DURECT Corporation

A Biopharmaceutical Company

March 19, 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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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
  - Conducting 3 Phase 2 trials in 2018
- Pipeline of late-stage 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
  - Conducting multiple Phase 2 studies in 2018

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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, 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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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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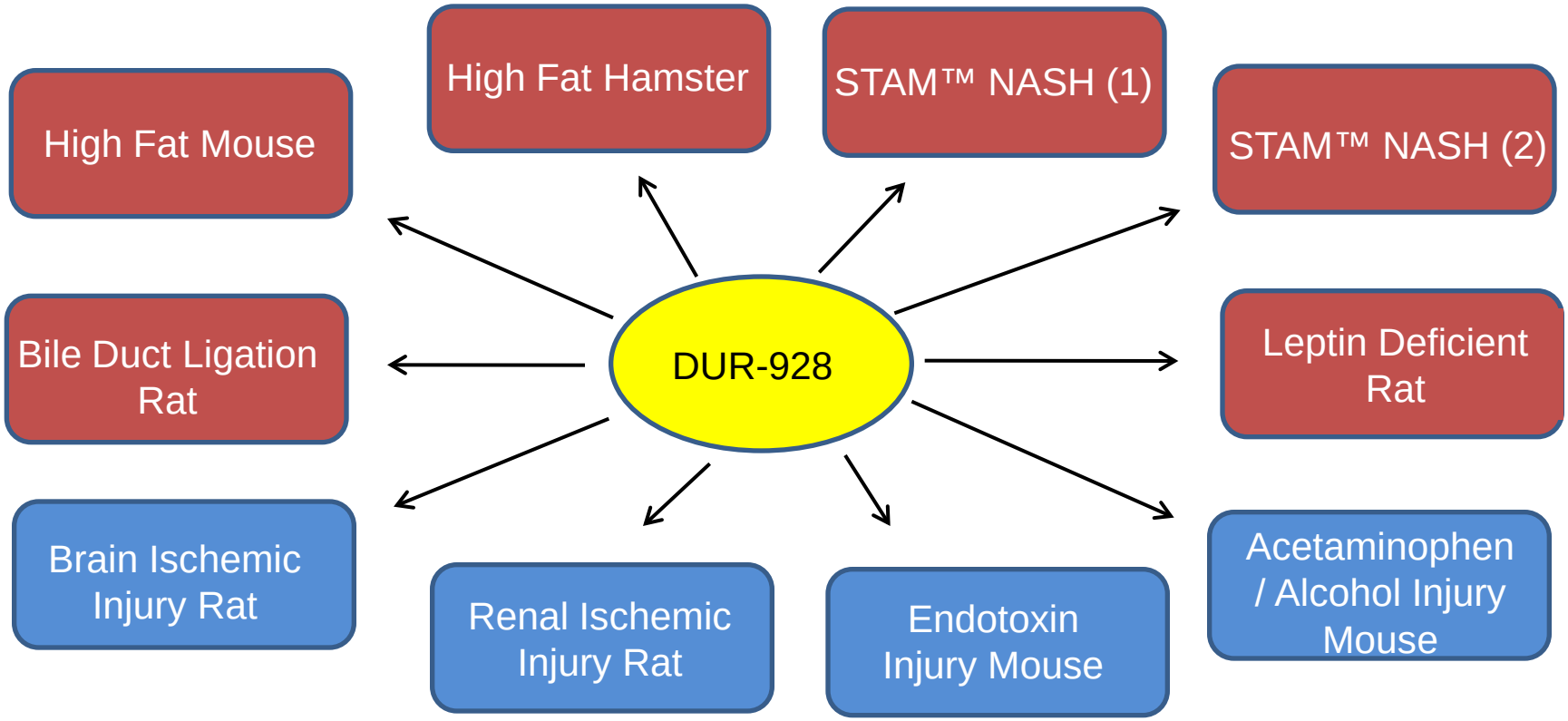
DUR-928
Compelling Animal Data



- 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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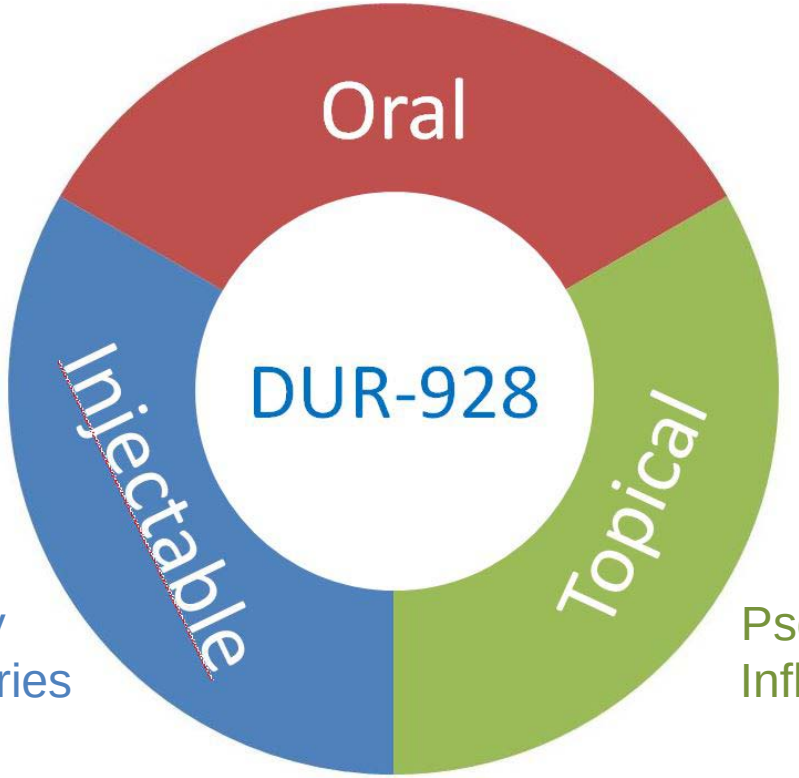
DUR-928 Development Programs
Orphan and broad based indications

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 dosed (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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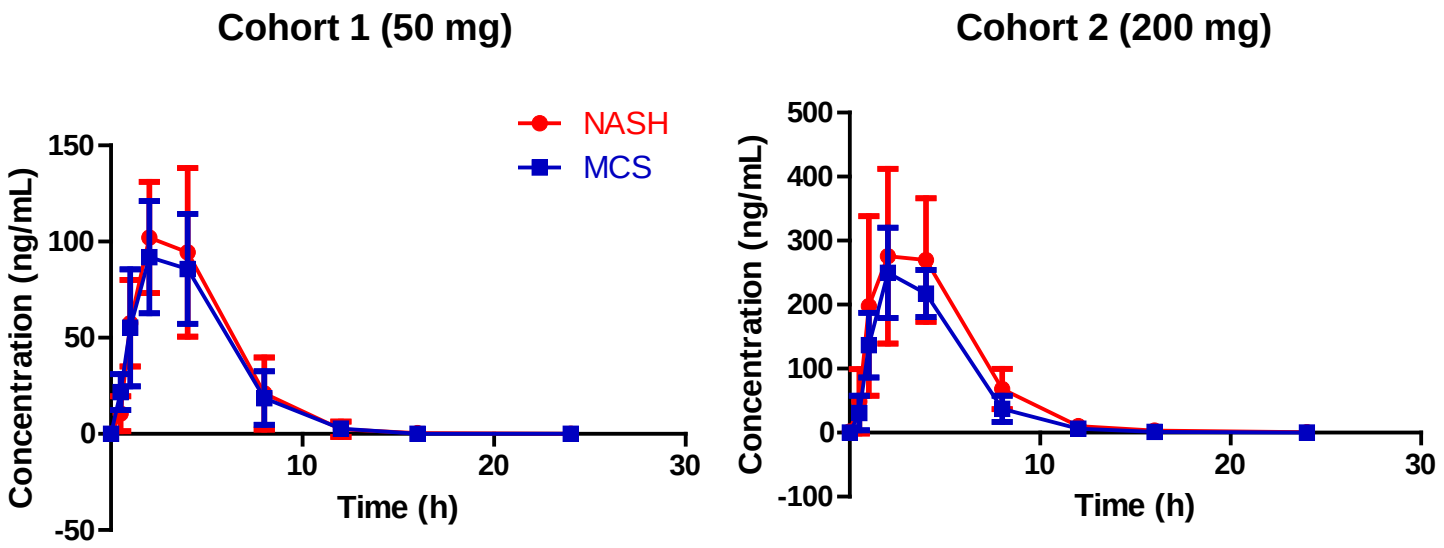
Phase 1b: NASH Patient Study

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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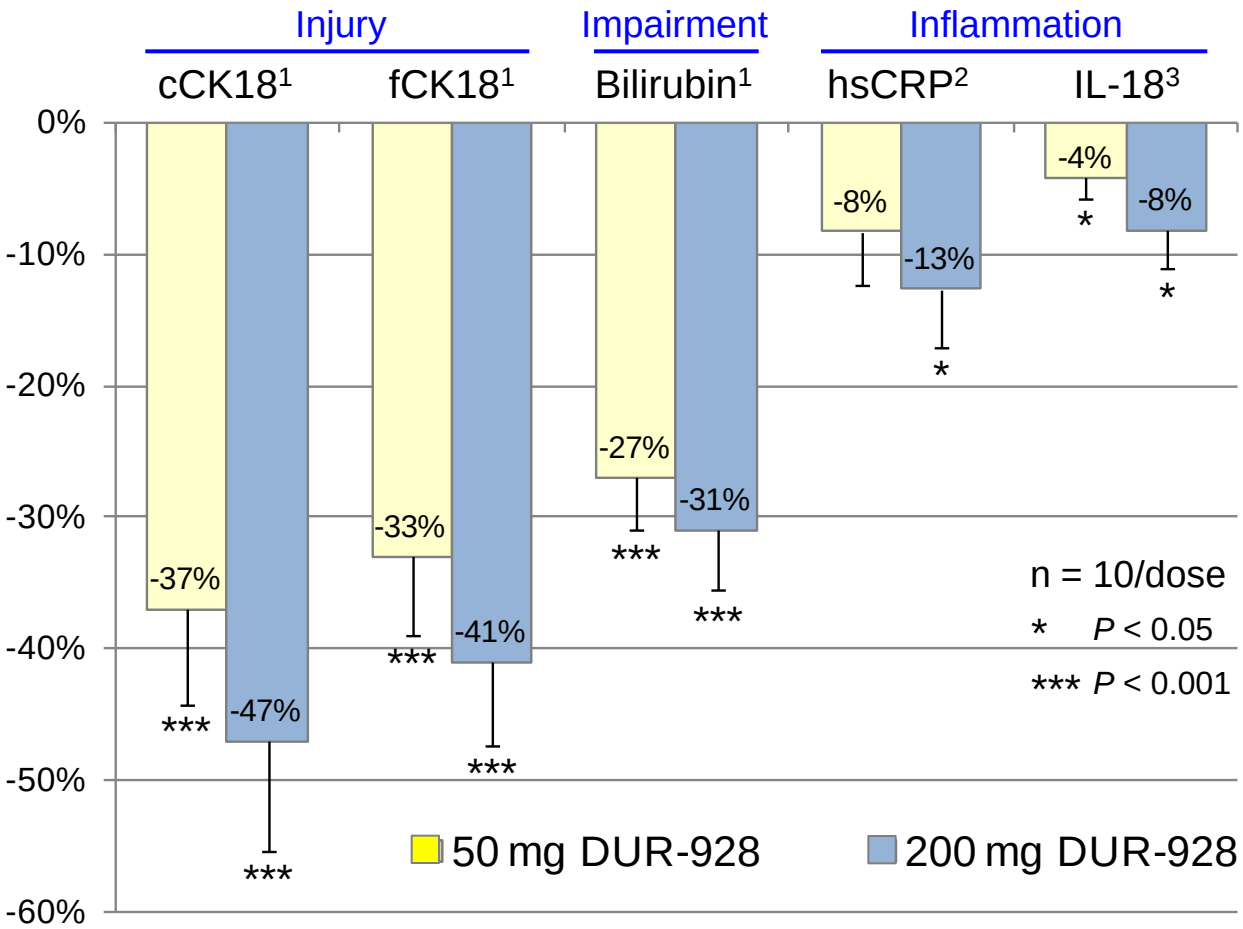
Phase 1b: NASH Patient Study

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 well tolerated among all subjects; PK parameters between kidney function impaired patients and matched controls 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 toxicology studies, covering oral 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 Planned Studies

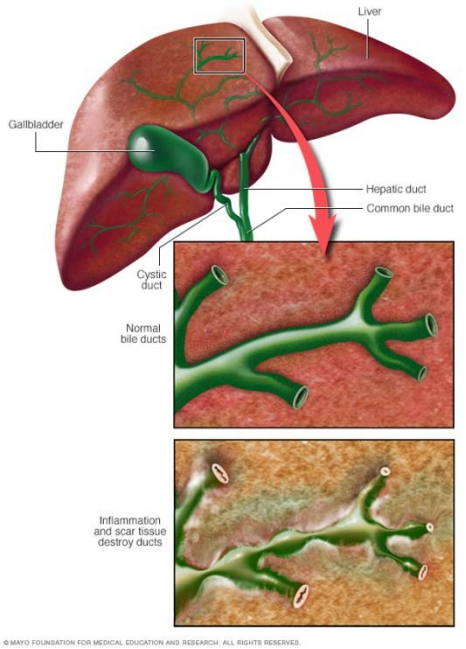
INDICATION	Preclinical	Phase 1	Phase 2	Phase 3	NDA	Patient Population
 Primary Sclerosing Cholangitis (PSC)	→					Orphan Indication
 Alcoholic Hepatitis (AH)		→				>320,000 hospitalized in the U.S.[1]
 Psoriasis		→				7.5 million in the U.S.[2]

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

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 fits the disease
  - Anti-inflammatory and anti-fibrotic properties of DUR-928
  - Improved hepatocyte function and survival
    - Reduction in bilirubin and cell death markers (CK-18s)

- Animal models that are relevant to PSC
  - 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
  - Data may be relevant to other chronic liver diseases, including NASH

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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
  - Low (10 mg) dose: n = 15-20
  - High (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 enhances recruitment, allows for interim looks at data
  - ALP is an accepted proof-of-concept marker for PSC
- Positive read-out may have implications for other liver diseases (NASH)
- Expected timing
  - Started enrolling Q1 2018
  - Initial data in 2018

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

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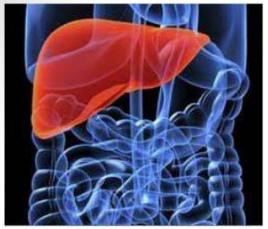
Alcoholic Hepatitis (AH)

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 exceeding 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

- Biology fits the disease
  - Anti-inflammatory and cell survival properties of DUR-928
  - Improvements to hepatocyte function (reduction in bilirubin) and reduction in cell death (CK-18s)

- Multiple animal models that are relevant to AH
  - Acetaminophen / Alcohol injury mouse & Endotoxin injury mouse models
  - High Fat Mouse & High Fat Hamster
  - STAM NASH model 1 and 2
  - Leptin Deficient Rat
  - Renal Ischemia model
  - Bile duct ligation rat
    - Collectively, these models show that DUR-928 has protective effects against acute injuries and liver diseases

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

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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
  - MELD (Model for End-Stage Liver Disease) is accepted proof-of-concept marker for AH
    - Calculated using bilirubin, creatinine and prothrombin time

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

- Expected timing
  - Start enrolling H1 2018, initial data in 2018

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DUR-928
2018 Planned Studies

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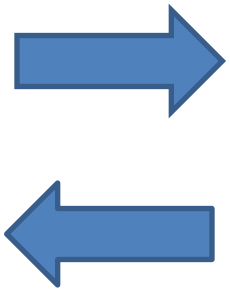
Indivior PLC

- Spun-out of Reckitt Benckiser in December 2014
- Indivior is traded on the London Stock Exchange (INDV), market cap of ~$4.0 billion[1]
- 2017 revenue of $1.1 billion and adjusted net profit of $270 million

[1] As of March 6, 2018

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

➢ December 12, 2017: Indivior announced the NDA for RBP-7000 was accepted for review; PDUFA date is July 28, 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 NDA for RBP-7000 accepted for review, PDUFA date is July 28, 2018

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]
- Indivior setting up separate business unit for the launch, anticipated in Q4 2018[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 15, 2018; assumes no material change in U.S. market circumstances

INDIVIOR

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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 and Sandoz are working to consider potential next steps

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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 rights licensed to Pain Therapeutics (PTIE)
  - PTIE controls and pays for development
  - DURECT eligible for a royalty of 6-11.5%, small milestone & excipient sales
- Complete Response Letter (CRL) received by PTIE Sept 23, 2016
  - PTIE met the FDA in February 2017; agreed on 2 abuse potential studies required for resubmission
  - On December 18, 2017, PTIE announced successful conclusion of a pre-NDA meeting with the FDA
  - On February 13, 2018, PTIE resubmitted the NDA
  - NDA accepted, Adcom date is June 26 and PDUFA date is August 7, 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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DURECT Corporation
Financial Overview

- Nasdaq: DRRX
- Recent Price: $1.94[1]
- Shares O/S: 153.3 MM[2]
- Market Cap: $298 MM[1]
- Cash & Investments: $37 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 Mar 16, 2018 [2] As of Mar 2, 2018 [3] As of Dec 31, 2017 [4] 2012-2017 [5] 2011-2017

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Potential Key Drivers Next 12-24 Months

2018

- Multiple Phase 2 studies (DUR-928), initial Phase 2 data
- Potential RBP-7000 approval (PDUFA date of July 28)
- REMOXY® ER: Potential approval (PDUFA date of August 7)
- New collaboration(s)

2019

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

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