DURECT Corporation

A Biopharmaceutical Company

September 6, 2018

DURECT

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."

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DURECT Corporation

A Biopharmaceutical Company with a Rich Pipeline

- DUR-928 is under development for potential treatment of acute organ injury, chronic metabolic diseases, inflammatory conditions, and orphan diseases
  - Lead molecule in our Epigenetic Regulator program
  - Regulation of lipid metabolism, inflammatory response, and cell survival
  - Compelling data from more than 10 animal models
  - Phase 1b studies completed in NASH, CKD and psoriasis
    - Signals of biological activity from a single dose
  - Initiating 3 Phase 2 trials in 2018
- Pipeline of 505(b)2 programs
- Approved product and cash flow positive product lines
  - PERSERIS™ (risperidone) approved July 2018
  - ALZET®
  - LACTEL®

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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®)

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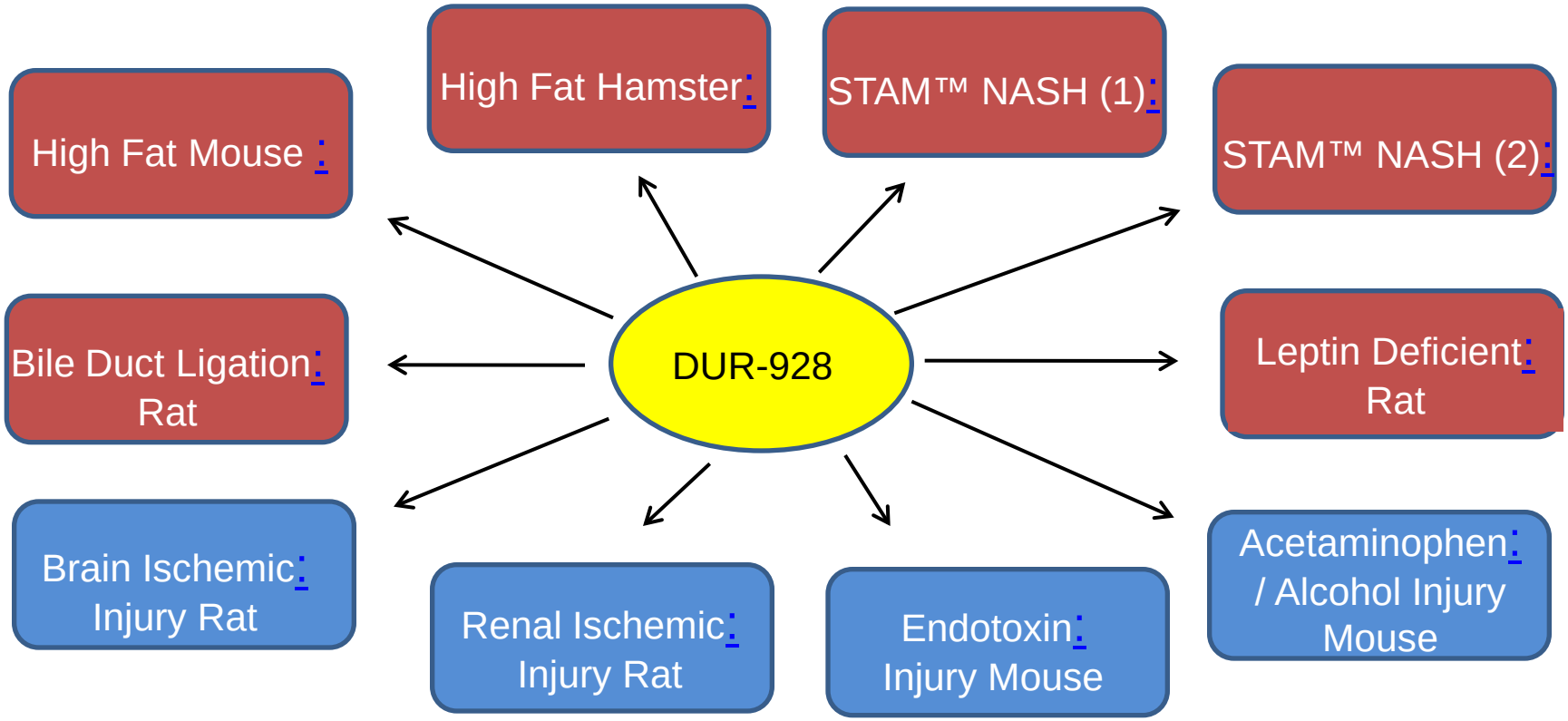
DUR-928
Compelling Animal Data



- Extensive, compelling pre-clinical data
- Positive data has been generated in each of the models shown
- Together, these have given us confidence in the activity of this drug candidate

Phase 1: Safety in healthy human subjects

- Over 140 individuals dosed (including Phase 1b studies)
- Oral, IV, IM and intradermal administration
- High doses resulted in plasma levels >1,000-fold higher than endogenous levels
- 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)

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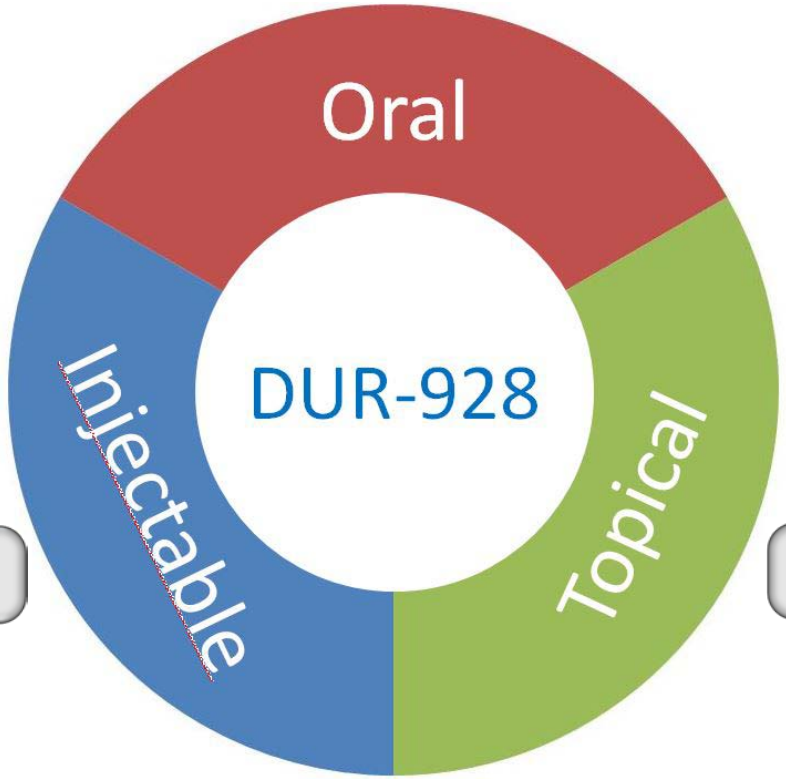
DUR-928 Development
Orphan and broad based indications

Chronic liver & metabolic disorders

NASH, PSC



Acute organ injuries

AH, AKI

Inflammatory skin disorders

Psoriasis, Atopic Dermatitis

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DUR-928
Potential in NASH

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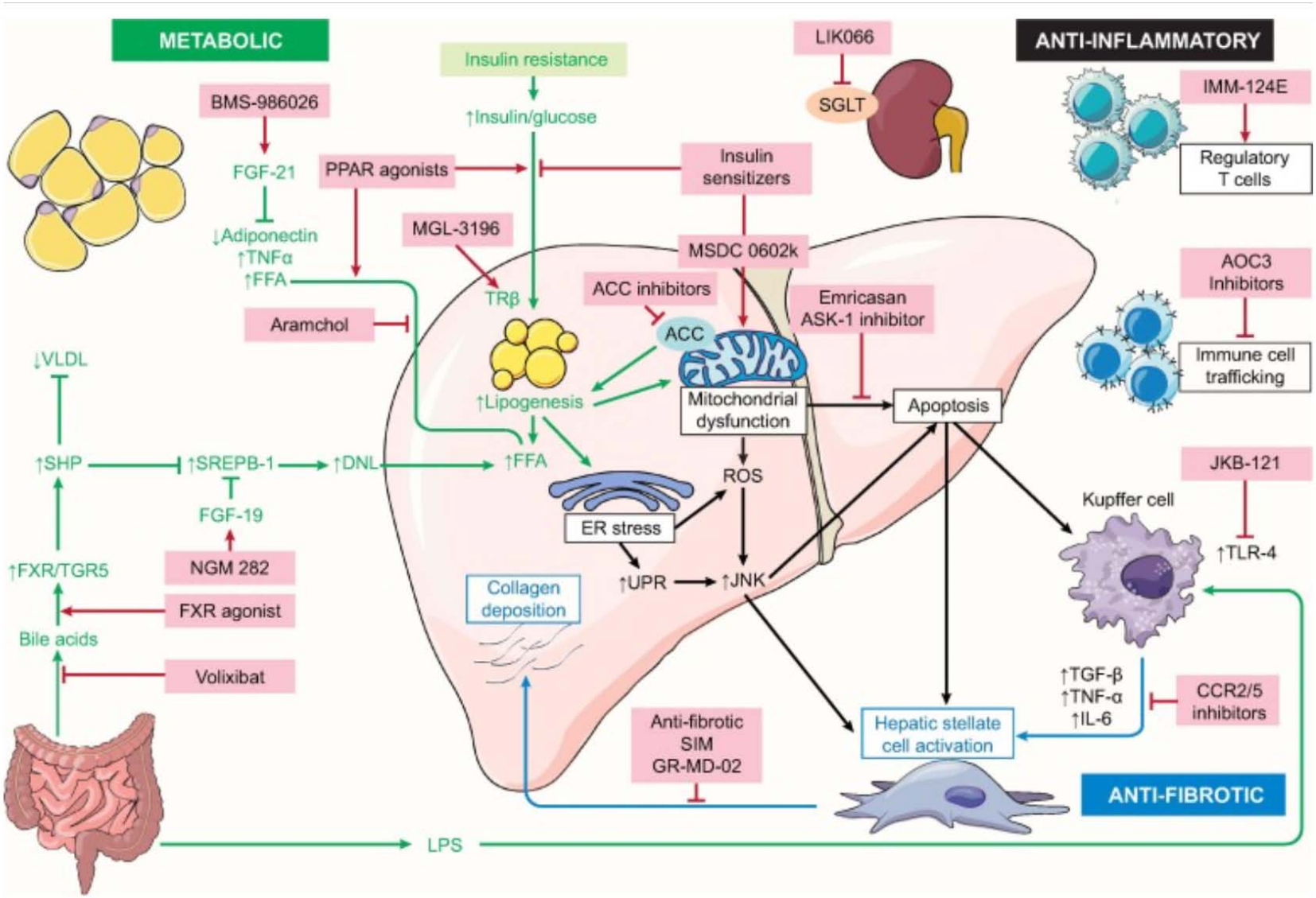
Mechanisms of Action of Pharmacologic Treatment for NASH are Complex



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

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DUR-928 may help simplify the solution

- Apoptosis **928**
  - Gilead, Conatus
- Inflammation **928**
  - Allergan/Tobera, BI, PPAR agonists (Genfit, etc)
- Lipogenesis/FFA **928**
  - Madrigal, Viking, Gilead/Nimbus, Galmed, NGM, BMS, PPAR agonists (Genfit, etc), FXR agonists (intercept, etc)
- Gluconeogenesis **928**
  - PPAR agonists (Genfit, etc), insulin sensitizers
- Collagen deposit **928**
  - Galectin
- Mitochondria dysfunction **928**
- Lipid transport **928**

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DUR-928 and NASH

- Cell culture and gene expression data
- Animal data
  - High Fat Diet mouse & hamster, Leptin deficient and STAM 1 & 2
  - Acute models of liver and kidney injury
- Phase 1b single dose data
- API manufacturing to commercial scale
- Long term toxicology is underway
- A 30 day dose ranging study is in planning

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DUR-928

Phase 1b: Initial Patient Study (NASH)

- Conducted in Australia, oral formulation
- 2 successive cohorts evaluating single doses of DUR-928:
  - 20 NASH patients and 12 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

➢ While not designed to assess efficacy, biologic activity was observed after a single dose in both cohorts

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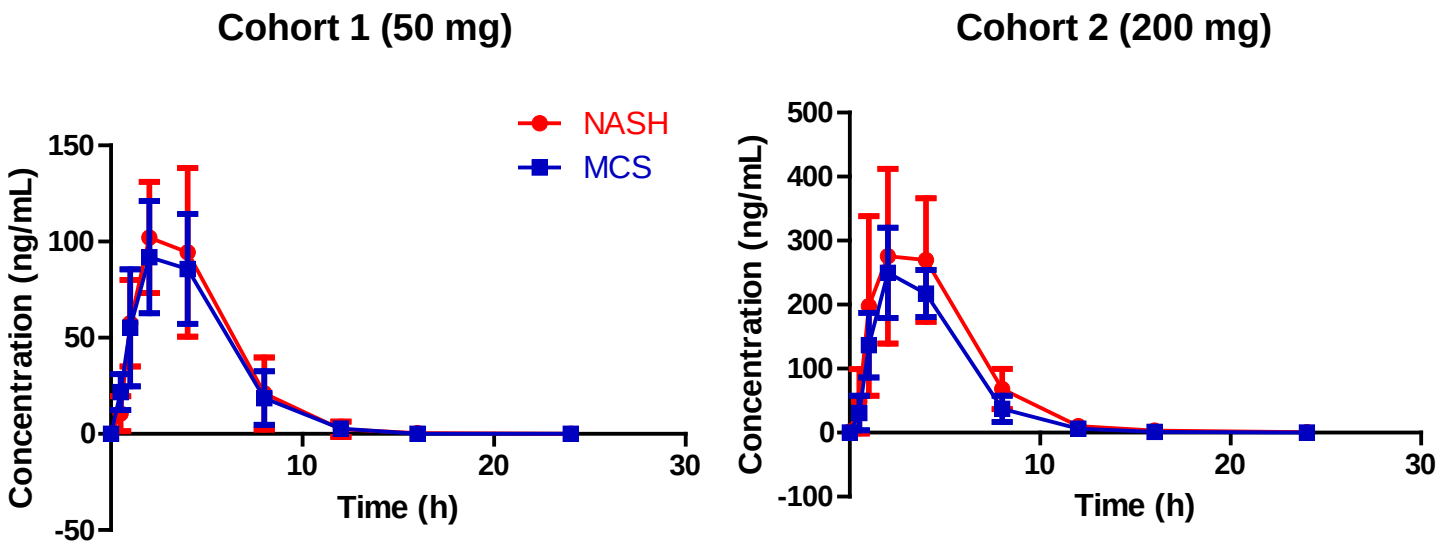
Phase 1b: NASH Patient Study

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



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

Note: NASH group includes cirrhotic and non-cirrhotic patients

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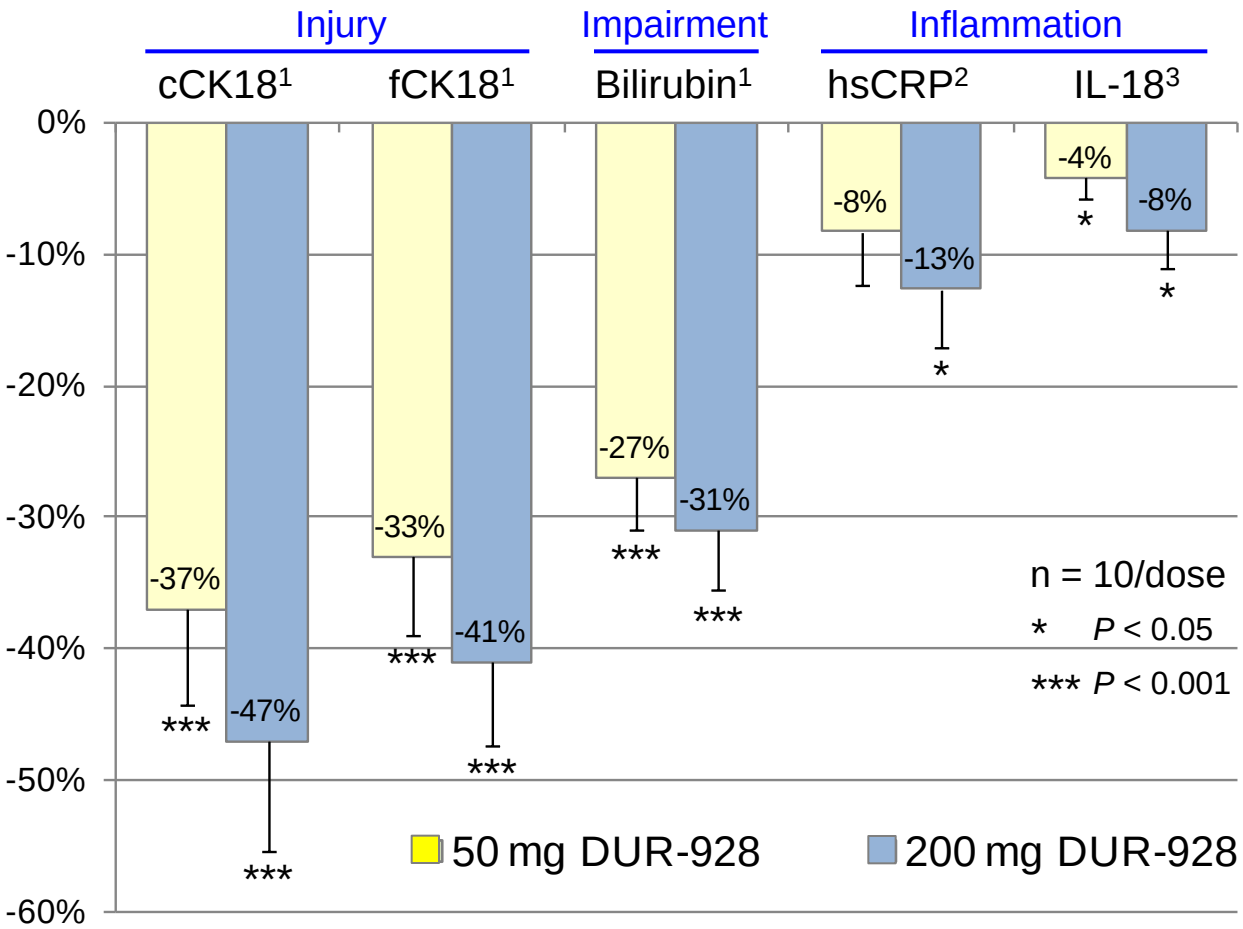
Phase 1b: NASH Patient Study

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



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

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Acute Organ Injury Program

Phase 1b: Initial Patient Study (renal impaired patients)

- Conducted in Australia, injectable (IM) formulation
- 2 successive cohorts evaluating single doses of DUR-928:
  - 11 renal function impaired patients (stage 3 and 4 chronic kidney disease) and 6 matched control subjects (by age, BMI, and gender) per cohort
  - Single-site, open label, dose ranging safety and PK study

- DUR-928 was well tolerated among all subjects; PK parameters between kidney function impaired patients and matched controls were comparable
- While the number of subjects was small, those with high baseline levels saw reductions in bilirubin and CK-18s at 12 hours, consistent with the NASH Phase 1b study

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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

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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

Disease Models:

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

Normal Animals:

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

Patients:

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

Healthy Subjects:

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

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DUR-928
2018 Phase 2 Studies

INDICATION	Preclinical	Phase 1	Phase 2	Phase 3	NDA	Patient Population
Alcoholic Hepatitis (AH)			→			>320,000 hospitalized in the U.S.[1]
Primary Sclerosing Cholangitis (PSC)			→			Orphan Indication
Psoriasis			→			7.5 million in the U.S.[2]

1 J Clin Gastroenterology. 2015 July; 49(6): 506-511
2 National Psoriasis Foundation

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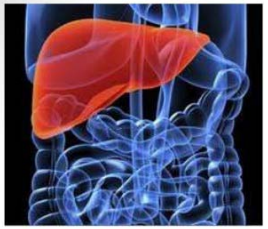
Alcoholic Hepatitis (AH)

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



Alcoholic Hepatitis

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

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Alcoholic Hepatitis (AH)
Rationale for DUR-928

- MELD Score (Model of End Stage Liver Disease)
  - MELD score & mortality rate (MELD 15=13%, 20=25%, 25=42%, 30=62%)
  - Accepted proof-of-concept marker for AH
  - Bilirubin, creatinine and prothrombin time
  - AH patients' MELD scores and CK-18 markers remain elevated for an extended time

- 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

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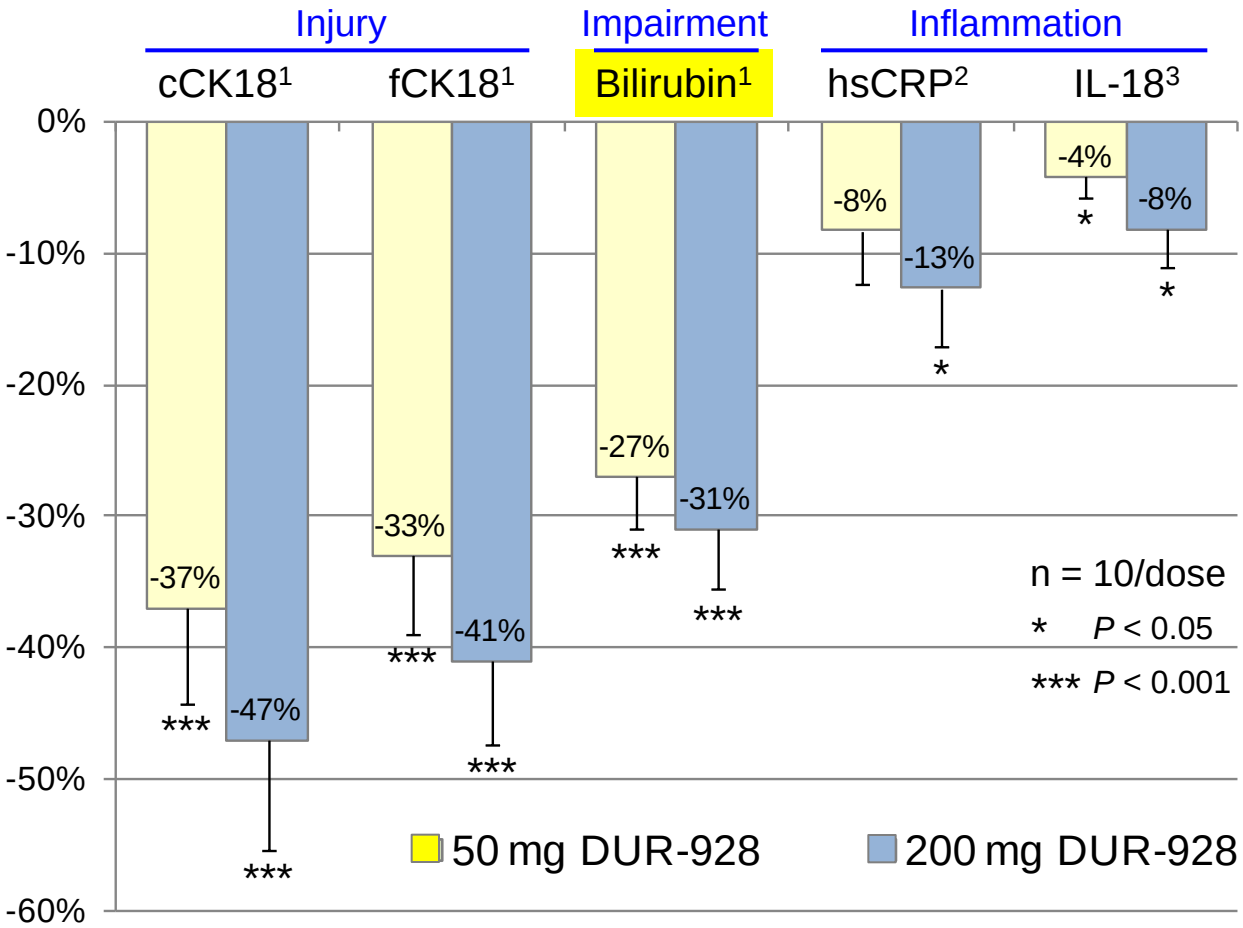
Phase 1b: NASH Patient Study

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



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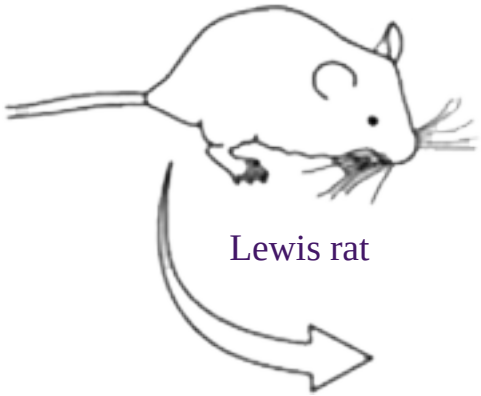
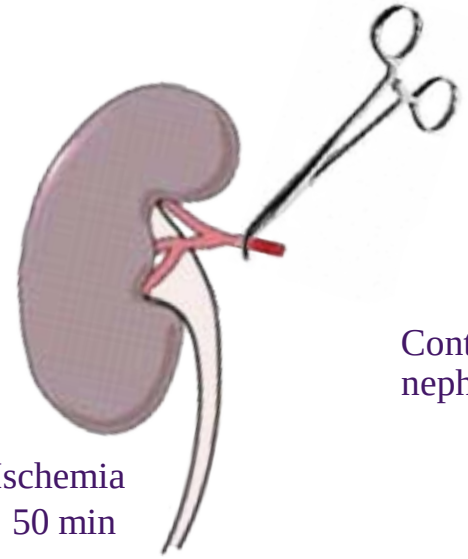
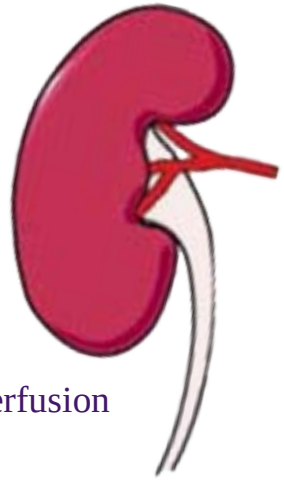
Renal ischemia / reperfusion injury
Effect of DUR-928 on temporary renal artery occlusion rat model

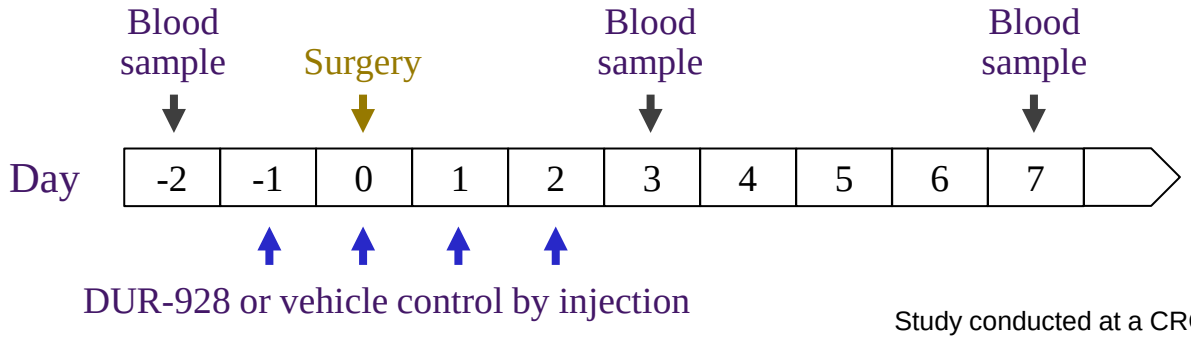
Ischemic Injury





Contralateral nephrectomy





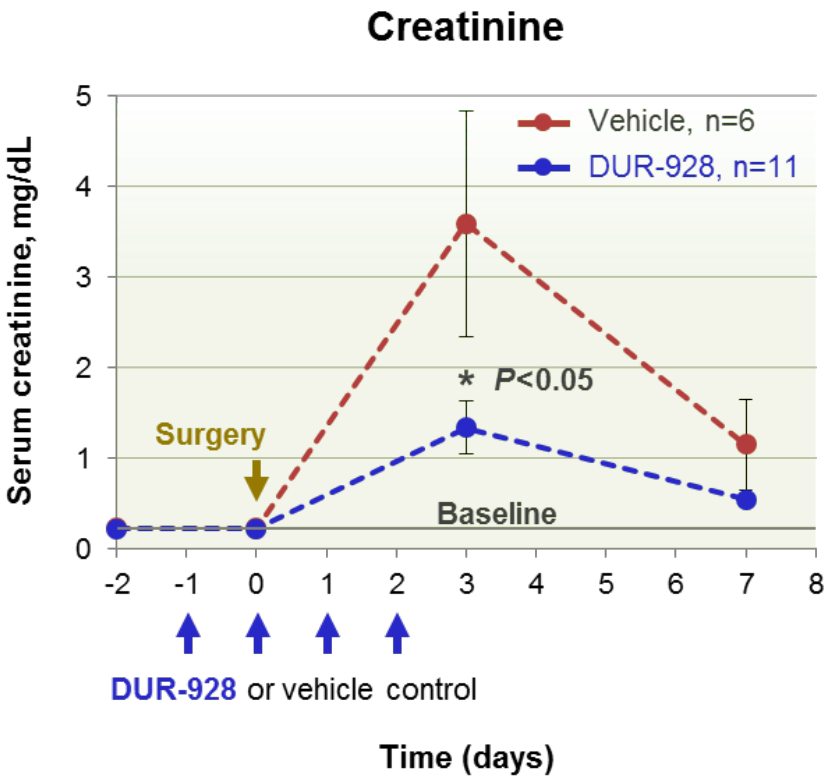
Note: study was repeated multiple times

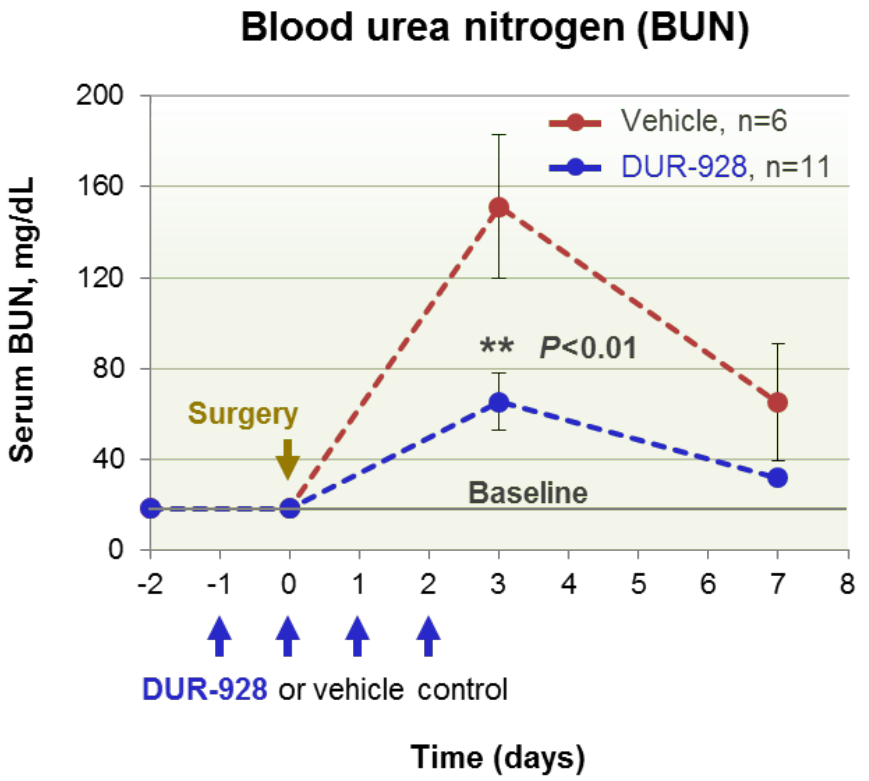
Study conducted at a CRO in Montreal
Data on file. DURECT Corporation

DURECT

Renal ischemia / reperfusion injury
Effect of DUR-928 on temporary renal artery occlusion rat model

Reductions in serum creatinine and BUN





Values are means±SD

Data on file. DURECT Corporation

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Alcoholic Hepatitis (AH)

Phase 2a study

- Open label, sequential dose escalation study (n = 24-36) 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 (tbd)

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

- Design features
  - Open label allows for interim looks at data

- Positive read-out may have implications for other liver diseases and other acute organ injuries

- Expected timing
  - Started enrolling Q2 2018, interim data in 2018

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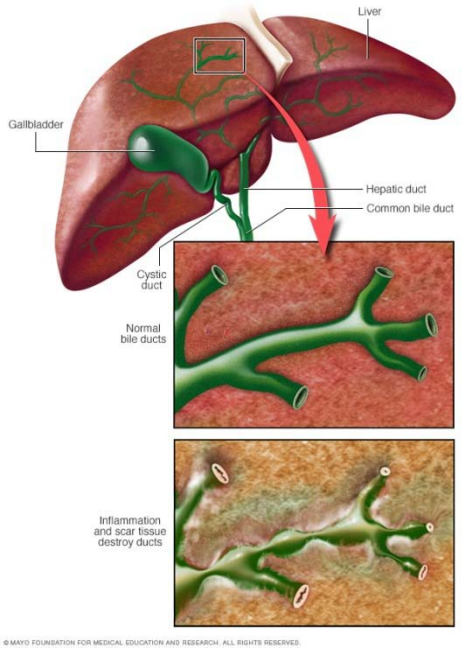
Primary Sclerosing Cholangitis (PSC)

Overview

- Autoimmune cholestatic liver disease
- Bile ducts carry digestive liquid bile from the liver to the small intestine
- Inflammation causes scars, narrowing bile ducts
- Leads to liver failure, infections and tumors of the bile duct or liver – ultimately requiring liver transplant
- ~75% of patients also have Inflammatory Bowel Disease (IBD)
- Typically marked by elevated serum ALP (alkaline phosphatase)
- Orphan disease: ~44,000 in the U.S.[1]
- No approved treatment



[1] Combination of (a) Bambha K, Kim WR, Talwalkar J, et al. Incidence, clinical spectrum, and outcomes of primary sclerosing cholangitis in a United States community. *Gastroenterology*. 2003;125(5):1364-1369; and (b) Bureau C. U.S. and World Population Clock. 2017; https://www.census.gov/popclock/. Accessed March 8, 2017.

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Primary Sclerosing Cholangitis (PSC)
Rationale for DUR-928

- Biology and Animal models
  - Improved hepatocyte function and survival
    - Reduction in bilirubin and cell death markers (CK-18s)
  - Bile duct ligation study: reduced bilirubin
  - STAM model and others: reduced ALP & hepatocyte nodule formation

- Phase 1b NASH & Chronic Kidney Disease data
  - Reductions seen in bilirubin and CK-18s from a single dose

- PSC may allow us to see a signal in 1 month using ALP and other biomarkers

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Primary Sclerosing Cholangitis (PSC)

Phase 2a study

- Randomized, open label, 2 dose groups, daily oral dosing for 4-weeks with follow-up for 4-weeks
  - 10 mg dose: n = 15-20
  - 50 mg dose: n = 15-20
- Objectives
  - Safety, PK and PD
  - % change from baseline of serum alkaline phosphatase (ALP), other biomarkers
- Design features
  - Open label allows for interim looks at data
  - ALP is an accepted proof-of-concept marker for PSC
- Expected timing
  - Started enrolling Q1 2018
  - Interim data in 2018

Note: We have Orphan Drug Designation for DUR-928 to treat PSC

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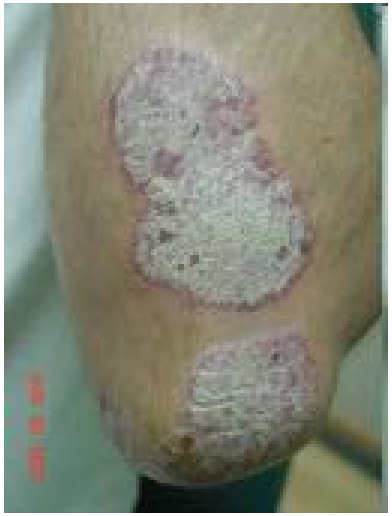
Psoriasis

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

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Psoriasis Phase 2 trial
DUR-928

- Psoriasis plaque microinjection Phase 1b study
  - Reduced LPSI (local psoriasis severity index) scores
- Reductions seen in inflammatory biomarkers and CK-18s from a single dose in Phase 1b NASH and CKD studies
- POC study with each patient receiving active and placebo topical formulations
  - Double blinded, placebo-controlled
  - Topical formulation dosed contralateraly with active and placebo
  - 2 month study duration per patient, including follow up

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DUR-928 Summary

- Impressive results from more than 10 animal models
- High doses resulted in plasma levels >1,000-fold higher than endogenous levels, well tolerated at all doses
- Encouraging data from Phase Ib single dose studies in NASH, CKD and Psoriasis patients
- Oral, IV, IM and topical formulations in place for clinical studies, API manufacturing at commercial scale
- Dosing in 2 Phase 2a studies underway with a third planned to initiate this year

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PERSERIS™ (risperidone) *extended-release injectable suspension*

Approved by FDA in July 2018

- Indicated for the treatment of schizophrenia in adults[1]
- PERSERIS is to be administered once monthly by subcutaneous injection by a healthcare professional[1]
- Neither a loading dose nor any supplemental oral risperidone is recommended[1]
- Robust Phase 3 and safety clinical trials comprising over 1150 patients

[1] Please see full prescribing information at www.indiviormedia.com

INDIVIOR

DURECT

PERSERIS™ (risperidone)

extended-release injectable suspension, for subcutaneous use

Please see full prescribing information at www.indiviormedia.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).

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PERSERIS™ (risperidone)

Market Opportunity

- >21 million people are affected world-wide[1], ~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]
- LAI U.S. Sales exceeded ~ $2.4B in 2016[5]
- Indivior peak sales projection for PERSERIS: $200-300 million[6]
- Indivior setting up separate business unit for the launch[6]
- Indivior reviewing appropriate launch timing[7]

1 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
2 Janssen's Invega Sustenna website https://www.invegasustenna.com/about-schizophrenia accessed 9/20/17
3 J Clin Psychiatry 2016;77(6):764–771
4 JAMA Psychiatry. 2015 August ; 72(8): 822–829.
5 IMS Sales, factored for schizophrenia
6 Indivior press release dated February 15, 2018; assumes no material change in U.S. market circumstances
7 Indivior press release dated July 30, 2018

INDIVIOR

DURECT

Patent Purchase Agreement with Indivior
Overview

- 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

➢ July 27, 2018: Indivior announced the NDA approval for PERSERIS™ (risperidone) extended-release injectable suspension, for subcutaneous use

POSIMIR®: Post-Operative Pain Control
SABER®-Bupivacaine

- Up to 3 days of post-op pain control, non-narcotic
- Designed for local control of post-surgical pain, plus reduced narcotic use and associated side effects and costs
- US commercialization rights licensed to Sandoz in May 2017
- Phase 3 clinical trial (PERSIST) in laparoscopic cholecystectomy (gallbladder removal) did not meet primary efficacy endpoint
  - We are evaluating and considering potential next steps

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DURECT Corporation
Financial Overview

- Nasdaq: DRRX
- Recent Price: $1.31[1]
- Shares O/S: 162.0 MM[2]
- Market Cap: $212 MM[1]
- Cash & Investments: $42.5 MM[3]
- Debt: $20 MM[3]

- Federal NOL's: $327 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 Aug 31, 2018 [2] As of July 30, 2018 [3] As of June 30, 2018 [4] 2012-2017 [5] 2011-2017

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Potential Key Drivers Next 12-18 months

- Phase 2 data in multiple indications (DUR-928)
  - AH
  - PSC
  - Psoriasis
  - Initiate other Phase 2 study or studies
- Product launch of PERSERIS™ by Indivior
- Decision on next steps with POSIMIR®
- Potential new collaboration(s)

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DURECT Corporation

A Biopharmaceutical Company

September 6, 2018

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