



Full Year 2021 Financial and Corporate Update

March 22, 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.

2021 Summary Highlights

- **2021, the year of Poxel's first approved and launched product...**
 - Imeglimin approved in June and TWYMEEG[®] launched in September in Japan as novel Type-2-Diabetes treatment
 - Poxel received JPY 1.75 billion (EUR 13.2 million) milestone payment for the approval of TWYMEEG
 - Triggered a third and final tranche of the IPF loan for EUR 13.5 million
 - Sumitomo Dainippon Pharma, market leader in diabetes, is responsible for commercialization
 - Poxel entitled to receive escalating royalties of 8 - 18% on net sales of TWYMEEG
- **...and the beginning of a new path in rare diseases:** Poxel increases strategic focus on rare metabolic indications and NASH
 - Recruitment for DESTINY-1, Phase 2 in Biopsy-Proven NASH Patients completed in September 2021
 - Rare diseases identified as strong and relevant scientific fit for Poxel to drive future value

Poxel's Key Investment Highlights

A New Chapter to Drive Shareholder Value

Strategic focus on **rare metabolic diseases** and **NASH**

Entitled to **significant royalties** following first drug approval and launch in Japan in 2021 for TWYMEEG® (Imeglimin) for Type 2 Diabetes

Proven capabilities to **build solid partnerships** and to **lead drug development**

Diversified Clinical Stage Pipeline with **Global Operations**

Highly **Experienced Management Team** in **Metabolic Diseases**



Launch of
TWYMEEG®

2021

**Expand in
Rare
Metabolic
Diseases**



**Internal
Opportunities**

D-TZD Platform

AMPK Platform



**External
Opportunities**

ALD*

PXL065

PXL770

2018

NASH

PXL065

PXL770


2009

Type 2 Diabetes

Imeglimin

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						<ul style="list-style-type: none"> Phase 2 results expected Q3 2022 505(b)(2) pathway
PXL770	NASH	AMPK ² Activator						<ul style="list-style-type: none"> Successful Phase 2a Study Evaluate next steps early 2023
Rare Metabolic Indications								
PXL770	ALD ³	AMPK Activator						<ul style="list-style-type: none"> Initiate Phase 2a midyear 2022⁷
PXL065	ALD ³	Non-Genomic TZD						<ul style="list-style-type: none"> Fast Track Designation granted Feb 2022 Initiate Phase 2a midyear 2022⁷
PXL770/Next-Gen AMPK	ADPKD ⁴	AMPK Activator						<ul style="list-style-type: none"> Completed preclinical; develop clinical strategy
Next-Gen D-TZD	Not Disclosed	Non-Genomic TZD						<ul style="list-style-type: none"> Select lead candidate(s)
Type 2 Diabetes (T2D)								
TWYMEEG® Japan / Asia ⁵ 	T2D	MRC ⁶ Modulator						<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						<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

TWYMEEG® (Imeglimin): Launched in Japan in 2021

Partnered in Asia¹ with Diabetes Market Leader, Sumitomo Dainippon Pharma

• Launch Update

- Launch activities and promotional efforts in Japan = High awareness among prescribers
 - full sales force mobilized, launching Phase 4 & medical affairs with KOLs
- As expected, modest initial trajectory post-launch (Sept 16, 2021)
 - new product prescriptions restricted to 2 weeks for first year
 - Covid-19 conditions impacting patient access to physicians & market education efforts required for innovative product with new MOA
- Ongoing preparations to commercialize in other Asian countries¹

• Commercial Strategy

- DSP #1 diabetes franchise; FY20 USD 890 M2
- TWYMEEG can be prescribed as add-on to any therapy (e.g. DPP4i's), and as monotherapy
 - DPP4i's are prescribed to 80% T2D patients³
- Supported by TIMES Phase III program, showing robust efficacy with favorable safety and tolerability profile
- Patent estate extends to 2036 (incl. potential 5-year patent term extension), with other patent applications ongoing



Collaboration Summary

Upfront payments
and clinical &
regulatory
milestones

JPY 7.0bn (EUR 53M) ✓

Royalties

Escalating royalties
on net sales

 8% paid
to receive 8-18%⁴ to
Merck⁵

Sales-based
payments

Up to JPY 26.5bn
(EUR 200m, USD
227m)

1. Including: Japan, China, South Korea, Taiwan, Indonesia, Vietnam, Thailand, Malaysia, the Philippines, Singapore, Myanmar, Cambodia, and Laos
2. Sumitomo Dainippon Pharma fiscal year April-March
3. IQVIA data FY2016 and NDB data FY2016
4. 8% royalties expected through Sumitomo FY22 (to March 2023)
5. First 8% of royalties on net sales of Imeglimin paid to Merck Serono

Financial Update

Full Year 2021



2021 Revenue*

Mainly reflecting the milestone payment for the approval of TWYMEEG

<i>EUR (in thousands)</i>	FY 2021 12 months	FY 2020 12 months
Sumitomo Agreement	13,377	6,787
Roivant Agreement	-	18
Other	20	1
Total revenues	13,397	6,806

- Revenues for 2021 include the following payments from Sumitomo Dainippon Pharma:
 - JPY 1.75 billion (EUR 13.2 million) **milestone payment for the approval of TWYMEEG** in Japan on June 23, 2021
 - JPY 7.5 million (EUR 58 thousand) of **royalty revenue** which represents 8% of TWYMEEG net sales in Japan

Statement of Comprehensive Income as of Dec. 31, 2021*

<i>EUR (in thousands)</i>	December 31, 2021	December 31, 2020 (adjusted)**	
Revenue	13,397	6,806	Mostly reflects a €13.2m milestone payment (approval of Imeglimin in Japan)
Cost of sales	(59)		
Gross margin	13,339	6,806	
Research and development			Represents royalties paid to Merck on sales of Imeglimin in Japan
Research and development expenses	(27,479)	(29,219)	
Tax credit & subsidies	2,305	2,517	
General and administrative	(10,627)	(9,923)	Mostly reflects clinical trials for PXL770 and PXL065
Operating profit	(22,463)	(29,819)	
Financial income/(expenses)	(2,082)	(5)	Includes interest on IPF debt
Foreign exchange gains/(losses)	785	(1,970)	
Profit before tax	(23,760)	(31,794)	
Income tax	(2)	(36)	
Net income	(23,763)	(31,831)	

Statements of Financial Position as of December 31, 2021*

Assets

EUR (in thousands)	December 31, 2021	December 31, 2020 Adjusted**
Intangible assets	16,631	16,642
Property, plant and equipment	1,716	2,224
Other non-current financial assets	206	246
Deferred tax assets	-	-
Total non-current assets	18,552	19,113
Trade receivables and related accounts	50	281
Other receivables	3,999	5,480
Current tax receivables	-	-
Cash and cash equivalents	32,287	40,203
Total current assets	36,337	45,964
Total assets	54,889	65,077

Mostly reflects DeuteRx portfolio acquisition in 2018

Change in cash (-€8m), includes the 3rd tranche of IPF loan (€13,5m) and the €13.2m payment from Sumitomo Dainippon Pharma following marketing approval of TWYMEEG in Japan

Statements of Financial Position as of December 31, 2021*

Shareholders' Equity and Liabilities

EUR (in thousands)	December 31, 2021	December 31, 2020 Adjusted**	
Total shareholders' equity	8,206	27,065	Mostly reflects FY2021 net loss
Employee benefits	370	395	
Non-current financial liabilities	30,094	20,986	Reflects IPF loan (€29m) & PGE (€6m)
Provisions	318	172	
Non-current liabilities	30,782	21,554	
Current financial liabilities	5,046	2,866	Litigation with Merck is closed & provision has been reversed accordingly
Derivative liabilities	153	691	
Provisions	-	2,409	
Trade payables and related accounts	8,417	8,362	
Other current liabilities	2,285	2,131	
Current liabilities	15,901	16,459	
Total liabilities	54,889	65,077	

Statements of Cash Flow as of Dec. 31, 2021*

<i>EUR (in thousands)</i>	December 31, 2021	December 31, 2020 Adjusted **
Cash flows from operating activities before change in WC	(18,791)	(26,040)
(-) Changes in working capital requirements	1,898	(292)
Cash flows from operating activities	(16,893)	(25,748)
Acquisitions of intangible assets	(49)	(46)
Other acquisitions	7	98
Cash flows from investing activities	(42)	52
Share capital increase	295	16,808
Other financing operations	8,730	11,838
Cash flows from financing activities	9,029	28,712
Increase (decrease) in cash and cash equivalents	(7,915)	3,016

Reflects net operating loss

Reflects 3rd tranche of IPF loan and start of repayment

Early 2022 Corporate Update Highlights

- **Actively pursuing various financing options to extend cash runway**, including dilutive and non-dilutive sources, as well as discussions with IPF Partners
- **Continuing preparation for launch of first clinical studies in rare diseases, starting with Phase 2a clinical Proof-of-Concept (POC) biomarker program in X-linked adrenoleukodystrophy (ALD), planned to initiate mid-2022**, subject to financing
- **PXL065 has been granted Fast Track Designation in ALD allowing for potential faster product approval**
- **Completed preclinical assessment of PXL770 and AMPK activation for the orphan kidney disease, ADPKD, which demonstrated robust efficacy in established models**
- **Ongoing efforts to further evaluate internal and external opportunities to enrich pipeline**

Accelerating & Expanding Rare Metabolic Disease Programs

Starting with existing platforms:

PXL065 - D-TZD's (Fast Track)

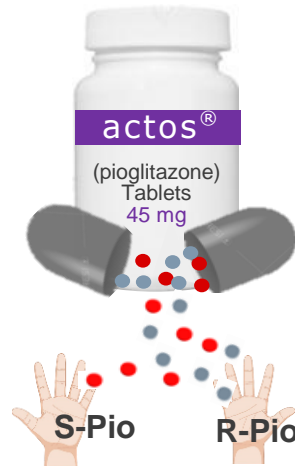
PXL770 - AMPK Activator



Two First-in-Class Advanced Lead Molecules

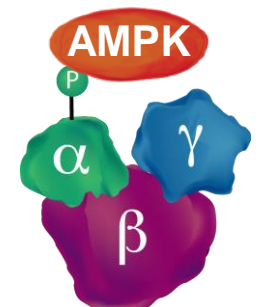
PXL065

- Deuterium stabilized R-stereoisomer of pioglitazone¹
- Preclinical:
 - no (PPAR γ -driven) weight gain/fluid retention
 - metabolic and anti-inflammatory efficacy
- Clinical
 - completed Phase 1
 - confirmed selective R-pio exposure
 - good safety profile in >130 human exposures (Phase 1 plus ongoing Destiny-1 NASH trial)
- Composition of matter IP
- 505(b)(2) regulatory path
- Open IND in ALD with Fast Track



PXL770

- Proprietary direct allosteric AMPK activator²
- Preclinical:
 - metabolic, anti-inflammatory, cytoprotective efficacy in NASH, diabetes, kidney (diabetes and ADPKD³), CV models
- Clinical
 - orally bioavailable; once daily PK profile
 - human target engagement and efficacy demonstrated (diabetes and NAFLD⁴)
 - well tolerated with favorable safety profile >200 human exposures up to 12 weeks
- Composition of matter IP
- Open IND in ALD



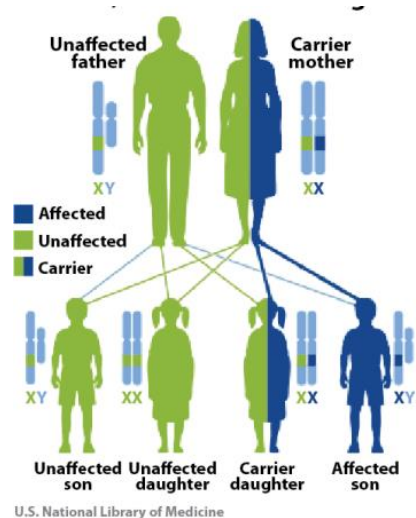
1. Approved Type 2 diabetes therapy (Actos); Jacques V et al. Hep Comm 2021; implicated in ALD - Brain 2013;136:2432-43
2. Gluais-Dagorn et al. Hep Comm 2021; implicated in ALD - Weidling I J Neurochem 2016
3. Autosomal dominant polycystic kidney disease
4. Non-alcoholic fatty liver disease

Adrenoleukodystrophy

A Not-so-Rare Orphan Neurometabolic Disease

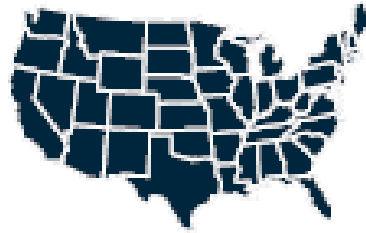
Genetics

- 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

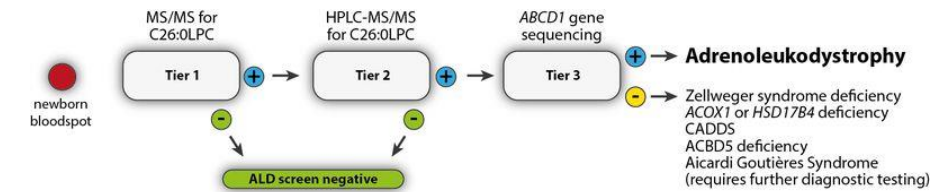


Estimated Global Prevalence¹
444,000 – 644,000



Diagnosis

- Newborn screening – increasingly common (now >60% of newborns in US)

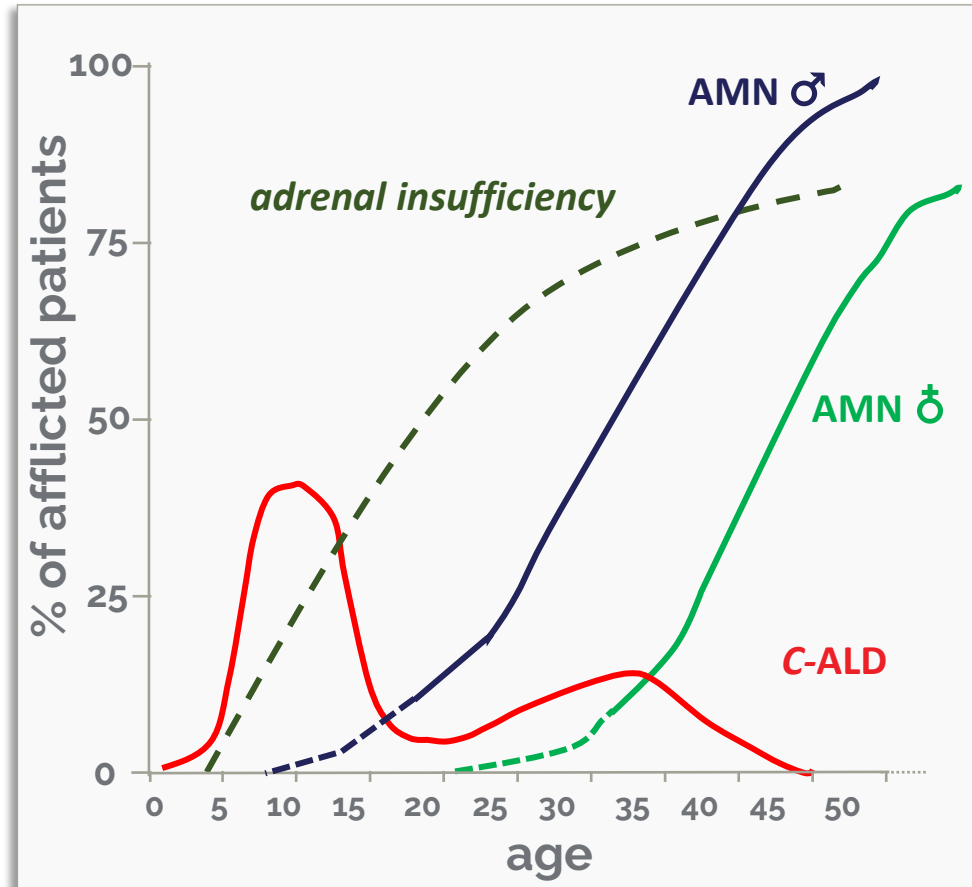


- Clinical presentation followed by measurement of VLCFA and genotyping

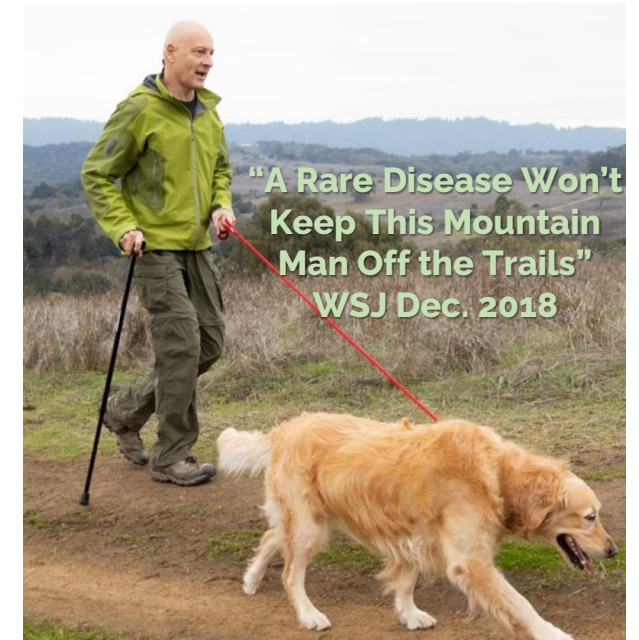
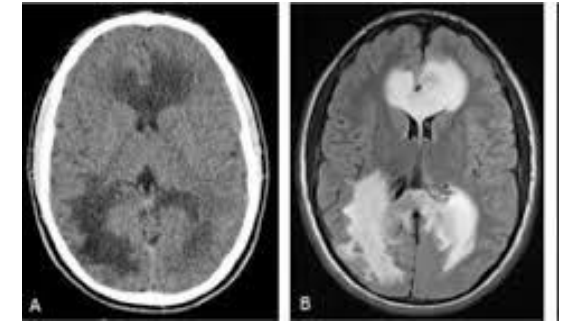
ALD Clinical Features and Disease Course

Three Major Overlapping Subtypes

- Addison's Disease
- Cerebral ALD (C-ALD):
 - damage to brain white matter; cognitive impairment; loss of vision/hearing; impaired balance-movement; death
- Adrenomyeloneuropathy (AMN):
 - slowly progressive; impaired gait-balance-movement; bladder-bowel dysfunction; also affects women



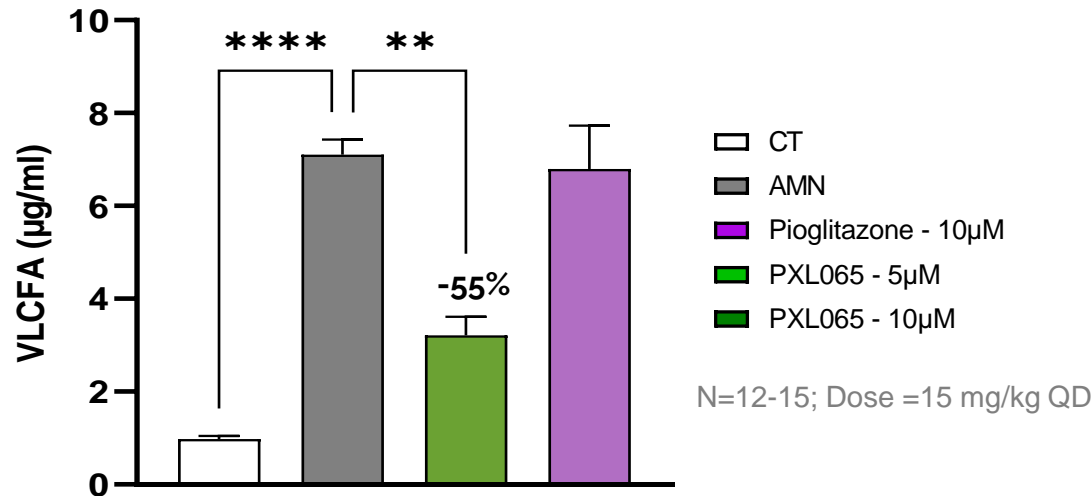
C-ALD Lesions (MRI)



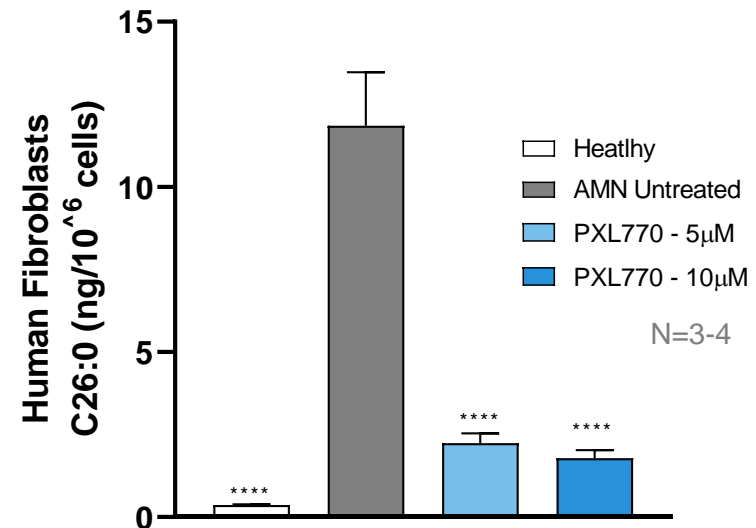
Both Poxel Lead Molecules are Active in ALD Models

- TZD's¹⁻⁴ and AMPK⁵⁻⁸ activation – independently implicated as therapeutic approaches
- *Both* PXL065 and PXL770:
 - correct disease pathology in cells from patients with C-ALD and AMN (fibroblasts and lymphocytes)
 - improve elevated VLCFA in vivo in plasma and key tissues – brain, spinal cord
- Example data shown here:

**Suppression of Elevated VLCFA (C26:0)
in Spinal Cord of ABCD1 Null Mice**



Suppression of Elevated VLCFA (C26:0) in Cells from Patients



1. J Neuroinflamm 2011; 8:91
 2. Exp Neurol 2017; 293:74
 3. Brain 2013;136:2432-43
 4. Sci Trans Med 2016; 8:368ra174

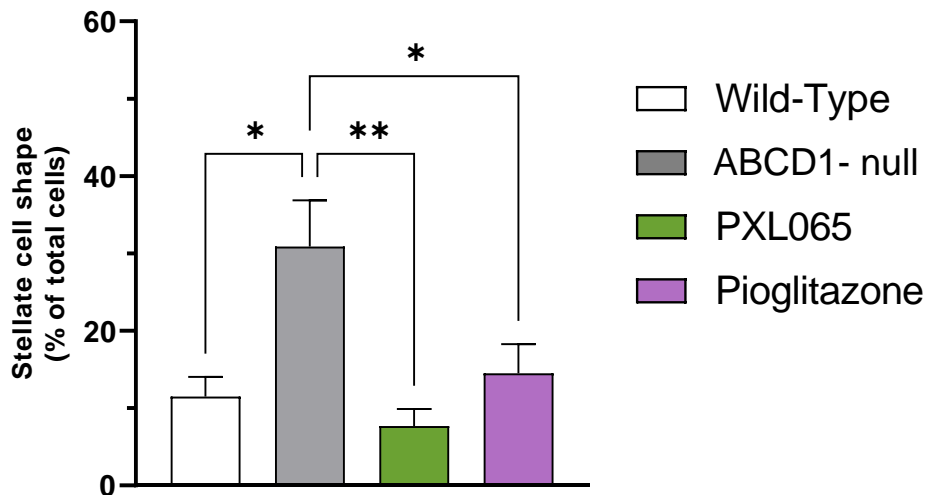
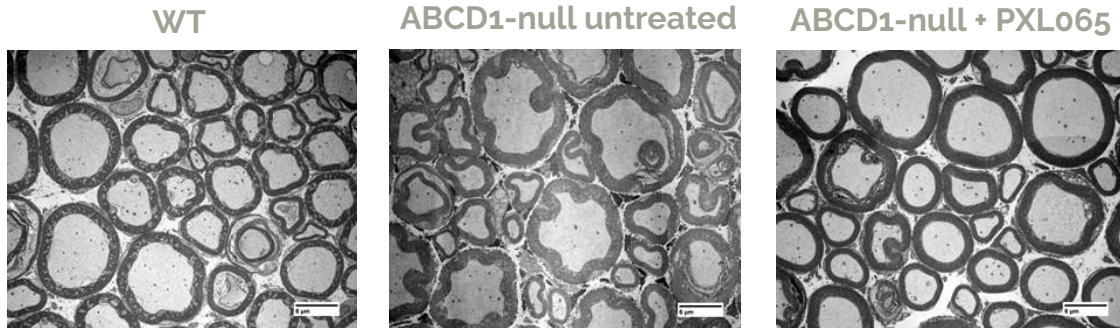
5. Mediators Inflamm 2015; 176983
 6. Biochem Biophys Res Comm 2014;445:126-
 7. J Neurochem 2016; 138:86-
 8. J Neurochem 2016; 138:10-

p<0.01, *p<0.001

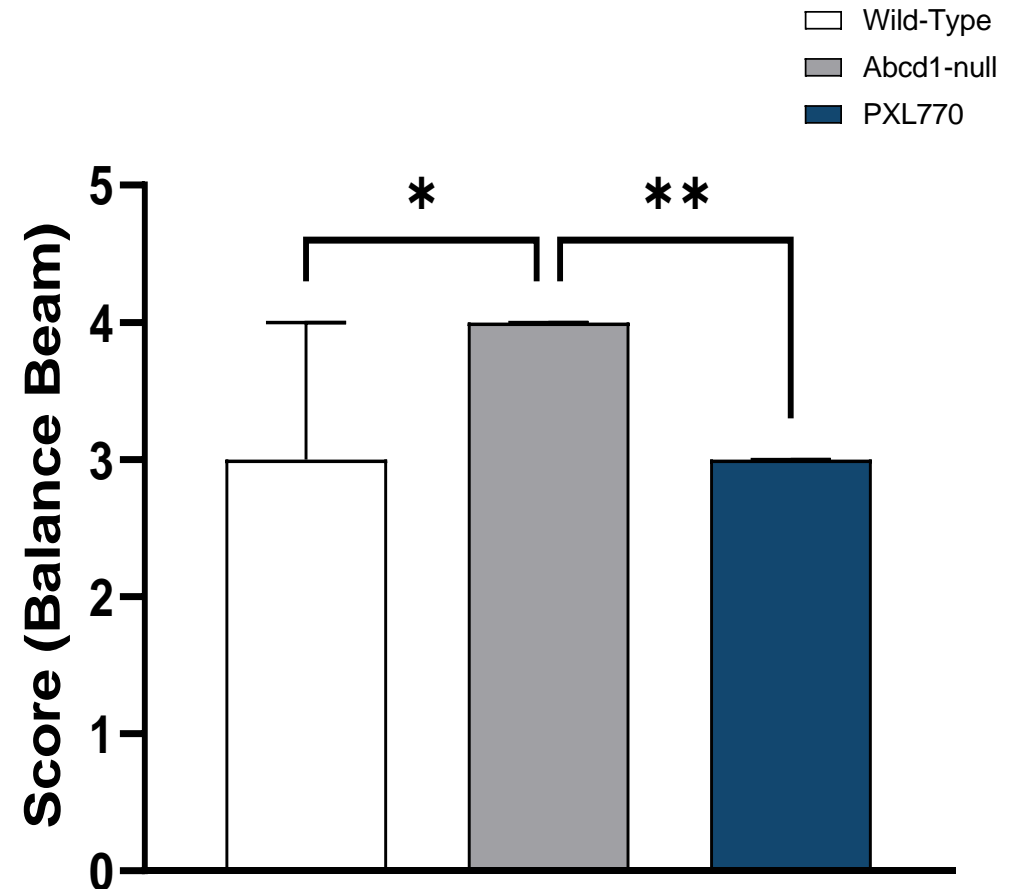
Both PXL065 and PXL770 Mediate Neurologic Benefits

ABCD1-Null Mouse (12 week Treatment)

Electronic Microscopy of Sciatic Nerve



Neurologic Tests (Balance Beam)

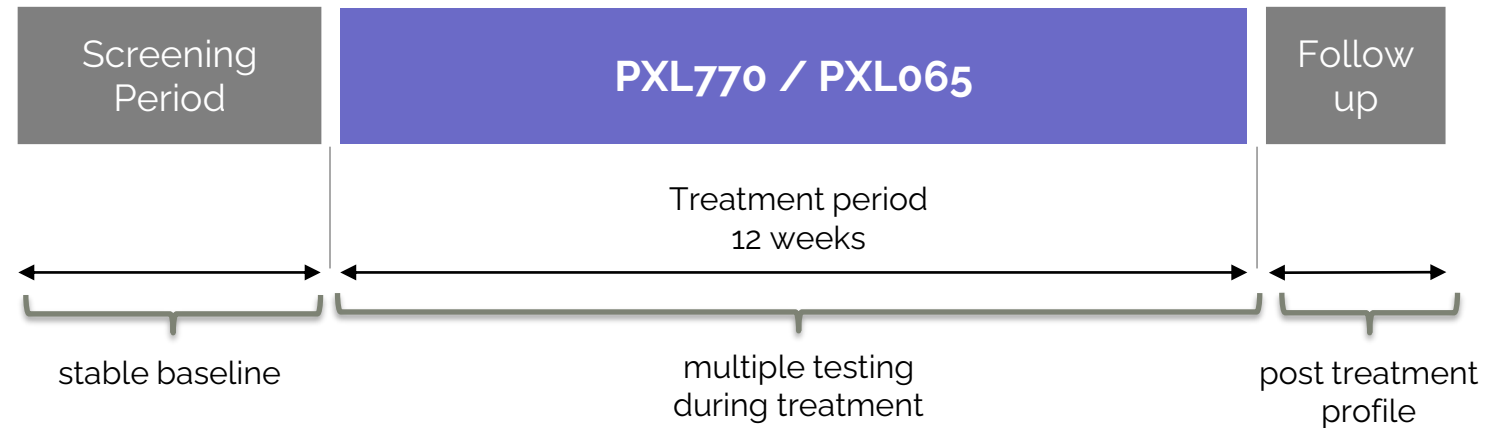


Planned Phase 2a Studies in ALD/AMN

PXL770 and PXL065 (Fast Track Designation) in Two Separate Identical Studies

Key inclusion criteria

- Males with AMN
- Age 18-65
- No active cerebral disease
- 12 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 initiation anticipated midyear – completion early 2023
Potential for Phase 3 Pivotal trial(s) to begin in 2023

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

Community Engagement

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

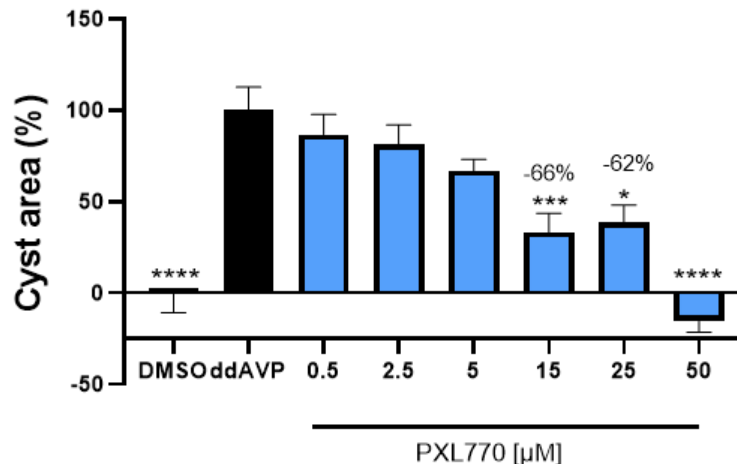


Opportunity in Polycystic Kidney Disease (ADPKD)

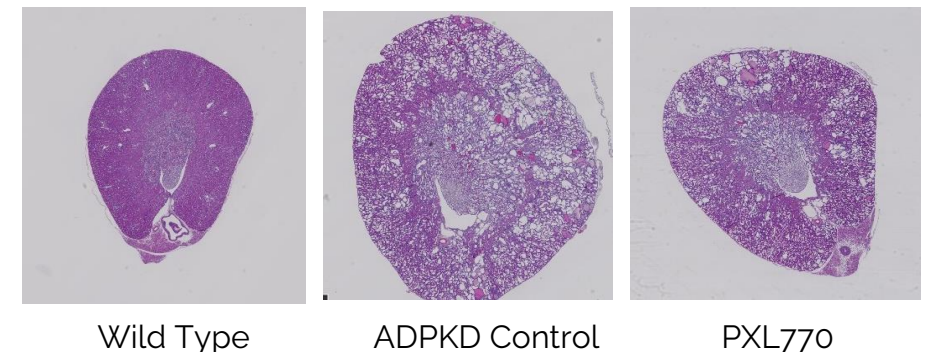
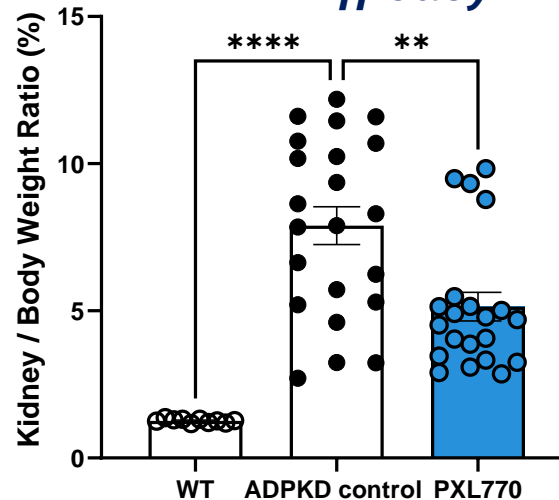
AMPK - a Compelling Target – PXL770 has Completed Preclinical Assessment

- Autosomal-dominant genetic form of kidney disease
 - prevalence ≈140,000 in US (qualifies for orphan designation)
 - high unmet need (>50% develop end-stage renal disease); one approved drug (tolvaptan) with significant safety-tolerability challenges
- 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)



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

NASH

PXL065

Non-Genomic Pathway D-TZD Modulator
for Treatment of NASH
Utilizing the 505(b)(2) Regulatory Pathway

PXL770

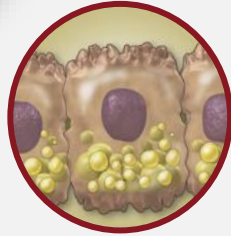
Direct AMPK Activator



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

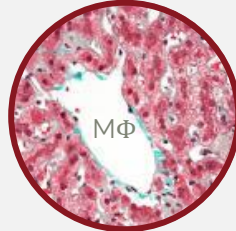


HALLMARKS OF NASH



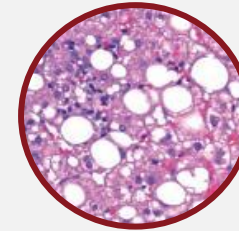
Lipid accumulation in hepatocytes

Steatosis



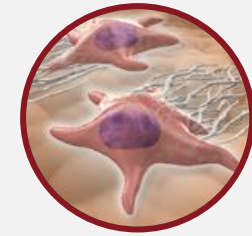
Immune cells (macrophages - MΦ)

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 (PXL770)
- derived from pioglitazone – proven NASH benefits (PXL065)

Daily oral administration

- combinable with other approaches

Innovative development approaches

- focus on patients with co-existing diabetes (PXL770)
- 505(b)(2) regulatory path (PXL065)

PXLo65 Ongoing Phase 2 in Biopsy-Proven NASH Patients

Topline Results Expected Q3 2022



Key inclusion criteria

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

Randomization
1:1:1:1

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 Endpoints

- 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

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

2022 Upcoming milestones

- **TWYMEEG[®] sales:**
 - Pursuing efforts to raise awareness and knowledge of TWYMEEG amongst prescribing physicians by our partner Sumitomo Dainippon Pharma following launch in September 2021
 - Poxel entitled to receive sales-based payments and escalating royalties of 8 - 18% on net sales of TWYMEEG: Poxel expects net royalties to be cash neutral through Sumitomo FY2022 (through March 2023) following 8% royalty repayment to Merck Serono.
- **Results of PXL065 Phase 2 (DESTINY-1) trial in NASH expected in Q3 2022**
- **Phase 2a clinical Proof-of-Concept (POC) biomarker program, subject to additional financing, planned to start midyear, with results to follow in early 2023**
- **Cash & cash equivalents: EUR 32.3 million (USD 36.6 million) as of 12/31/2021**
- **Actively pursuing various financing options to extend cash runway, including dilutive and non-dilutive sources**
- **Ongoing efforts to evaluate internal and external opportunities to further enrich pipeline**



Question & Answer Session

- Participants can submit questions in the chat

