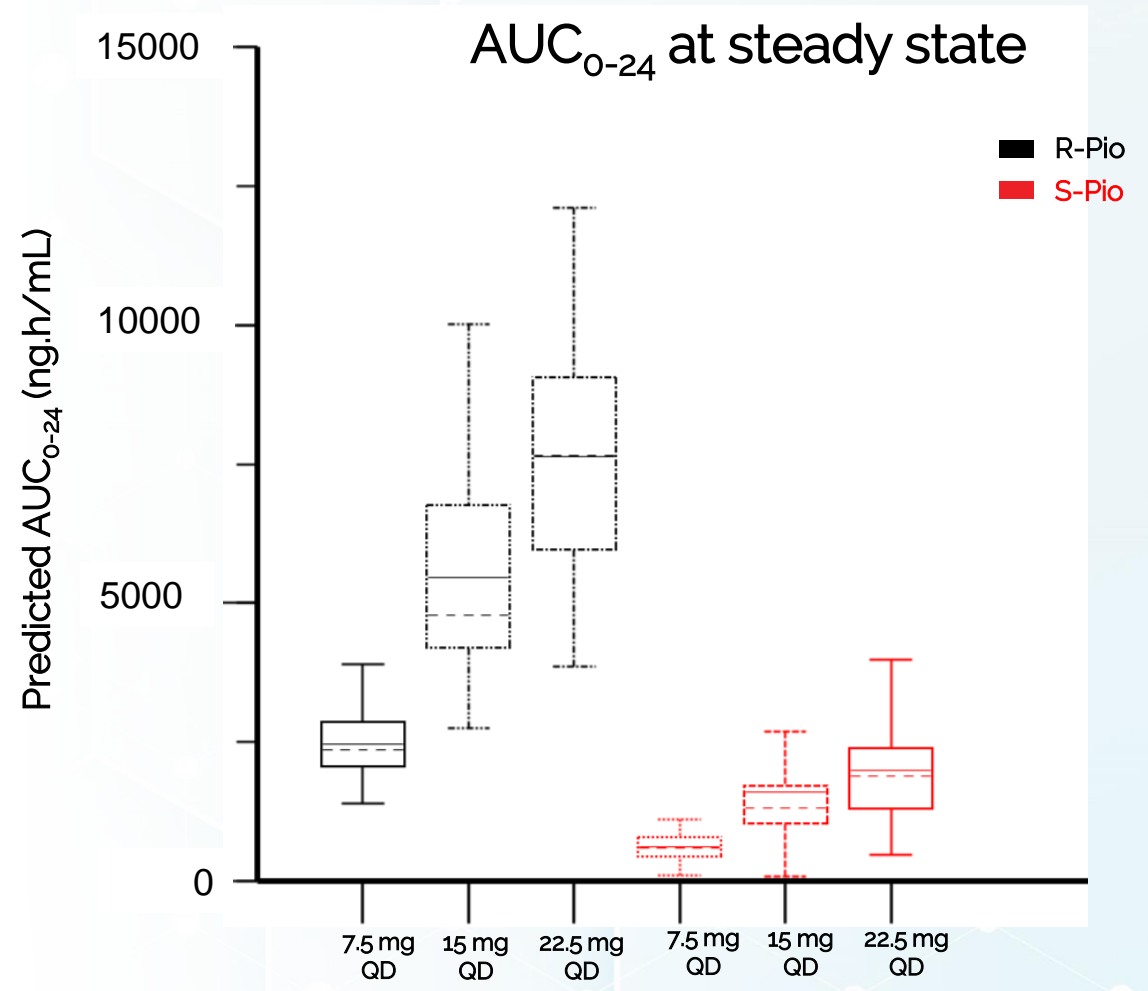
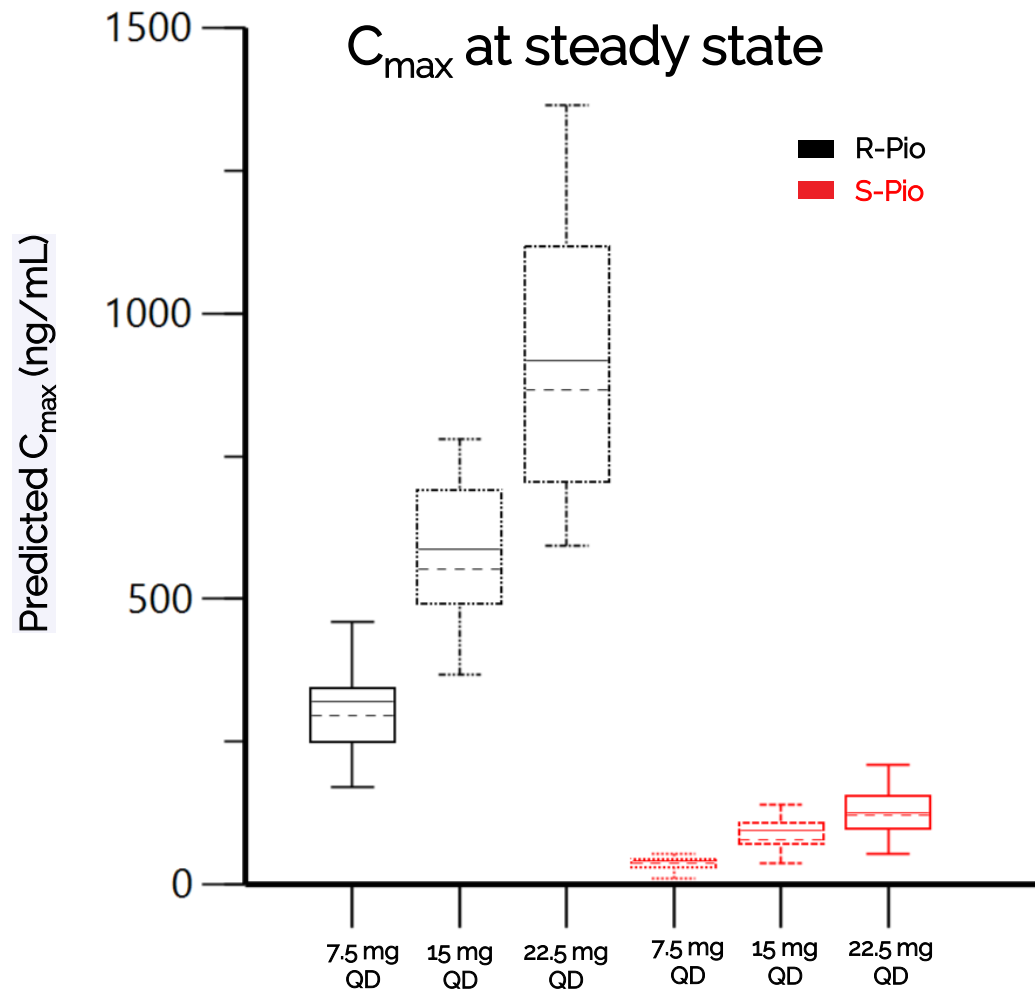
Overall Frequency of Treatment Emergent Adverse Events

Safety Endpoint - Safety Set

- 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

Dose Proportionality in Exposure

Greater R- vs. S-stereoisomer as previously reported from Phase 1



Conclusions

- Achieved primary endpoint (liver fat content) at all 3 doses
- Non-invasive NASH tests show positive effects
- Strong effect to reduce fibrosis (and prevent worsening); favorable trends in other histology endpoints including increasing number of patients who reach *both* endpoints of fibrosis improvement and NASH resolution versus placebo
- Improved glucose control and insulin sensitivity
- Good safety-tolerability with no dose dependent weight gain; no increase in edema
- PK consistent with Phase 1 results (dose dependent increase in R-enantiomer; limited exposure to S-enantiomer); modest adiponectin increases also consistent with lower PPAR γ target activity vs. Pio
- PXL065 is a differentiated NASH development candidate - results confirm potential to retain beneficial hepatic and metabolic effects with reduced PPAR γ -driven side effects
- These results are very promising. Next steps to include:
 - pivotal trial design and dose selection (including external expert input)
 - pursue regulatory interactions leading to End of Phase 2 meeting

Next Steps & Conclusion



Strategic Focus on NASH and Rare Diseases

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

Next steps

NASH

- PXL065 prioritized for further development in NASH
 - Discussions for a potential pivotal program in NASH will be 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

