DURECT Corporation

A Biopharmaceutical Company

November 3, 2017

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

- Epigenetic NCE's for orphan diseases (PSC), acute organ injury and chronic metabolic diseases (including NAFLD/NASH), and inflammatory conditions (including psoriasis)
  - Family of endogenous small molecules
  - DUR-928: lead molecule with compelling data from more than 10 animal models
  - More than 140 people dosed in Phase 1 studies
  - Phase 1b activity in NASH and psoriasis patients
- Pipeline of 505(b)2 programs
  - Including RBP-7000, POSIMIR® and REMOXY® ER
- Cash flow positive product lines
  - ALZET® and LACTEL®

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Epigenetic Regulator Program

- Family of ENDOGENOUS epigenetic regulators and analogues
  - Sulfated oxysterols: a new class of therapeutics
  - Regulation of lipid metabolism, inflammatory response, and cell survival
  - In-licensed in 2012; exclusive WW rights with patents issued and pending

- 3 programs, many potential orphan & broad-based indications
  - Chronic metabolic disorders . . . . . Oral administration
  - Acute organ injuries . . . . . Injection (SC, IM, IV)
  - Inflammatory skin disorders . . . . . Topical

- Lead molecule: DUR-928
  - Compelling data from more than 10 animal models
  - Phase 1b studies completed in NASH, CKD and psoriasis
    - Signals of biological activity from single dose
  - Initiating multiple Phase 2 studies

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DUR-928
Biology

- Made in association with the mitochondria
  - Insulin is one of the mechanisms that regulate its production
  - Shown to stabilize mitochondrial membranes
- Modulates Lipid Metabolism
  - Decreases fatty acid, cholesterol and triglyceride synthesis (HMGCR, ACC, FAS, others)
  - Regulates lipid absorption and transportation
  - Improves insulin sensitivity and glucose tolerance
- Regulates inflammation responses (including modulation of IL-1, IL-6, IL-18, hsCRP, TNFα, and other mediators during the inflammation state)
- Improves cell survival (including reduction of full length and cleaved CK-18)

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Epigenetic Regulator Program
Endogenous molecules

- 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
- 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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Compelling Animal Data

- Activity demonstrated in multiple metabolic disorders, inflammatory conditions and acute organ injury
  - Chronic model observations:
    - Suppresses inflammatory responses
    - Reduced fibrosis, hepatocyte ballooning, and lipid accumulation
    - Improved glucose tolerance, insulin sensitivity, and liver morphology
    - Improved cholestatic liver injury
  - Acute model observations:
    - Reduced mortality, inflammation, and cell death
    - Improved histology across multiple organs
- Treatment duration covering 1-2 injected doses (acute), to daily oral administration (chronic)

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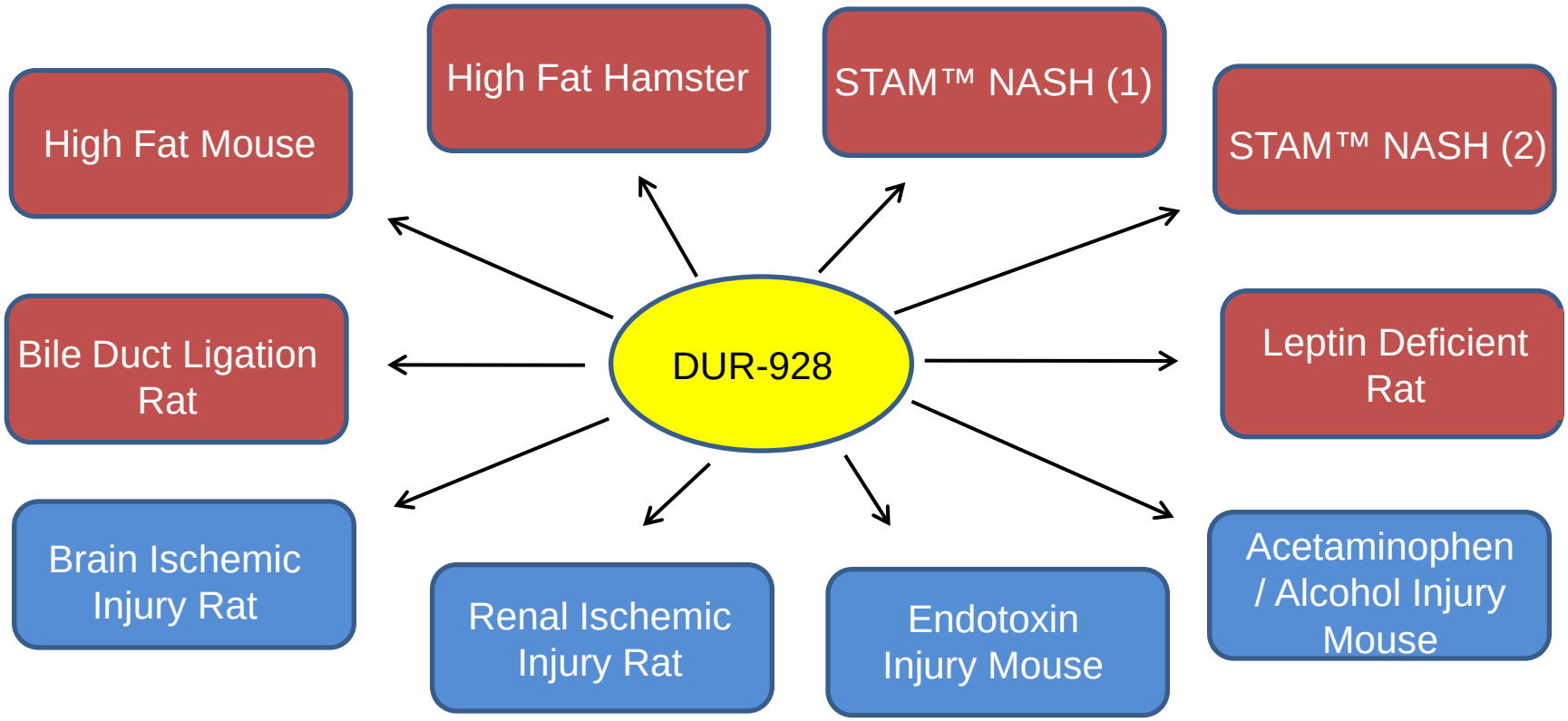
DUR-928
Compelling Animal Data



- 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

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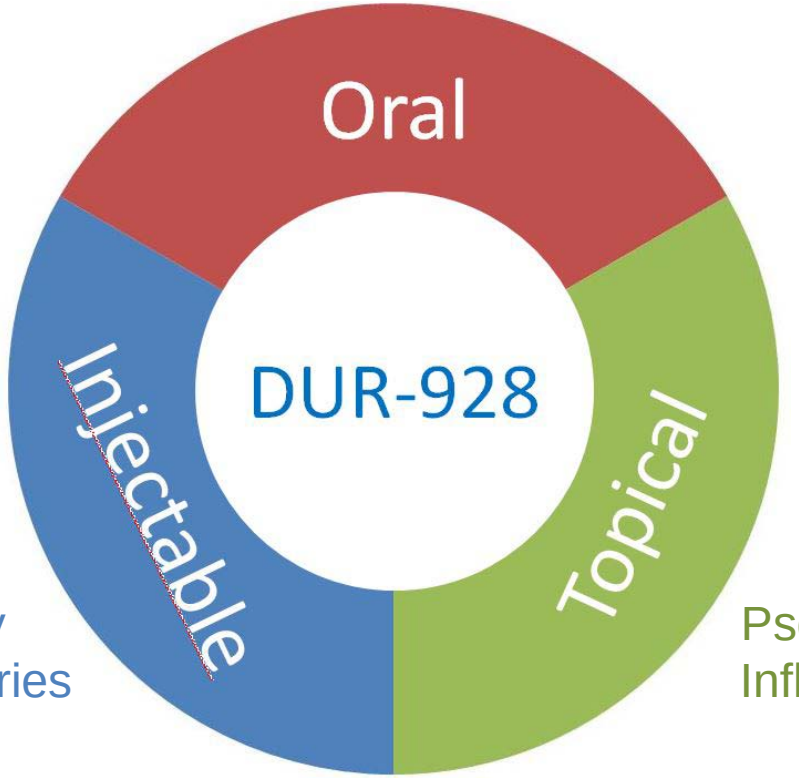
DUR-928 Development Programs
Orphan and broad based indications

NASH/ASH
Cholestatic liver diseases,
Other metabolic disorders



Liver / Kidney
Acute organ injuries

Psoriasis / atopic dermatitis
Inflammatory skin disorders

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Phase 1: Safety in healthy human subjects

Single-site, randomized, double-blind, placebo controlled studies

Oral Administration

- Single-ascending dose in 30 subjects
- Multiple-ascending dose in 20 subjects (5 consecutive days)
- Food effect in 8 subjects

Injectable Administration

- Single-ascending dose in 24 subjects
- Multiple-ascending dose in 10 subjects (5 consecutive days)
- IV infusion in 16 subjects

- Over 140 individuals treated (including Phase 1b studies)
- 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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Chronic Metabolic Disease Program

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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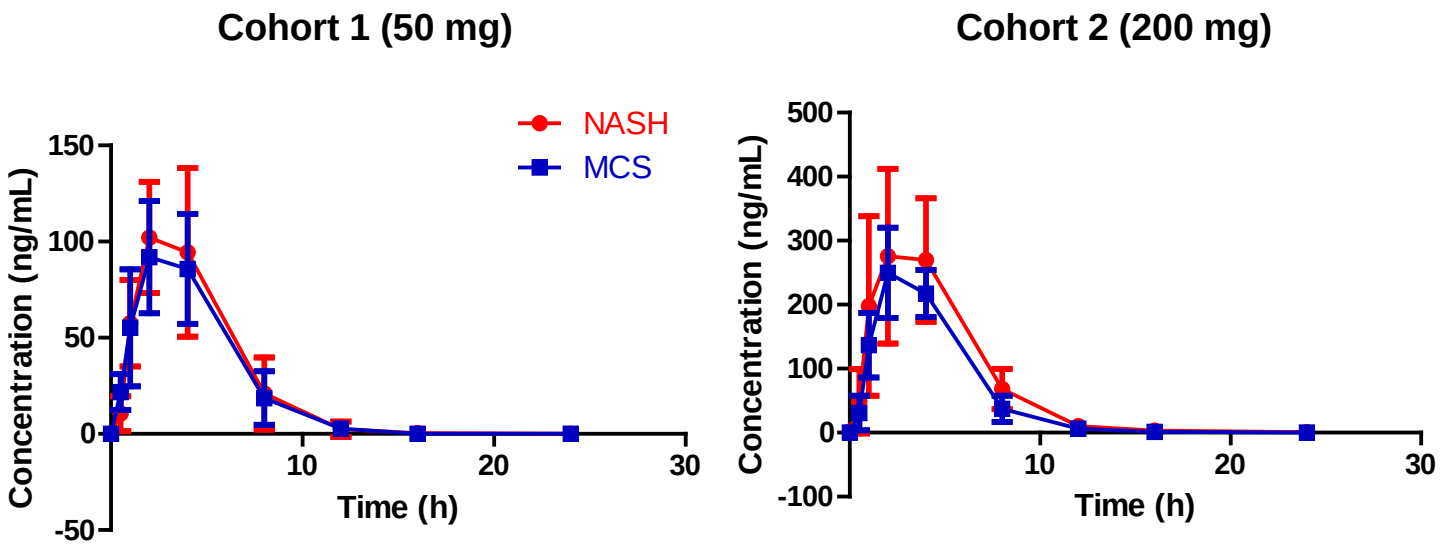
Phase 1b: NASH Patient Study

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 per cohort

Note: NASH group includes cirrhotic and non-cirrhotic patients

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Phase 1b: NASH Patient Study

High-sensitivity C-reactive Protein (hsCRP)

A marker of inflammation

	NASH Group 24 hour Mean Decrease
Low Dose	8%
High Dose	13%

IL-18

An inflammatory mediator implicated in both liver and kidney diseases

	NASH Group 8 hour Mean Decrease
Low Dose	4%
High Dose	8%

Periods shown are those of greatest effect

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

Note: NASH group includes cirrhotic and non-cirrhotic patients

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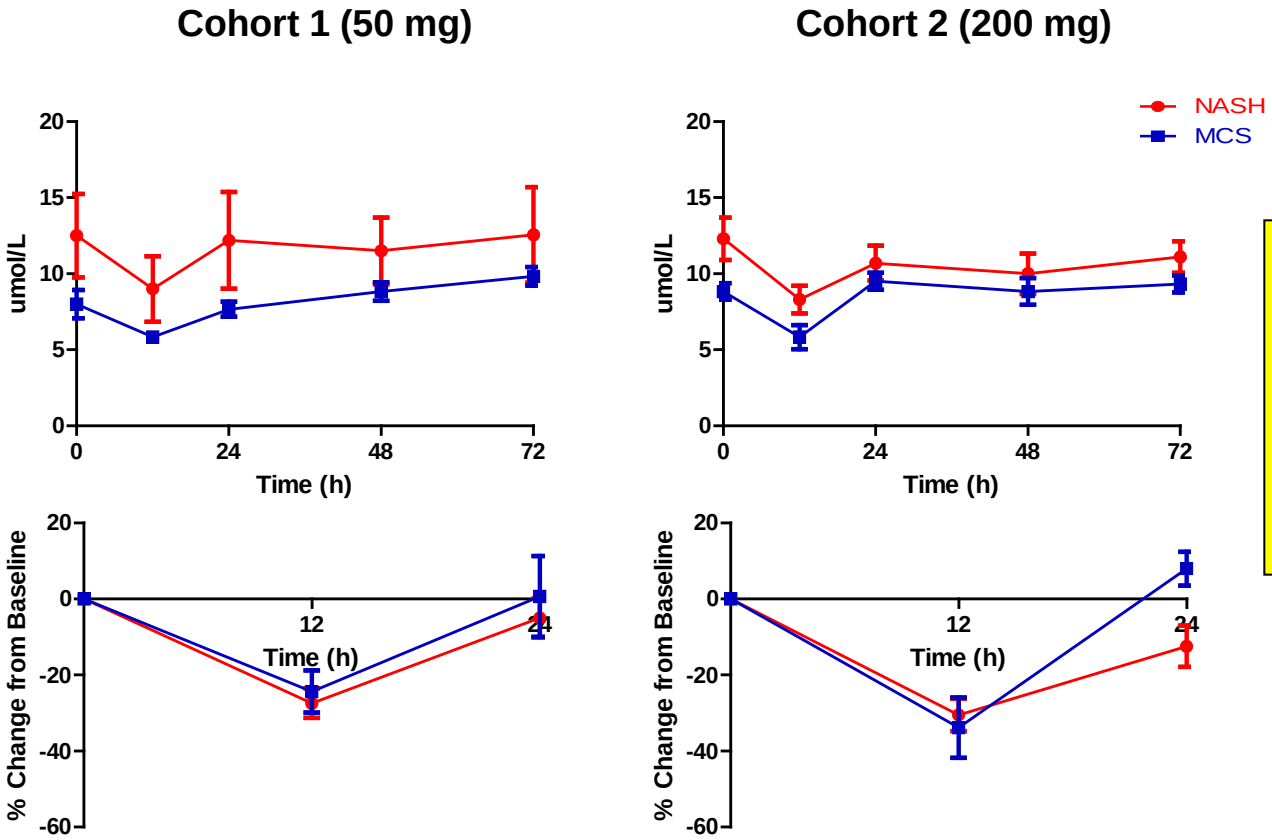
Phase 1b: NASH Patient Study

Total Bilirubin



	NASH Group 12 hour Mean Decrease
Low Dose	27%
High Dose	31%

Period shown is that of greatest effect

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

Note: NASH group includes cirrhotic and non-cirrhotic patients

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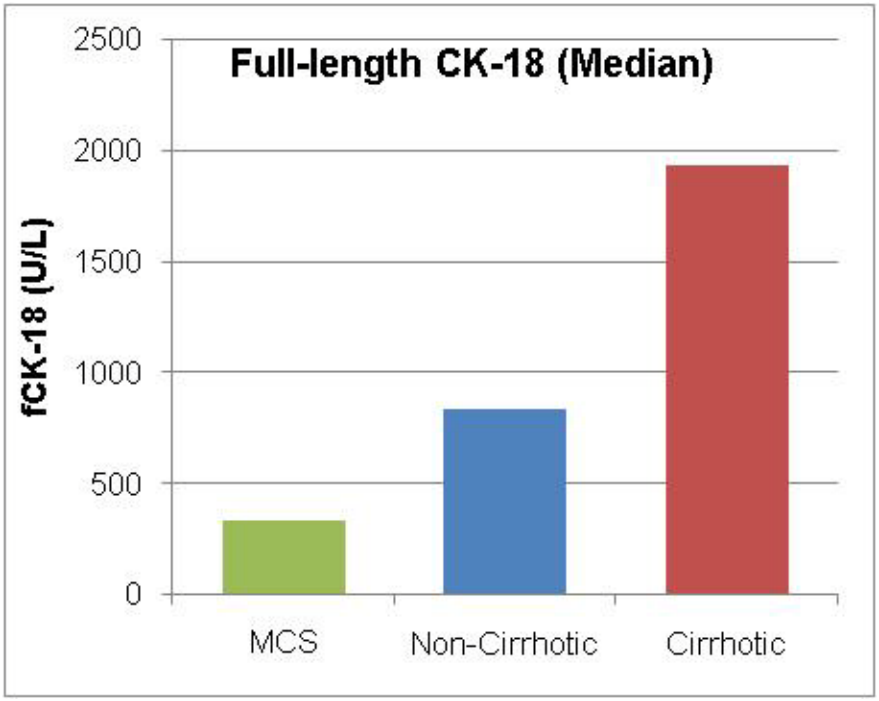
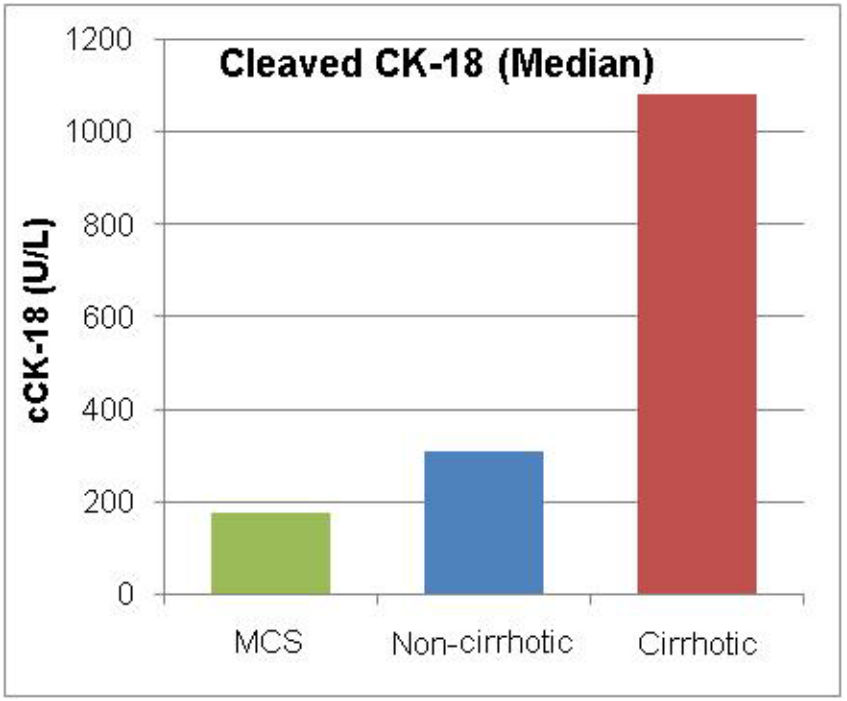
Phase 1b: NASH Patient Study

CK-18 – cell death marker

Baseline Value in Study Subjects





N = 10 NASH patients, 6 Matched Control Subjects – from low dose cohort

Note: NASH group includes cirrhotic and non-cirrhotic patients

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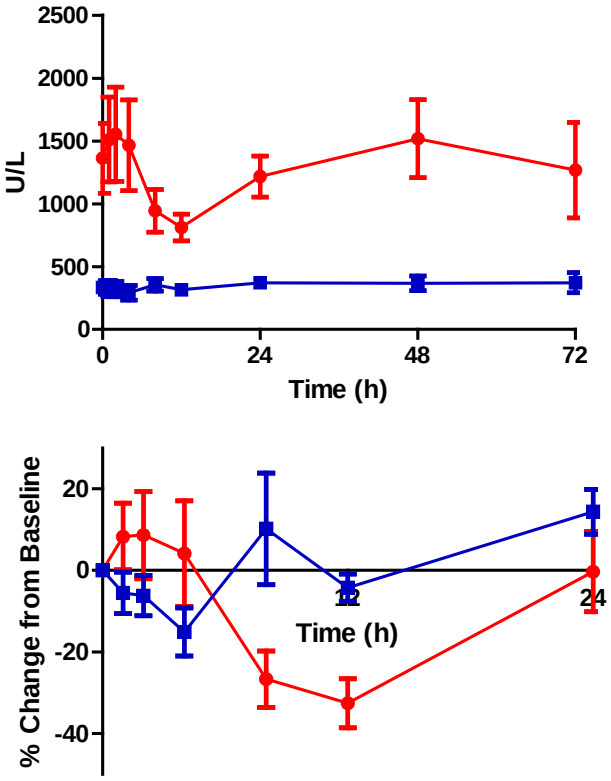
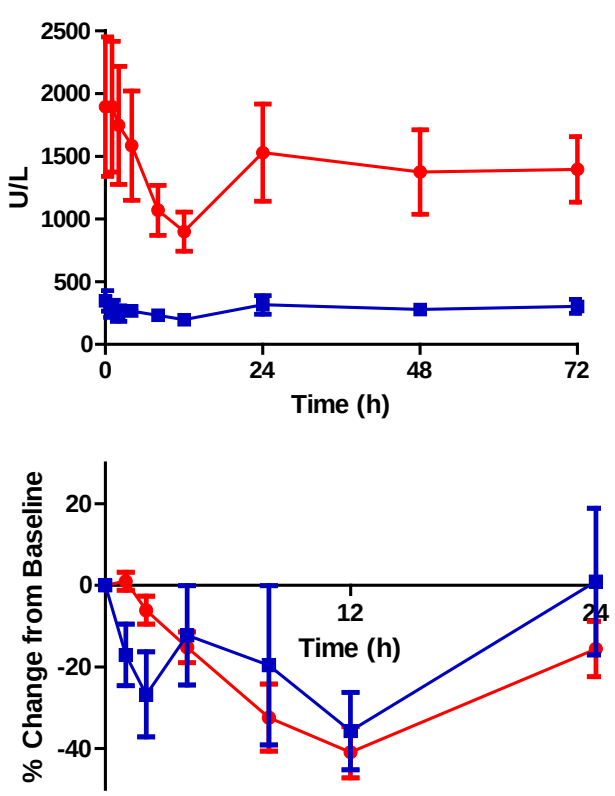
Phase 1b: NASH Patient Study

Full-length CK-18

Cohort 1 (50 mg)



Cohort 2 (200 mg)



	NASH Group 12 hour Mean Decrease
Low Dose	33%
High Dose	41%

Period shown is that of greatest effect

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

Note: NASH group includes cirrhotic and non-cirrhotic patients

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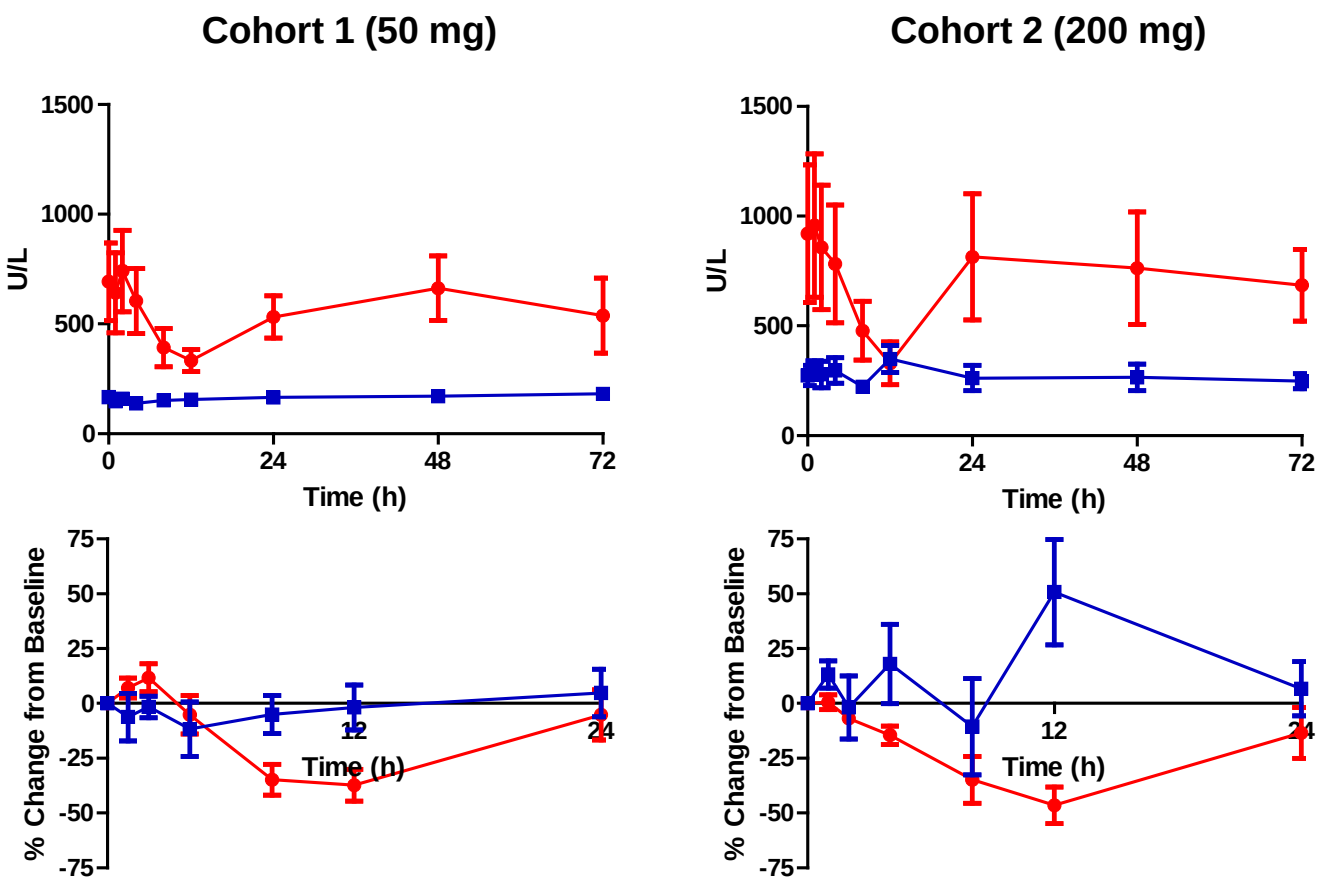
Phase 1b: NASH Patient Study

Cleaved CK-18



	NASH Group 12 hour Mean Decrease
Low Dose	37%
High Dose	47%

Period shown is that of greatest effect

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

Note: NASH group includes cirrhotic and non-cirrhotic patients

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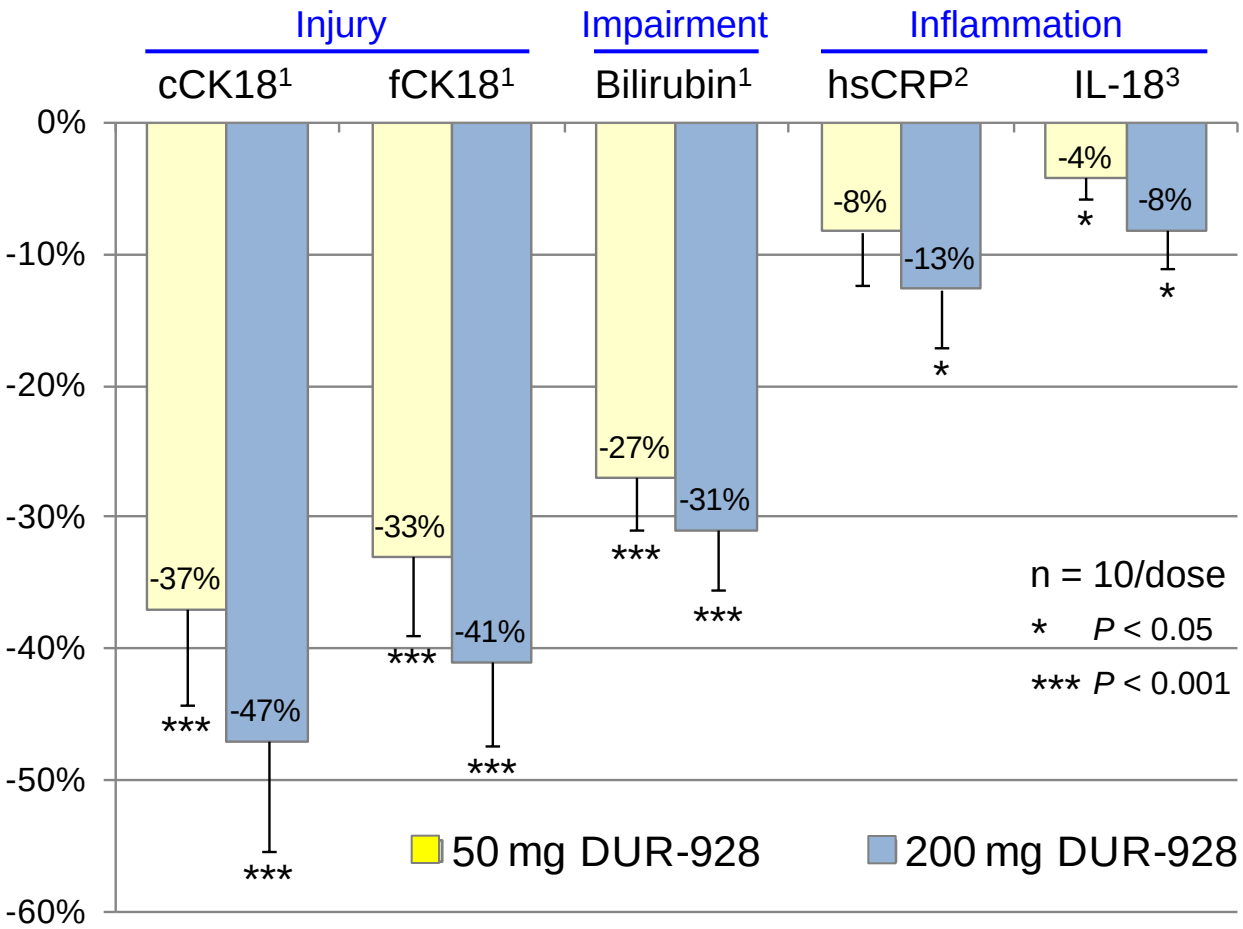
Phase 1b: NASH Patient Study

Biomarkers 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 well tolerated among all subjects; PK parameters between kidney function impaired patients and matched controls comparable

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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 development of a topical formulation of DUR-928 and a Phase 2 proof-of-concept study

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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 toxicology studies, covering oral and injectable administrations

Patients:

Demonstrated biologic activities in NASH 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 Development Programs: Next steps

- Oral Administration
  - Commence Phase 2 in PSC
- Injectable Administration
  - Commence Phase 2 in one or more acute indications
- Topical Administration
  - Proof-of-concept Phase 2 in psoriasis

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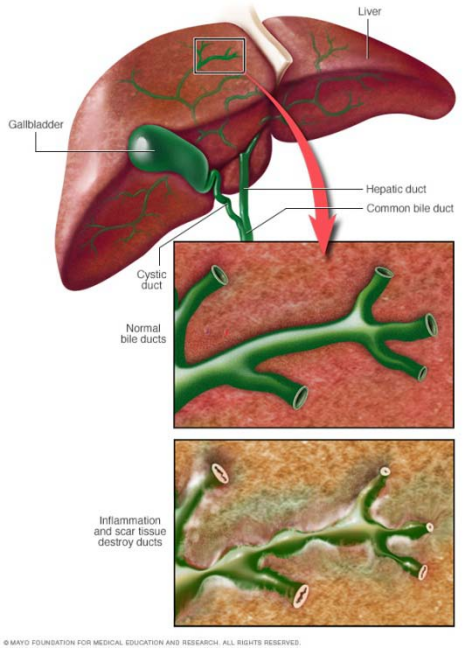
Primary Sclerosing Cholangitis (PSC)

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 IBD
- Typically marked by elevated serum ALP (alkaline phosphatase)
- Orphan disease: ~44,000 in the U.S.
- No approved treatment



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Primary Sclerosing Cholangitis (PSC)
Rationale for DUR-928

- Biology fits the disease
  - Anti-inflammatory and anti-fibrotic properties of DUR-928
  - Improvements to hepatocyte function (reduction in bilirubin) and reduction in cell death (CK-18)
- Animal models that are relevant to PSC
  - Bile duct ligation study
  - STAM mouse model and others
- Phase 1b NASH data
  - Reductions seen in bilirubin, inflammatory biomarkers and CK-18 from a single dose
- PSC may allow us to see a signal in 1 month without subjecting patients to a liver biopsy
  - Any signal may be relevant to other chronic liver diseases (e.g., NASH)

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Primary Sclerosing Cholangitis (PSC)

Phase 2 study

- Open label, 2 dose groups, daily oral dosing for 4-weeks with follow-up for 4-weeks
  - Low dose: n = 15-20
  - High dose: n = 15-20
- Primary endpoints
  - Safety
  - % change from baseline of serum alkaline phosphatase (ALP), other biomarkers
- Design features
  - Open label enhances recruitment, allows for interim looks at data
  - ALP is an accepted proof-of-concept marker for PSC
  - Utilize serum biomarkers rather than invasive liver biopsy
- Positive read-out may have implications for other liver diseases (NASH)
- Expected timing
  - Start enrolling Q4 2017
  - Initial data in 2018

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

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

- Up to 3 days of post-op pain control
- Unmet need: non-narcotic analgesia, 24-72 hours after surgery
- Designed for local control of post-surgical pain
- Plus reduced narcotic use and associated side effects and costs
  - Nausea, vomiting, ileus, constipation, respiratory depression
  - Potential for earlier hospital discharge

- US commercialization rights licensed to Sandoz in May 2017
- DURECT rights to the rest of the world

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POSIMIR®
Phase 3 Trial

PERSIST

- Phase 3 clinical trial in laparoscopic cholecystectomy (gallbladder removal)
- Part 1: POSIMIR vs. Placebo, n = 92
- Part 2: POSIMIR vs. Bupivacaine HCl, n = 296
  - Primary efficacy endpoint: pain intensity on movement during first 48 hours after surgery

➢ PERSIST did not meet the primary efficacy endpoint

  - We and Sandoz are working to understand the trial results more fully

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Indivior PLC

- Spun-out of Reckitt Benckiser in December 2014
- Indivior is traded on the London Stock Exchange (INDV), market cap of ~$3.6 billion[1]
- 2016 revenue of ~$1.1 billion and adjusted net profit of ~$254 million

[1] As of October 31, 2017

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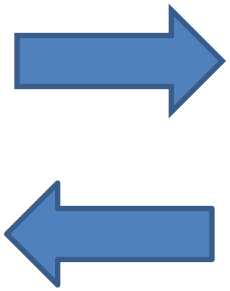
Patent Purchase Agreement with Indivior
Overview

- DURECT assigns certain U.S. patents to Indivior
- Patents are relevant to RBP-7000



- 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

➢ Indivior recently submitted an NDA for RBP-7000, implying potential approval in 2018

RBP-7000

- A once-monthly injectable risperidone to treat schizophrenia
  - Key late-stage pipeline product for Indivior

- Positive top-line results from Phase III safety and efficacy trial reported in May 2015
- Positive top-line data reported from long-term safety extension trial in March 2017
- US Health Economics & Outcomes Research completed

- Pre-NDA meeting held in August 2016
  - Indivior reported FDA agreement with proposed stability testing timelines & NDA submission strategy

➢ Indivior submitted the NDA for RBP-7000 on Sept. 28, 2017

INDIVIOR

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RBP-7000

PHASE III & HEOR DATA SUMMARY: RBP-7000[1]

- Once-a-month dosing
- Rapid onset of action
- No loading dose with initiation of treatment
- No supplemental dosing during treatment
- Demonstrated clinical efficacy & safety in schizophrenia
- Overall well tolerated
- Measurable quality of life and medication satisfaction benefits

[1]Indivior R&D Day | December 9th 2016 slide 91

INDIVIOR

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RBP-7000

Schizophrenia

- >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 RBP-7000: $200-300 million[6]

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 22, 2017; assumes no material change in U.S. market circumstances

INDIVIOR

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REMOXY® ER (oxycodone) extended-release capsules CII

- Extended-release oxycodone based on ORADUR® technology
  - Gel cap formulation intended to deter common methods of abuse
  - True-twice a day dosing and 5 mg dosage strength
- Exclusive development and commercialization rights licensed to Pain Therapeutics (PTIE)
  - PTIE controls and pays for development
  - DURECT eligible for a royalty of 6-11.5%, small milestone, and potential excipient sales
- Complete Response Letter (CRL) received by PTIE Sept 23, 2016
  - PTIE met with the FDA in February 2017
  - PTIE stated that they agreed with the FDA on 2 abuse potential studies required for resubmission, which they have substantially completed
  - Per PTIE, pre-NDA guidance meeting with FDA planned for November 14, 2017 and PTIE plans to resubmit the NDA in Q1 2018

REMOXY ER is an investigational drug candidate, not currently authorized by the FDA for marketing in the U.S. for any indication

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Company Financials

Shares Outstanding (October 27, 2017)		148.5	
Recent Share Price (November 3, 2017)	$	0.95	
Market Value	$	141.1	MM

June 30, 2017			
Cash and Investments	$	41.8	MM
Debt		19.9	MM

Federal NOL carryforward at 12/31/16	$	327	MM
State NOL carryforward at 12/31/16	$	216	MM

Insider selling	None	
Insider buying 2012-2016	>2.5 MM	shares
Insider ownership (excl. options)	~4.7%	
Options paid in lieu of cash bonuses [1]	>$5.7 MM	
Reduced salaries / BOD fees for options [2]	>$1.5 MM	

[1] 2012-2016
[2] 2011-2016

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Potential Key Drivers Next 12-24 Months

Next 12 months

- Start of Phase 2 (DUR-928), initial Phase 2 data
- Potential RBP-7000 approval
- REMOXY® ER data generated by Pain Therapeutics to support resubmission in Q1 2018, potential approval
- New collaboration(s)

Next 24 months

- Phase 2 data in multiple indications (DUR-928)
- Potential RBP-7000 launch
- Potential REMOXY® ER launch
- New collaboration(s)

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