TRANSFORMING MEDICINE
RESTORING WELLBEING

DURECT Corporation

A Biopharmaceutical Company

March 11, 2019

Forward-Looking Statements

The statements in this presentation regarding DURECT's and its collaborative partners' products in development, anticipated product benefits, anticipated product markets, clinical trial results and plans, DURECT's future business plans and projected financial results and DURECT's emergence as an innovative biopharmaceuticals company are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, DURECT's (and that of its third-party collaborators', where applicable) abilities to successfully enroll and complete clinical trials, complete the design, development, and manufacturing process development of the product candidates, obtain product and manufacturing approvals from regulatory agencies and manufacture and commercialize the product candidates and marketplace acceptance of the product candidates, as well as DURECT's ability to fund its growth and operations. Further information regarding these and other risks is included in DURECT's most recent Annual or Quarterly Report on Form 10-K or 10-Q filed with the SEC under the heading "Risk Factors."

DURECT Investment Highlights

01

DUR-928, member of a New Class of Therapeutics in Phase 2:
Epigenetic Regulator of Metabolism, Inflammation & Cell Survival

02

Opportunity in multiple underserved indications:
NASH, Alcoholic Hepatitis & other Liver Diseases, Acute Organ Injury, Inflammatory Skin Diseases

03

505(b)2 Development Programs & Approved Products, and Cash Flow Positive Product Lines
POSIMIR (bupivacaine extended-release solution), PERSERIS™ (risperidone) launched by Indivior, ALZET® & LACTEL®

04

Multiple Potential Value-Creating Catalysts in 2019

2019 Clinical Plan for DUR-928

Indication	Preclinical	Phase 1	Phase 2	Design/Timing	Patient Population
NASH (Oral)				28-day daily dosing, Phase 1b open-label study to evaluate safety, PK and signals of biological activity. Enrollment planned to begin Q1, with initial data 2H 2019	9-16 million in the U.S.[1]
Psoriasis (Topical)				Phase 2a proof-of-concept study, 28-day, multicenter, randomized, double-blind, vehicle-controlled. Enrollment planned to begin Q1, with top line data 2H 2019	7.5 million in the U.S.[2]
Alcoholic Hepatitis (Injectable)				Phase 2a open label, dose escalation study in moderate and severe AH patients.	>320,000 hospitalized in the U.S.[3]

1. Estes C, et al. Hepatology, 2018;67:123-133. 2. National Psoriasis Foundation. 3. J Clin Gastroenterology. 2015 July; 49(6): 506-511

Epigenetic Regulator Program

DUR-928 is an endogenous small molecule

- Endogenous = produced naturally by the body
- DUR-928 is highly conserved and found in similar plasma concentrations in healthy state in all mammals studied to date:
  - Humans, mice, rats, hamsters, monkeys, dogs, rabbits, pigs
- Endogenous molecules have been approved in various therapeutic areas:

Insulin	Corticosteroids
Thyroid hormone	Erythropoietin (Epoetin alfa; Epogen®/Procrit®)
Growth hormone	G-CSF (Filgrastim; Neupogen®/Neulasta®)

DUR-928: Mechanism of Action

Derived from Mitochondria

Cholesterol levels & Insulin regulate its production

Shown to stabilize mitochondrial membranes

Epigenetic Regulation

Regulates: SREBP-1c&2, NFκB, PPAR, LXR & others

Modulates Lipid Metabolism

Decreases fatty acid, cholesterol and triglyceride synthesis (HMGCR, ACC, FAS & others)

Regulates lipid absorption and transportation (MTP, PCSK9 & others)

Improves insulin sensitivity and glucose tolerance

Regulates inflammation responses, Autophagy & Improves cell survival

Modulation of IL-1, IL-6, IL-8, COX-2, TNFα, and other mediators during the inflammation state

Including reduction of IL-18, hsCRP, full length and cleaved CK-18 in patients

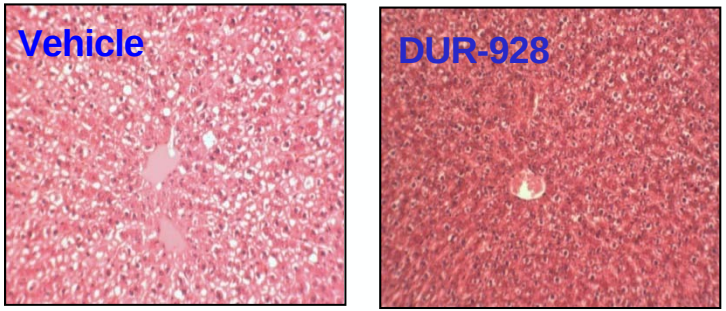
Back

DUR-928: Epigenetic Regulation and NASH

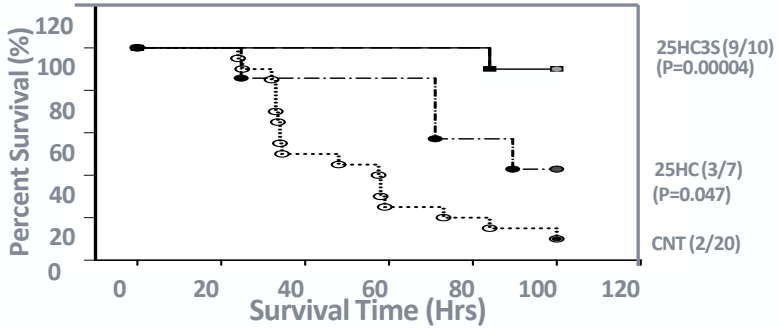
DUR-928 regulates hundreds of genes associated with metabolism, inflammation, autophagy and cell survival; many of the functions controlled by these genes are primary targets for the treatment of NASH

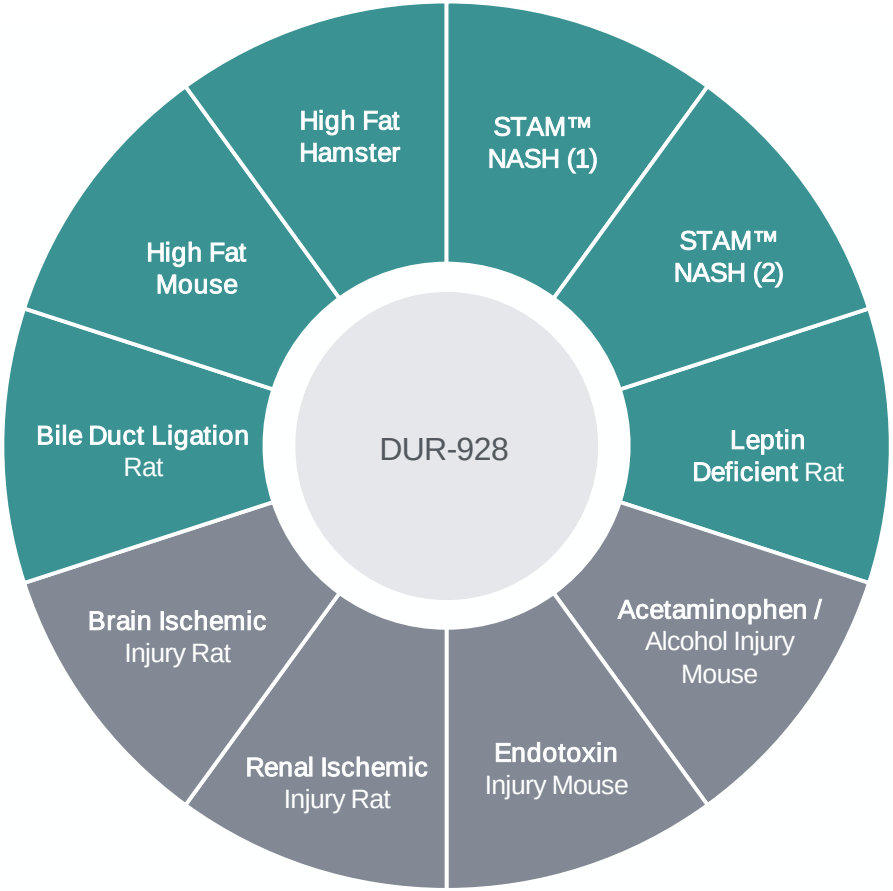
H&E staining of Zucker Rat Liver

(100x)



Effect of DUR-928 on survival of Endotoxin Dosed Mice





DUR-928
Compelling Proof-of-Concept in Animals

Extensive, compelling pre-clinical data

Positive data have been generated in each of the models shown

Together, these have given us confidence in the activity of this drug candidate

DUR-928 Phase 1

Safety in healthy human subjects

	Over 150 individuals dosed (including Phase 1b studies)
	High doses resulted in plasma levels >1,000-fold higher than endogenous levels
	Oral, IV, IM and intradermal administration
	Minimal food effect observed
	Well tolerated at all doses
	No accumulation in plasma concentrations observed with repeated dosing, dose related increases in plasma concentrations observed
	Drug-drug interaction studies clean (oral and IV)

DUR-928 Dosage Forms

Chronic liver & metabolic disorders	Acute organ injuries	Inflammatory skin disorders
NASH & Others	AH, AKI	PSORIASIS, ATOPIC DERMATITIS
		
ORAL	INJECTABLE	TOPICAL

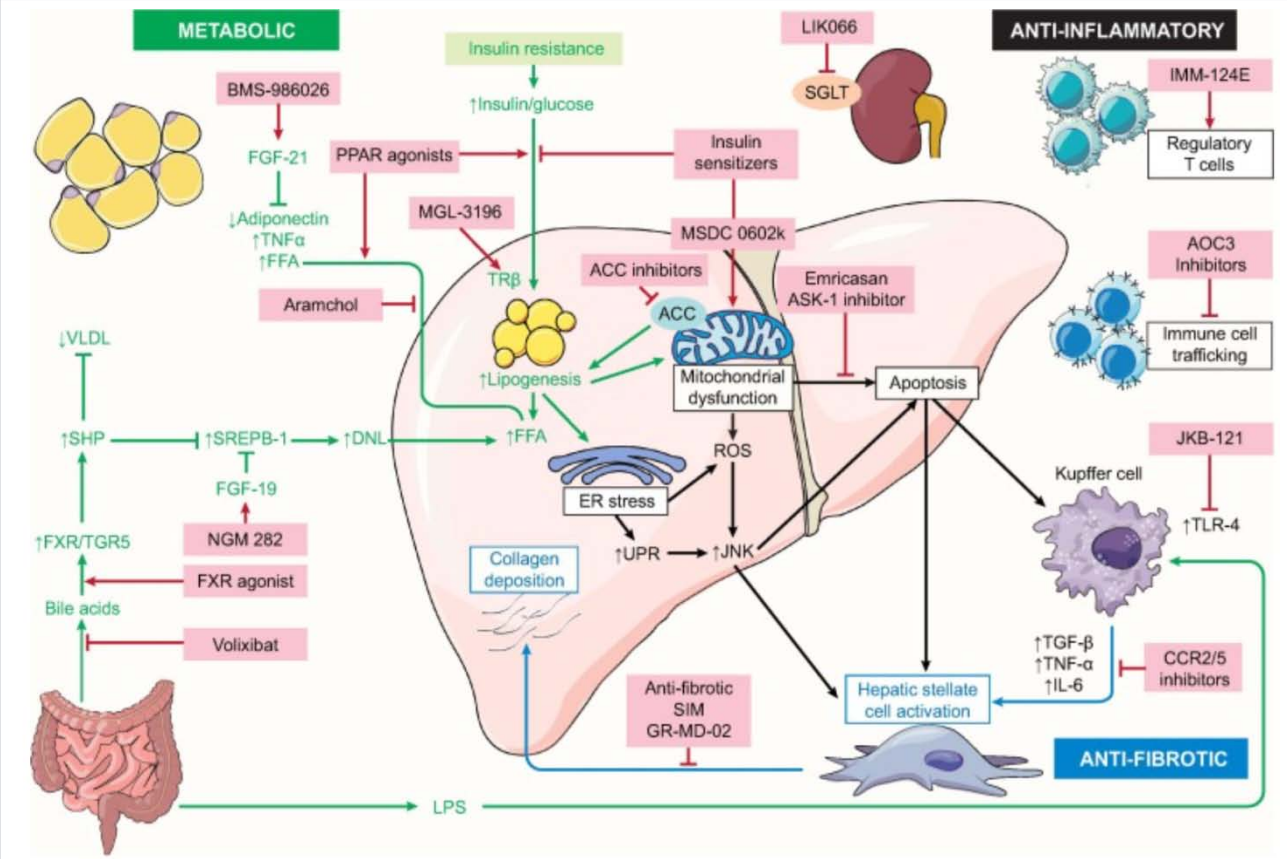
DUR-928
Potential in NASH

NASH

Nonalcoholic Steatohepatitis Overview

	Affects 3-5% of the US population; expected to increase ~2x by 2030
	Worldwide surge in obesity fueling increasing prevalence of NAFLD and NASH
	There are no treatments currently approved for NASH
	As early as 2020, NASH is expected to surpass Hepatitis C as the leading cause of liver transplants in the U.S.
	Total direct costs of illness for NASH will continue to be substantial with annual predicted economic burden of NASH with and without fibrosis estimated to be >$10B in the U.S. and major European markets

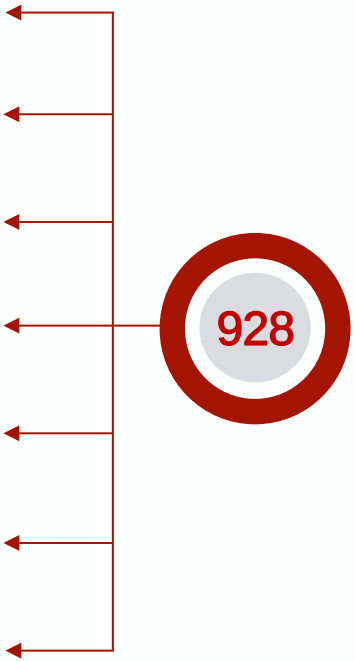
Mechanisms of Action of Potential Treatments for NASH are Complex



Konerman M et al, J Hepatol 2018;68:362-75. Courtesy of Dr. I Jacobson

DUR-928 may help simplify the solution

Apoptosis	Gilead, Conatus
Inflammation	Allergan/Tobira, BI, Genfit, Intercept
Lipogenesis/FFA	Madrigal, Viking, Gilead, Gilead/Nimbus, Galmed, NGM, BMS, Genfit, Intercept, Ionis
Gluconeogenesis	Genfit, Cirius
Collagen deposit	Galectin, Gilead/Scholar Rock
Mitochondria dysfunction	CohBar
Lipid transport	Gilead, Intercept, Albireo



DUR-928 and NASH

Cell culture and gene expression data

API manufacturing to commercial scale

Animal data (High Fat Diet mouse & hamster, Leptin deficient and STAM 1 & 2, Acute models of liver and kidney injury)

Long term toxicology is ongoing

Phase 1b single dose data

Multi-dose study initiation planned for Q1 2019

DUR-928 *Phase 1b*

Initial Patient Study (NASH)

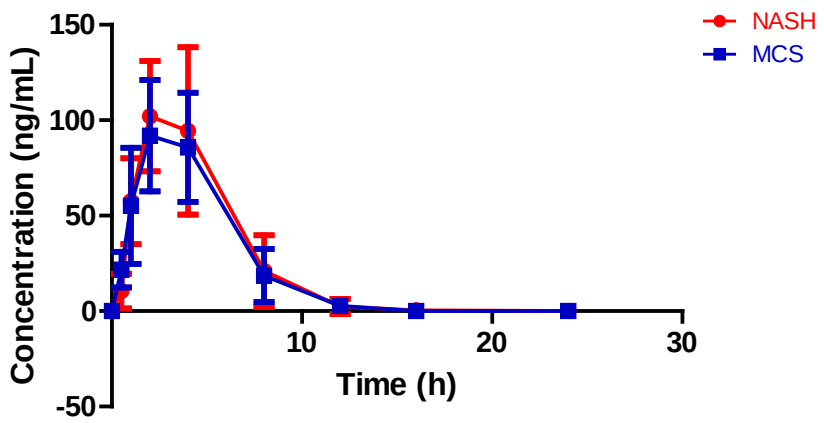
- Conducted in Australia, oral formulation
- 2 successive cohorts evaluating single doses of DUR-928:
- Each cohort had 10 NASH patients and 6 matched control subjects (by age, body mass index and gender, but with normal liver function)
- Single-site, open label, dose ranging safety and PK study
- Safety and PK results:
  - Safe and well tolerated, with one possibly treatment related serious adverse event (shortness of breath)
  - PK parameters between NASH patients and matched controls comparable

Biologic activity was observed after a single dose in both cohorts

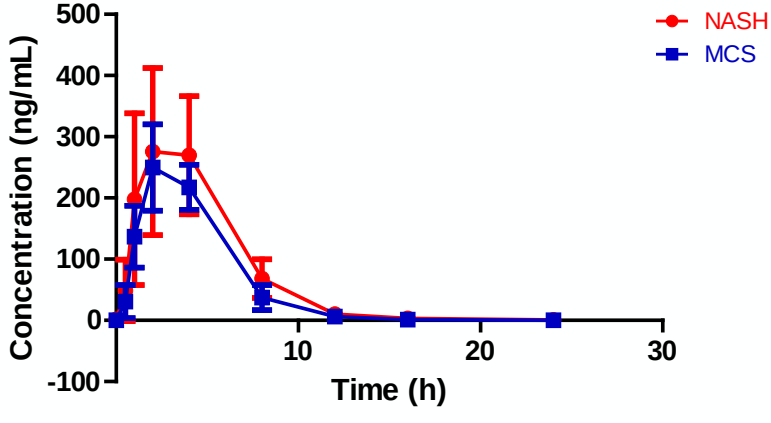
Phase 1b: NASH Patient Study

Plasma exposure not significantly increased in NASH patients compared to matched control subjects with normal liver function

Cohort 1 (50 mg)



Cohort 2 (200 mg)

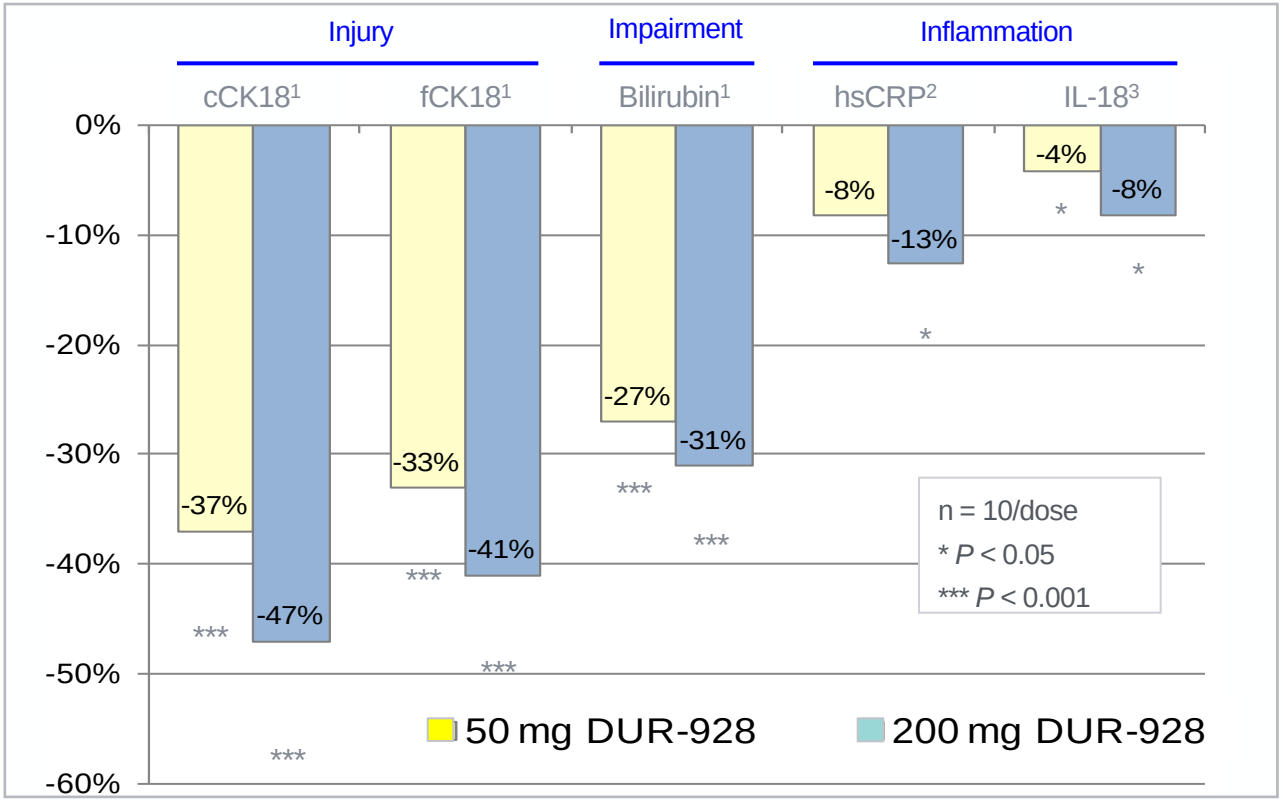


N = 10 NASH patients, 6 Matched Control Subjects (MCS) per cohort

Note: NASH group includes cirrhotic and non-cirrhotic patients

Phase 1b: NASH Patient Study

Biomarker Changes in NASH Patients After a Single Oral Dose of DUR-928



Single dose of 928 was able to reduce cell injury, impairment and inflammation

1. The reductions of cCK-18, fCK-18, and bilirubin were the greatest at 12 hours after dosing
2. The reduction of hsCRP was more noticeable at 24 hours after dosing
3. The reduction of IL-18 was noticeable at 8 hours after dosing

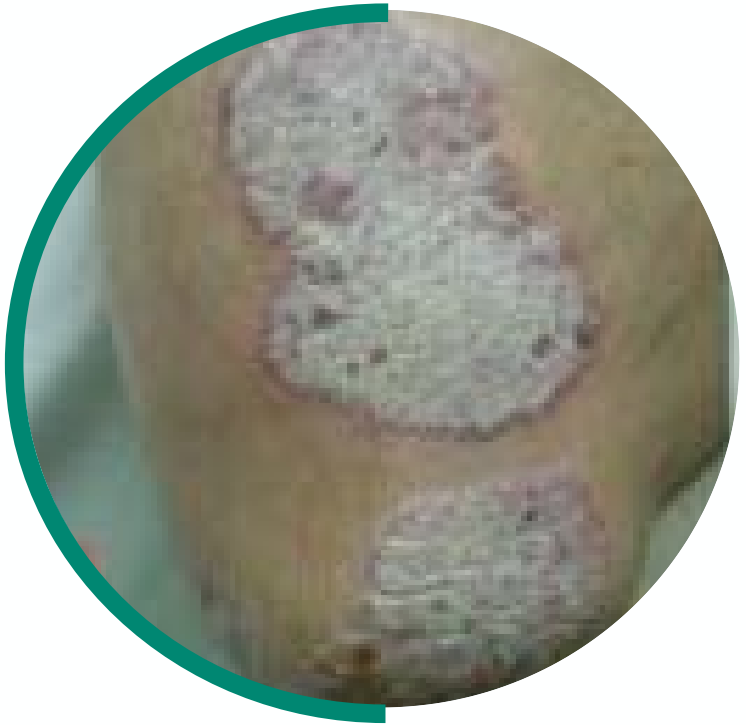
2019 DUR-928 NASH Trial

1. Orally-administered DUR-928 in NASH patients planned to begin enrolling patients Q1, 2019
2. This study will be an open-label, Phase 1b trial to evaluate safety, pharmacokinetics and signals of biological activity of DUR-928 in patients with NASH
3. It will be conducted in the U.S.
4. Patients will be administered DUR-928 orally for 28 consecutive days
5. We expect to announce initial data from this trial in the second half of this year

DUR-928
Potential in Psoriasis & Atopic Dermatitis

Psoriasis Overview

- Most common autoimmune disease in the U.S., affecting ~7.5 million people
- Painful, scaly, inflamed patches of skin (plaques)
  - Affects quality of life
  - Up to 30% of patients also develop psoriatic arthritis
- Treatment by anti-inflammatory agents
  - Topicals - first line therapy
  - Systemic medications
- Psoriasis is generally considered to be undertreated and there is treatment dissatisfaction[1]



[1] *JAMA Dermatol.* 2013;149(10):1180-1185.

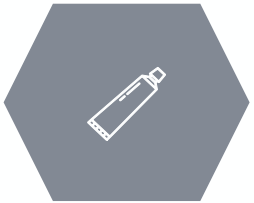
Inflammatory Skin Condition Program

Phase 1b: Initial Patient Study (Psoriasis)

- Conducted in Australia, intralesional injection
- Evaluating a single dose of DUR-928:
  - 9 psoriatic patients (moderate to severe)
  - Micro-plaque assay, self-control
  - 2 formulations, double-blinded, safety and efficacy study
  - Kenalog as positive control
  - Evaluated LPSI (local psoriasis severity index) scores

Proceeding with a Phase 2a proof-of-concept study with topically applied DUR-928

2019 Psoriasis Phase 2a Trial: DUR-928



Phase 2a proof-of-concept trial with topical DUR-928 in patients with mild to moderate plaque psoriasis beginning in the first quarter of 2019

- n=20
- Multicenter, randomized, double-blind, vehicle-controlled
- To be conducted in the U.S.
- DUR-928 will be applied topically once-daily for four weeks
- Patients will serve as their own controls, as each patient will have similar contralateral plaques
- DUR-928 will be applied to one plaque and the vehicle control will be applied to the contralateral plaque daily for four weeks
- Additional four week follow up
- Primary efficacy endpoint will be improvement in local psoriasis scores in the DUR-928-treated plaque compared to the vehicle-treated plaque

We expect to announce top line data from this trial in the second half of 2019

DUR-928
Potential in Alcoholic Hepatitis & Acute Kidney Injury

Alcoholic Hepatitis (AH) Overview

- Acute form of alcoholic liver disease (ALD)
- Spectrum ranging from mild injury to severe, life-threatening injury
- AH is characterized by inflammation and hepatocellular injury
- AH is believed to occur in 10-35% of heavy drinkers
- ~ 320,000 AH-related hospitalizations in the U.S.[1]
  - Alcohol Use Disorder (AUD) in the U.S. affects 15.1 million adults (6.2%)
  - 50% of all cases of cirrhosis have alcohol contribution
- No approved treatment
  - Short term mortality rate exceeds 30% in severe cases

[1] Hospitalizations in 2010 with a primary or secondary diagnosis of AH. J Clin Gastroenterology. 2015 July; 49(6): 506-511.

Alcoholic Hepatitis (AH) *Rationale for DUR-928*

Encouraging data from Phase 2a trial in initial dosing group (30 mg)

- MELD (Model of End Stage Liver Disease) scores
- Bilirubin levels
- Lille scores

Biology fits the disease

Anti-inflammatory and cell survival properties of DUR-928

Reduction in bilirubin and reduction in cell death markers (CK-18s) indicate potential to improve hepatocyte function

Phase 1b NASH and CKD data, multiple animal models

Reductions seen in bilirubin, inflammatory biomarkers (NASH) and CK-18s from a single dose in Phase 1b studies

Animal models demonstrate DUR-928 has protective effects against acute injury and liver disease

Alcoholic Hepatitis (AH) Phase 2a Study

Open label, dose escalation study with DUR-928 administered by IV infusion

- Part A: moderate AH (MELD scores of 11-20) 3 doses (30, 90 and 150 mg)
- Part B: severe AH (MELD scores of 21-30) 3 doses (30 mg, 90 mg and tbd)

Objectives

- Safety and Pharmacokinetics (PK)
- Pharmacodynamic (PD) signals
  - Biochemical: improvement in liver biochemistry, MELD and Lille scores
  - Biomarkers: improvement in biomarkers

In parallel, DURECT is assisting Dr. Craig McClain at the University of Louisville to conduct a trial of DUR-928 in AH patients using an NIH grant

DUR-928: An Endogenous Sulfated Oxysterol

An epigenetic regulator, highly conserved, and a new class of therapeutics

In vitro: Regulation of genes in Lipid metabolism, inflammatory responses, and cell survival

Normal Animals

Demonstrated excellent safety in all tox studies, covering oral, topical and injectable administrations

Healthy Subjects

Well tolerated at all doses (single, multi, oral administration, injection, IV infusion)

Disease Pre-Clinical Models

Demonstrated activity in more than 10 models, covering chronic and acute conditions

Disease Clinical Models

Demonstrated biologic activities in NASH, CKD and psoriasis patients (single dose)

DUR-928 Summary

01	Impressive results from more than 10 animal models
02	High doses resulted in plasma levels >1,000-fold higher than endogenous levels, well tolerated at all doses
03	Encouraging data from Phase Ib single dose studies in NASH, CKD and Psoriasis patients
04	Oral, IV, IM and topical formulations for clinical studies, API manufacturing at commercial scale
05	NASH and Psoriasis trials to begin Q1 with data read-outs in 2H 2019; AH trial encouraging data in 30 mg cohorts, advancing to 90 mg cohort in severe AH patients

Additional Proprietary Programs

Product / Indication	Phase 1-2	Phase 3	NDA Filed	Approved	Commercial	Comments
POSIMIR® (Post-operative pain)						Received complete response letter - DURECT plans to submit full response H1 2019
PERSERIS™ (Schizophrenia)						Commercially available as of Nov. 2018 - fully launched by Indivior in Feb. 2019 with 50 representatives (1)
Methydur (ADHD – Taiwan)						Approved in Taiwan - Orient Pharma plans to launch during 2019 in Taiwan (1)
ORADUR® - Methylphenidate (ADHD - other countries)						Phase 3-ready or NDA-filing-ready based on clinical work performed in Taiwan

1. DURECT to receive earn-outs or royalties based on net sales of specified products by Indivior and Orient Pharma

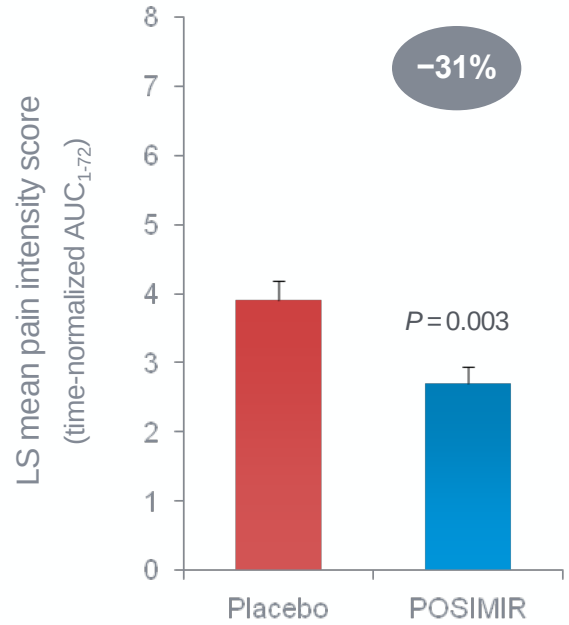
POSIMIR® (bupivacaine extended-release solution)

Post-Operative Pain Control Utilizing SABER™ Techonology

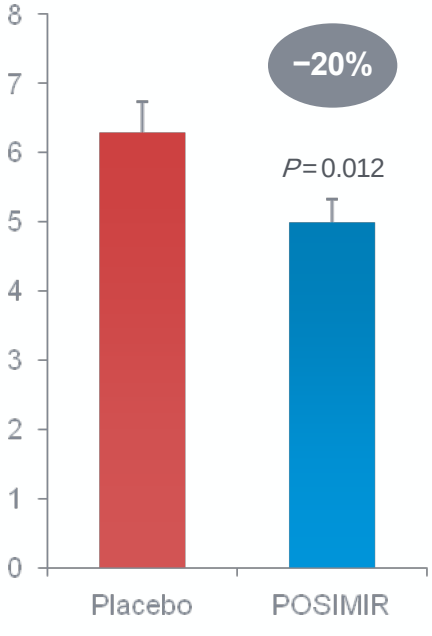
- Up to 3 days of post-op pain control, non-narcotic
- Investigational product designed for local control of post-surgical pain, plus reduced narcotic use and associated side effects and costs
- Plan to submit full response to CRL in H1 2019, with potential NDA approval in 2019

POSIMIR®: Reduction in Pain on Movement

Hernia Surgery

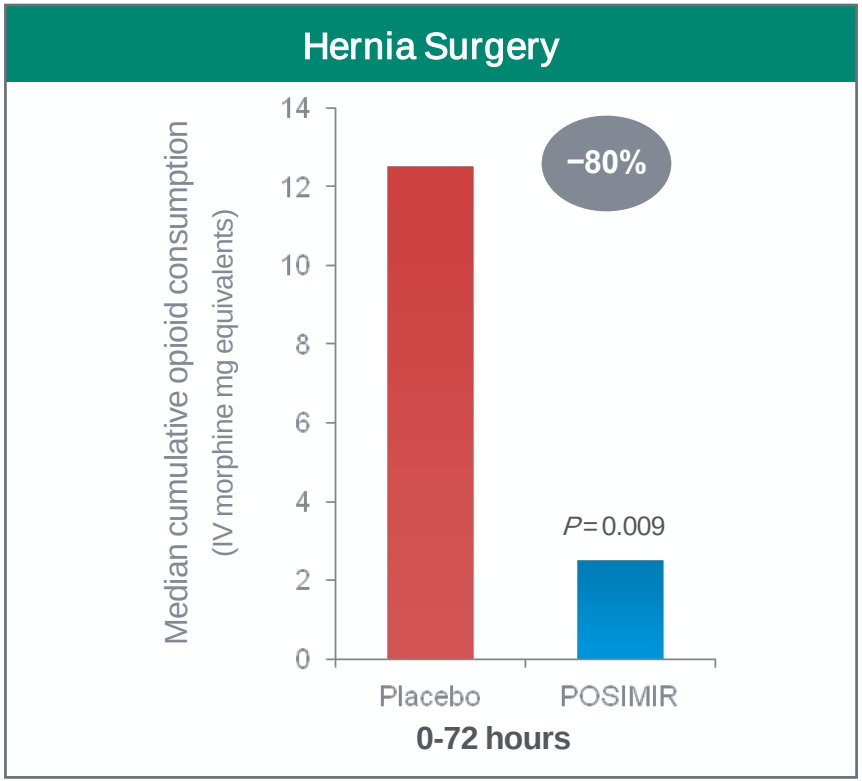


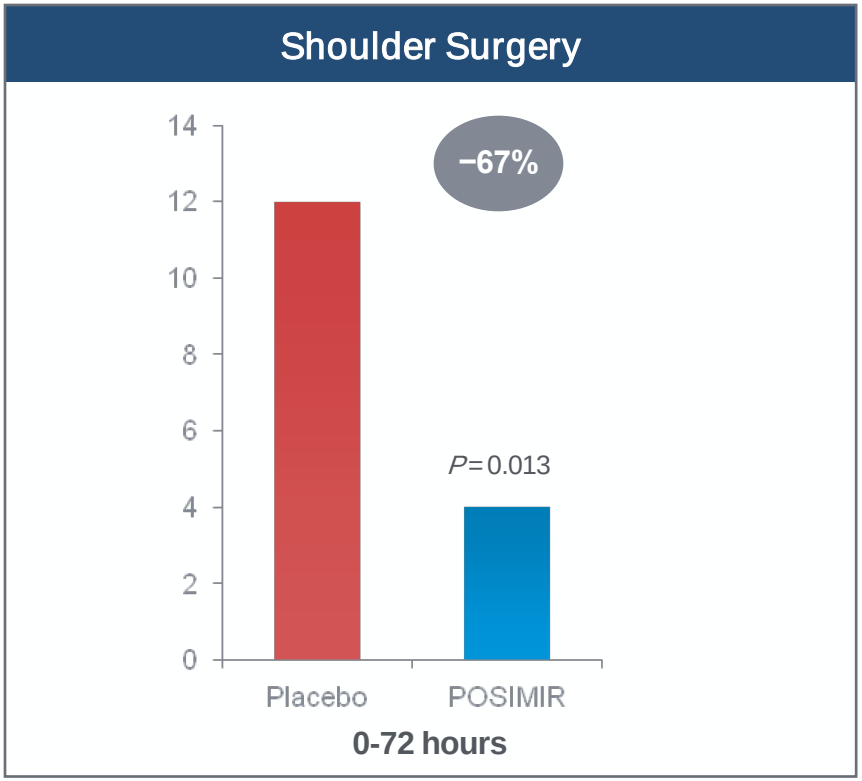
Shoulder Surgery



P-values derived from ANOVA.

POSIMIR®: Reduction in Opioid Use

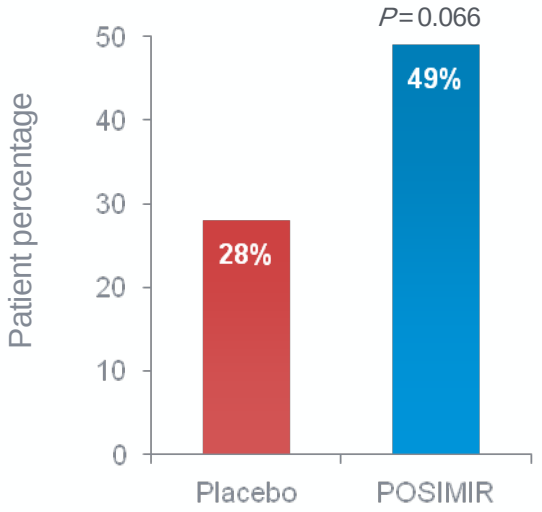




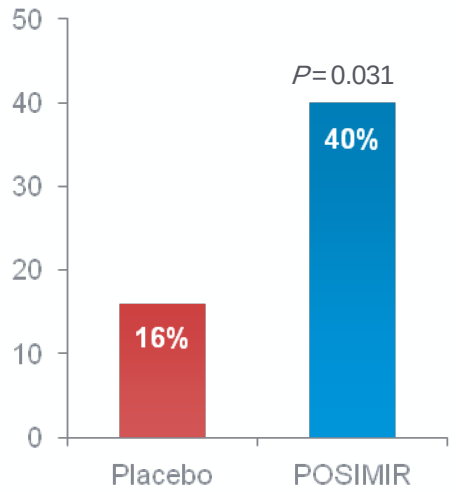
P-values derived from nonparametric Wilcoxon Rank Sum test.

POSIMIR®: Proportion of Patients NOT Taking ANY Supplemental Opioid

Hernia Surgery



Shoulder Surgery



% of Patients Not Taking Opioids, 0-72 hours

>20% more patients did not require a single opioid

P-values derived from CMH Chi-Square test adjusted by study sites.

POSIMIR®: Commercial Opportunity

>70 million surgeries
per year in the U.S.

~30 million procedures
as a potential available market

Large and underserved market

Compelling product concept for surgeons, anesthesiologists, and payers to get behind

- Better for patients
- Potentially large healthcare cost savings
- Benefits to administration technique
- Underlying desire for non-opioid, extended post-surgical pain relief

PERSERIS™ (risperidone)

Market Opportunity

- >21 million people are affected world-wide1, ~2.4 million adult Americans[2]
- Economic burden estimated at $156B in direct and indirect costs in the US[3]
- Long Acting Injectables (LAI) have been shown to increase adherence and lower rates of relapse & psychiatric hospitalizations compared to oral therapy[4]
- U.S. LAI schizophrenia market >$3.0B in 2017, grew 34% CAGR 2011-2017[5]
- Indivior setting up separate business unit for the launch[6]
- Indivior peak sales projection for PERSERIS: $200-300 million[7]
- PERSERIS was available in the U.S. in late 2018, with full promotional launch by Indivior with 50 reps in February 2019[7]

PERSERIS is a trademark of Indivior UK Limited

DURECT assigned certain U.S. patents to Indivior

Patents are relevant to PERSERIS™

Indivior payments to DURECT

$12.5 million upfront non-refundable

$5 million milestone on FDA approval

Single digit % Earn-Out based on U.S. net sales

PERSERIS™ (risperidone)

Extended-release injectable suspension, for subcutaneous use

Please see full prescribing information at www.perserishcp.com

INDICATION

- PERSERIS™ (risperidone) is indicated for the treatment of schizophrenia in adults.

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

See full prescribing information for complete boxed warning.

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.**
- **PERSERIS is not approved for use in patients with dementia-related psychosis.**

CONTRAINDICATIONS

- PERSERIS should not be administered to patients with known hypersensitivity to risperidone, paliperidone, or other components of PERSERIS.

WARNINGS AND PRECAUTIONS

- Cerebrovascular Adverse Reactions, Including Stroke in Elderly Patients with Dementia-Related Psychosis: Increased risk of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities. PERSERIS is not approved for use in patients with dementia-related psychosis.
- Neuroleptic Malignant Syndrome (NMS): Manage with immediate discontinuation and close monitoring.
- Tardive Dyskinesia: Discontinue treatment if clinically appropriate.
- Metabolic Changes: Monitor for hyperglycemia, dyslipidemia and weight gain.
- Hyperprolactinemia: Prolactin elevations occur and persist during chronic administration. Long-standing hyperprolactinemia, when associated with hypogonadism, may lead to decreased bone density in females and males.
- Orthostatic Hypotension: Monitor heart rate and blood pressure and warn patients with known cardiovascular disease or cerebrovascular disease, and risk of dehydration or syncope.
- Leukopenia, Neutropenia, and Agranulocytosis: Perform complete blood counts (CBC) in patients with a history of a clinically significant low white blood cell count (WBC) or history of leukopenia or neutropenia. Consider discontinuing PERSERIS if a clinically significant decline in WBC occurs in absence of other causative factors.
- Potential for Cognitive and Motor Impairment: Use caution when operating machinery.
- Seizures: Use caution in patients with a history of seizures or with conditions that lower the seizure threshold.

ADVERSE REACTIONS

- The most common adverse reactions in clinical trials (≥ 5% and greater than twice placebo) were increased weight, sedation/somnolence and musculoskeletal pain. The most common injection site reactions (≥ 5%) were injection site pain and erythema (reddening of the skin).

DURECT Corporation

Financial Overview

Nasdaq	DRRX
Recent Price	$0.75[1]
Shares O/S	162.1 MM[2]
Market Cap	$122 MM[1]
Cash & Investments	$34.5 MM[3]
Debt	$20.5 MM[3]
Federal NOL's	$348 MM[3]
Insider Buying	>2.5 MM shs[4]
Options in lieu of bonus	>$7.3 MM[4]
Reduced salaries and board fees for options:	>$2.2 MM[5]

Cupertino, CA headquarters

[1] As of March 11, 2019 [2] As of March 4, 2018 [3] As of December 31, 2018 [4] 2012-2017 [5] 2011-2017

Potential Key Drivers In 2019

Epigenetic Regulatory Program (DUR-928)

NASH multi-dose trial

- Planned for initiation in Q1 2019 with initial data in 2H 2019
- Supported by Phase 1b and pre-clinical data
- Early-stage clinical data can be a meaningful valuation catalyst

Psoriasis POC trial

- Planned for initiation in Q1 2019 with data in 2H 2019
- Supported by Phase 1b and pre-clinical data
- Partnering opportunity in psoriasis / atopic dermatitis

AH trial

- Advancing to higher dose in severe patients and assisting the set up of a parallel trial by Dr. Craig McClain at the University of Louisville, where the trial will be funded by grants

Product launch of PERSERIS™ by Indivior

Submission of full response to CRL for POSIMIR® in H1 2019

- Potential NDA approval in 2019

DURECT

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Appendix

Appendix

1	Epogen®,Procrit®, Neupogen®, Neulasta® - are all registered trademarks of their respective owners	Page 5
2	World Health Organization Website http://www.who.int/mental_health/management/schizophrenia/en/ accessed 9/15/17. National Institutes of Health Website https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=67 accessed 9/15/17	Page 32
3	Janssen's Invega Sustenna website https://www.invegasustenna.com/about-schizophrenia accessed 9/20/17	Page 32
4	J Clin Psychiatry 2016;77(6):764–771	Page 32
5	JAMA Psychiatry. 2015 August; 72(8): 822–829.	Page 32
6	According to IQVIA, per Jefferies research report dated October 11, 2018	Page 32
7	Indivior press releases dated December 18, 2018, February 14 and 27, 2019	Page 32