



DURECT

**TRANSFORMING MEDICINE.
RESTORING WELLBEING.**

DURECT Corporation

A Biopharmaceutical Company

October 2, 2017



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 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 patients
- Pipeline of 505(b)2 programs
 - Including the late-stage post-op pain product: POSIMIR®
 - Other late-stage product candidates: RBP-7000 and REMOXY® ER
- Cash flow positive product lines
 - ALZET® and LACTEL®

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 study (NASH) completed, signal of biological activity from single dose
 - Phase 1b study (CKD) completed
 - Phase 1b study (Psoriasis) completed, advancing to topical formulation

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, TNF α , and other mediators during the inflammation state)
- **Improves cell survival** (including reduction of full length and cleaved CK-18)

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:

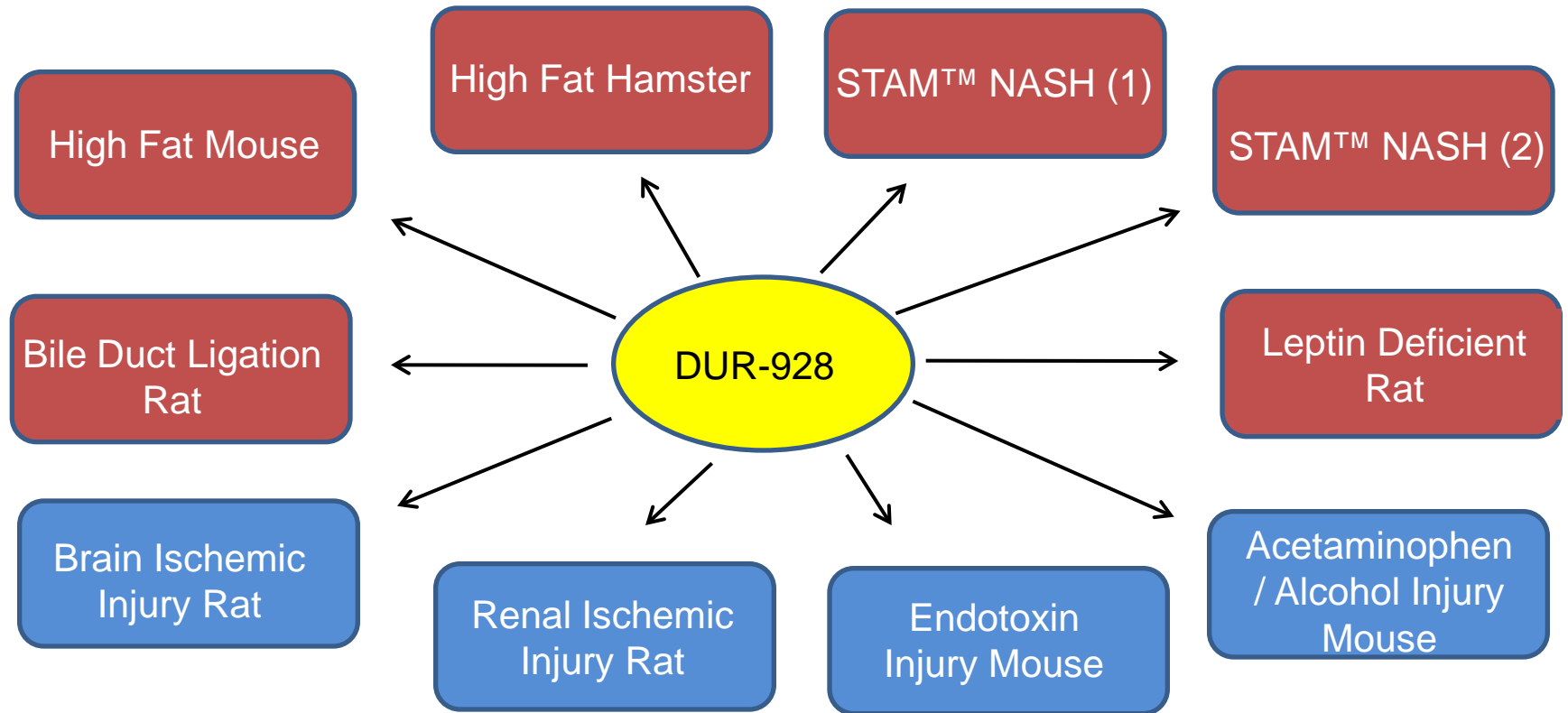
Insulin	Corticosteroids
Thyroid hormone	Erythropoietin (Epoetin alfa; Epogen [®] /Procrit [®])
Growth hormone	G-CSF (Filgrastim; Neupogen [®] /Neulasta [®])

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)

DUR-928

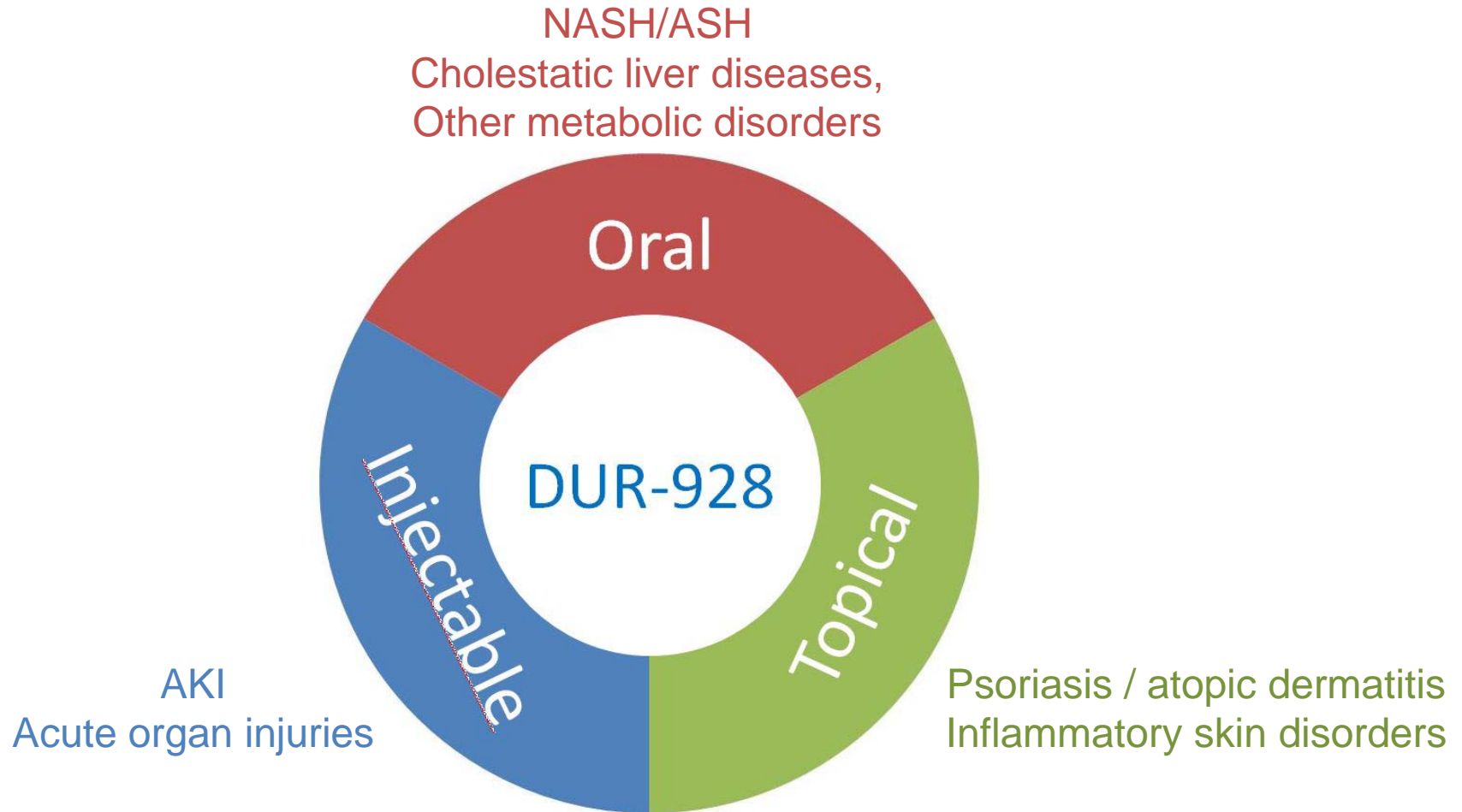
Compelling Animal Data



- 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

DUR-928 Development Programs

Orphan and broad based indications



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)

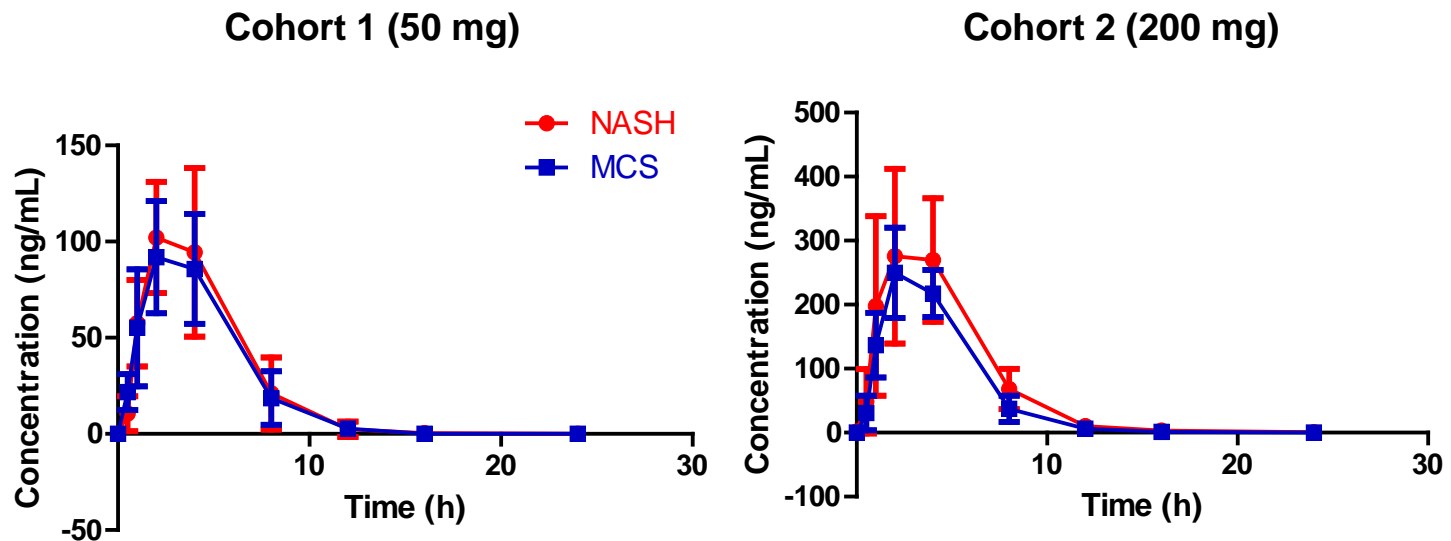
Chronic Metabolic Disease Program

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

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

Phase 1b: NASH Patient Study

High-sensitivity C-reactive Protein (hsCRP)

A marker of inflammation

	NASH Group 24 hour <u>Mean Decrease</u>
Low Dose	8%
High Dose	13%

IL-18

An inflammatory mediator implicated
in both liver and kidney diseases

	NASH Group 8 hour <u>Mean Decrease</u>
Low Dose	4%
High Dose	8%

Periods shown are those of greatest effect

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

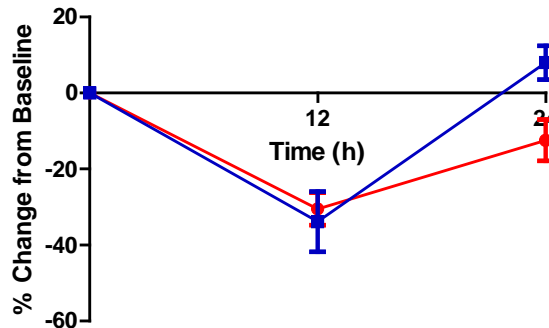
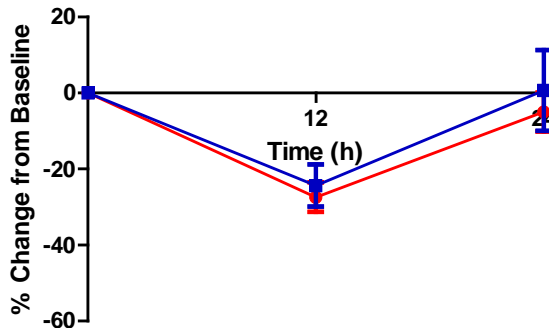
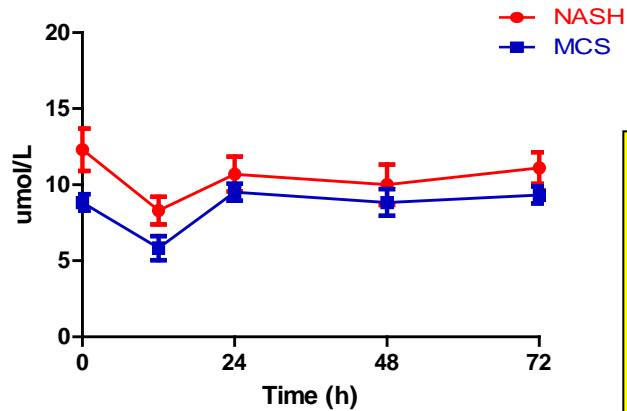
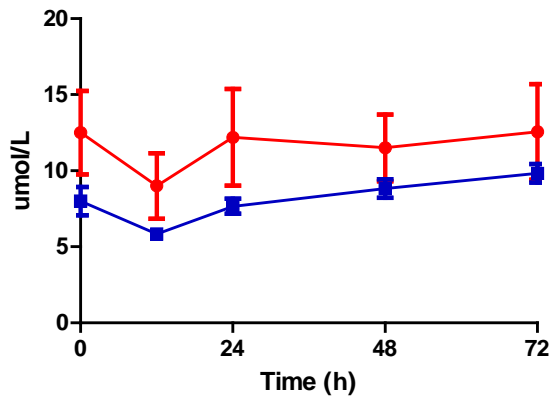
Note: NASH group includes cirrhotic and non-cirrhotic patients

Phase 1b: NASH Patient Study

Total Bilirubin

Cohort 1 (50 mg)

Cohort 2 (200 mg)



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

Period shown is that of greatest effect

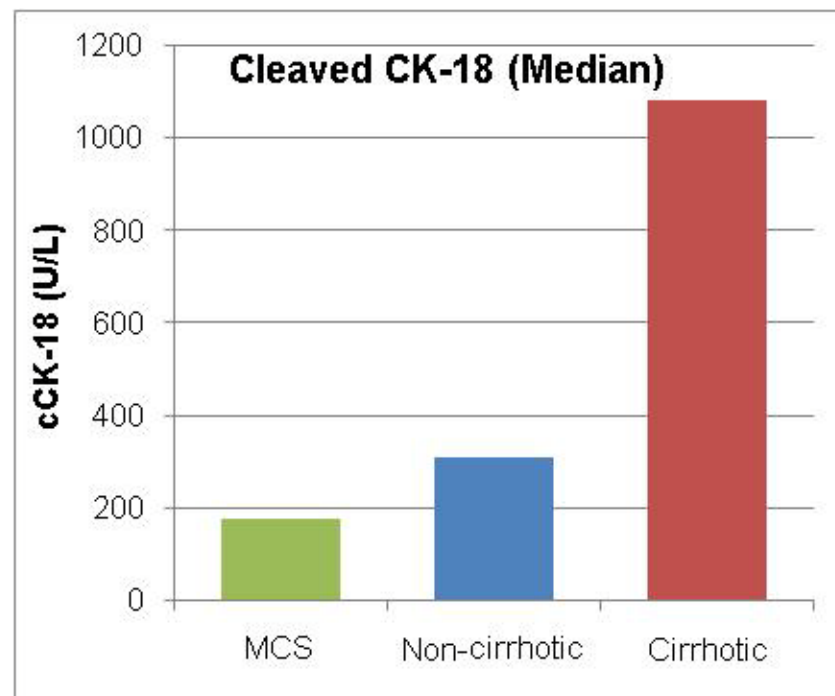
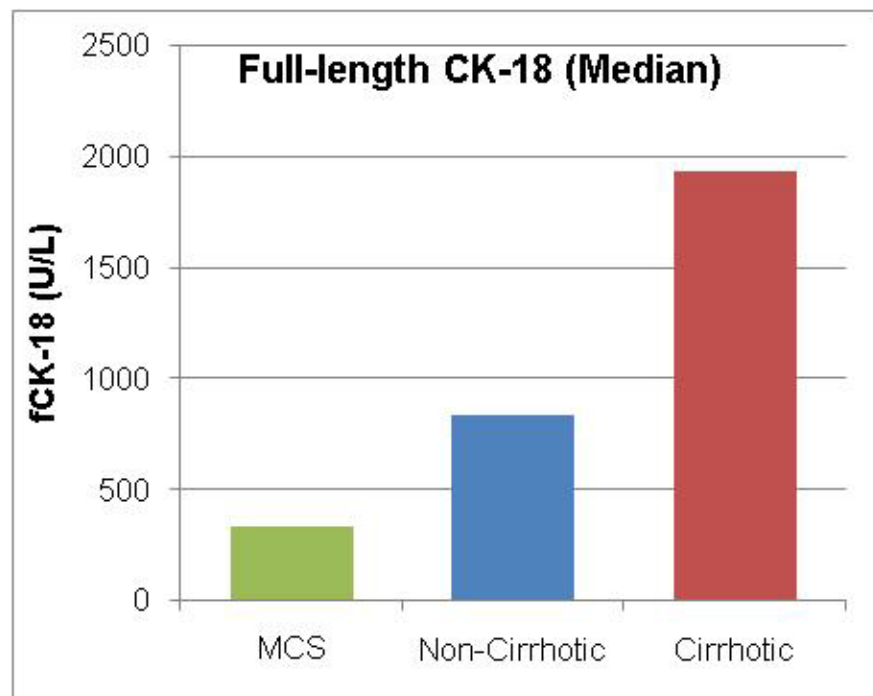
N = 10 NASH patients, 6 Matched Control Subjects per cohort

Note: NASH group includes cirrhotic and non-cirrhotic patients



Phase 1b: NASH Patient Study

CK-18 – cell death marker Baseline Value in Study Subjects

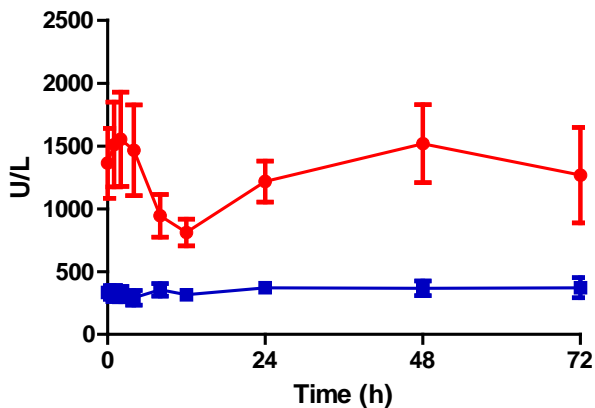


N = 10 NASH patients, 6 Matched Control Subjects – from low dose cohort

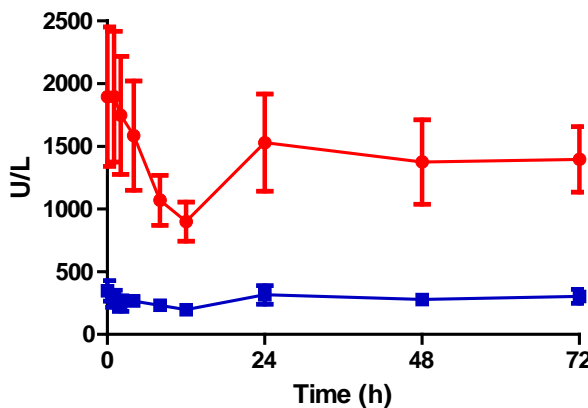
Phase 1b: NASH Patient Study

Full-length CK-18

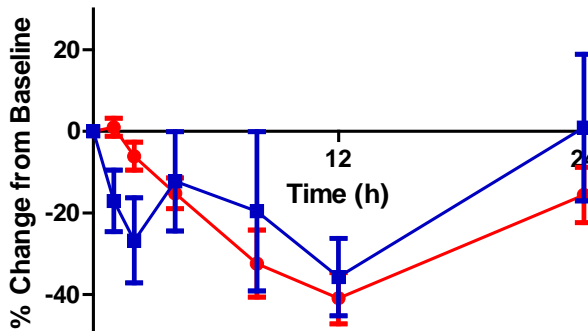
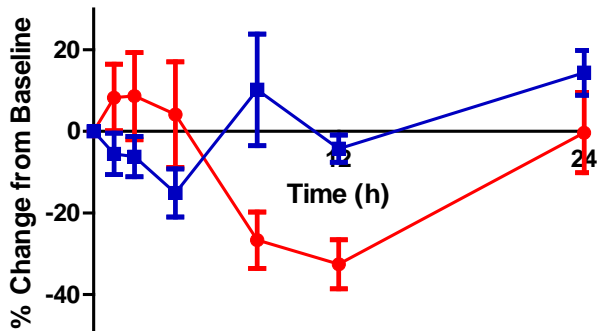
Cohort 1 (50 mg)



Cohort 2 (200 mg)



● NASH
■ MCS



	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

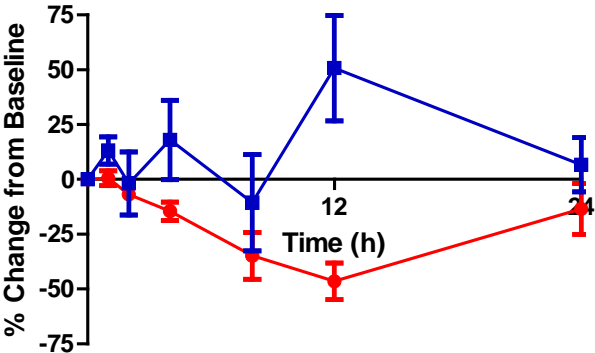
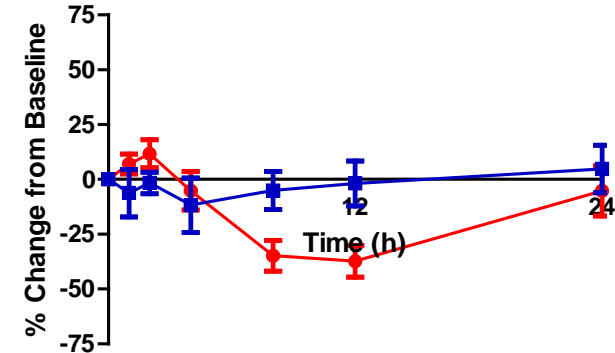
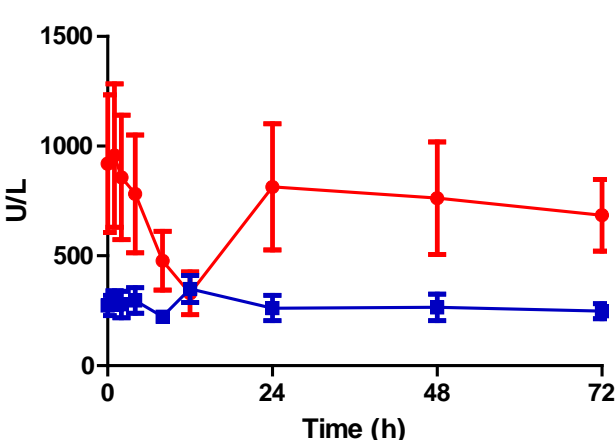
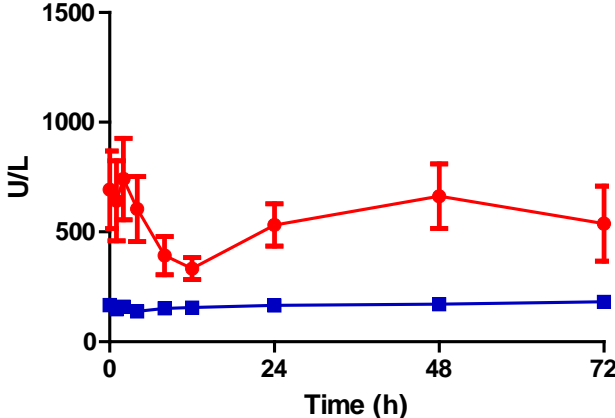


Phase 1b: NASH Patient Study

Cleaved CK-18

Cohort 1 (50 mg)

Cohort 2 (200 mg)



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

Period shown is that of greatest effect

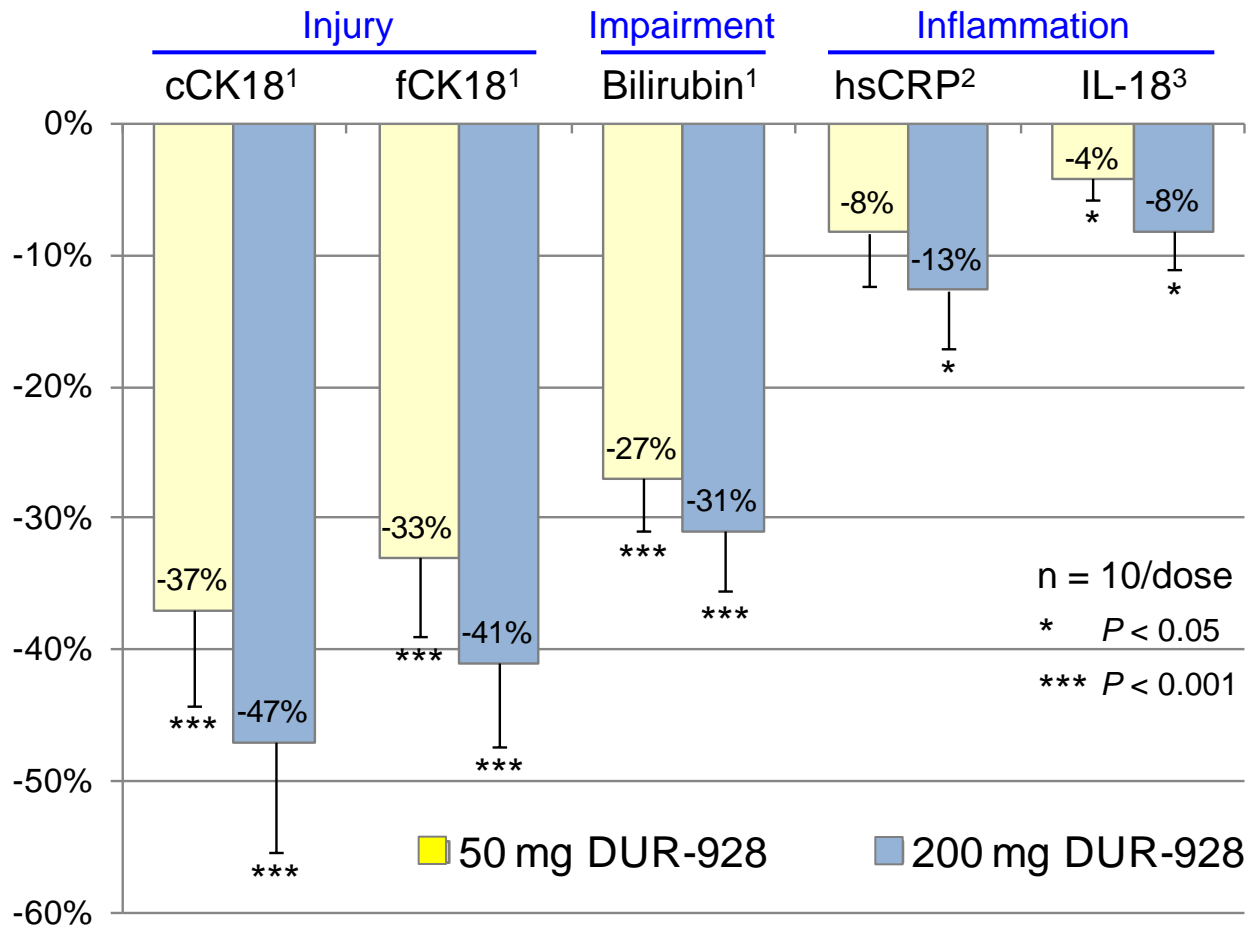
N = 10 NASH patients, 6 Matched Control Subjects per cohort

Note: NASH group includes cirrhotic and non-cirrhotic patients



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

Acute Organ Injury Program

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

- Conducting 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

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

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

Patients:

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

Normal Animals:

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

Healthy Subjects:

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

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

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

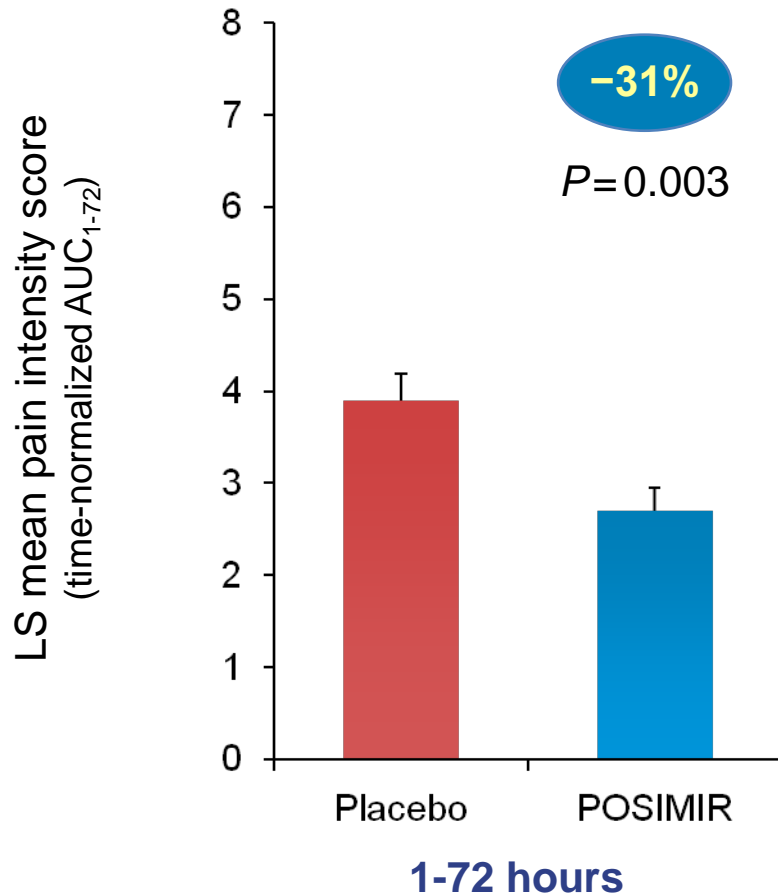


- Up to 3 days of post-op pain control
- Unmet need: non-narcotic analgesia, 24-72 hours after surgery
- Designed for local control of post-surgical pain
- Plus reduced narcotic use and associated side effects and costs
 - Nausea, vomiting, ileus, constipation, respiratory depression
 - Potential for earlier hospital discharge
- US commercialization rights licensed to Sandoz in May 2017
- DURECT rights to the rest of the world

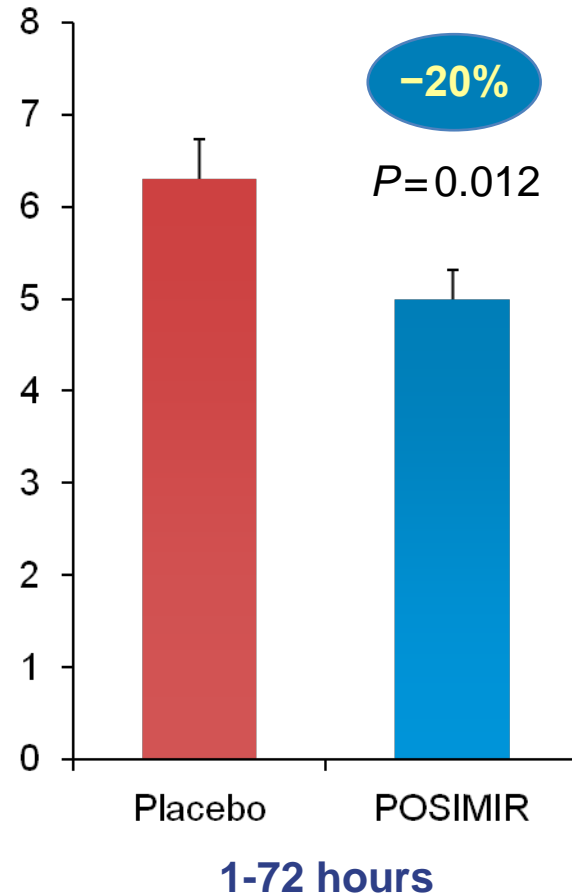
POSIMIR[®]

Reduction in Pain on Movement

Hernia Surgery



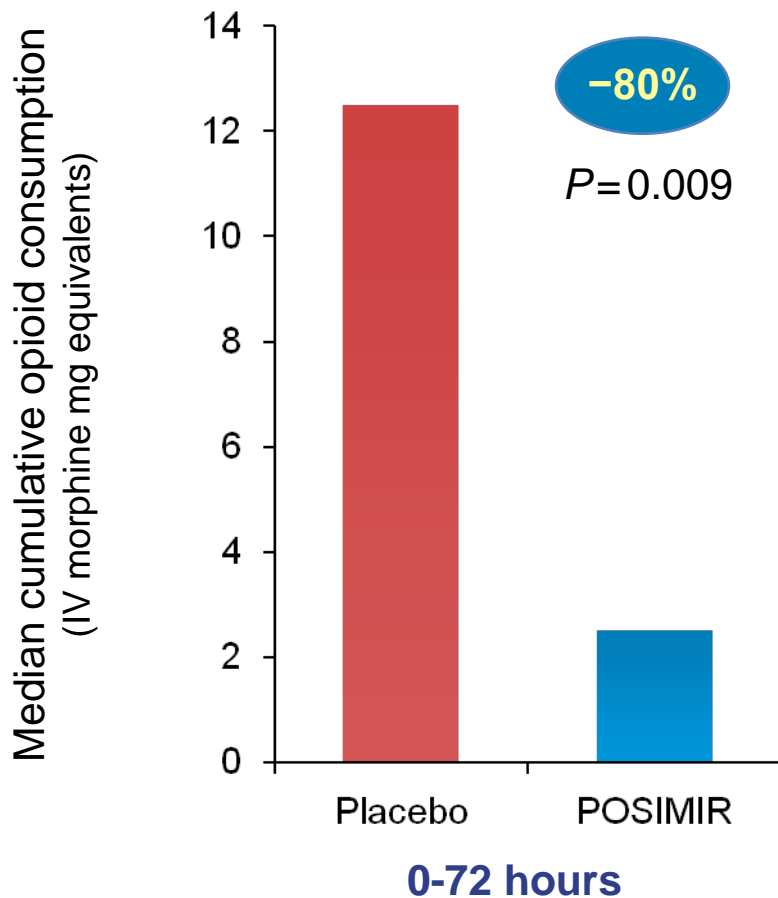
Shoulder Surgery



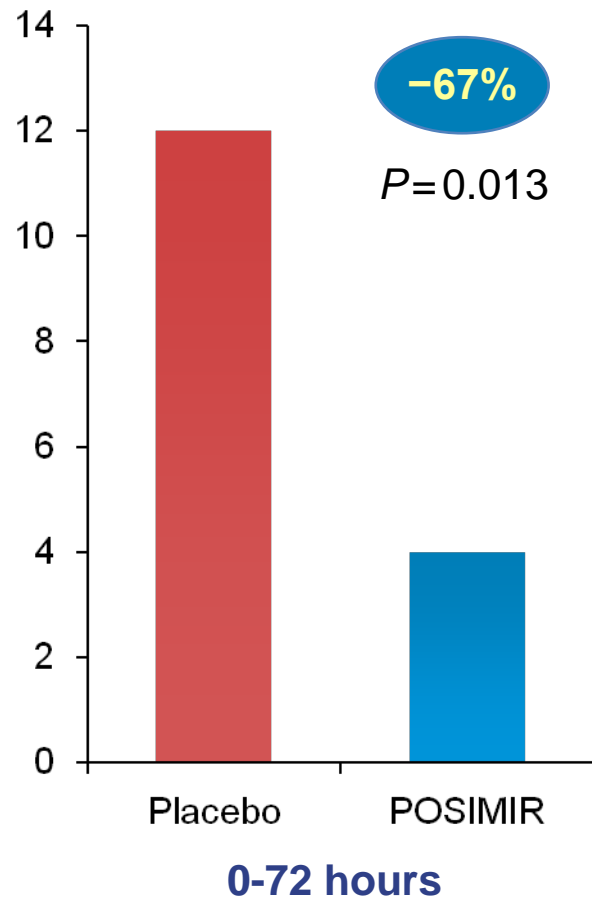
POSIMIR[®]

Reduction in Opioid Use

Hernia Surgery



Shoulder Surgery

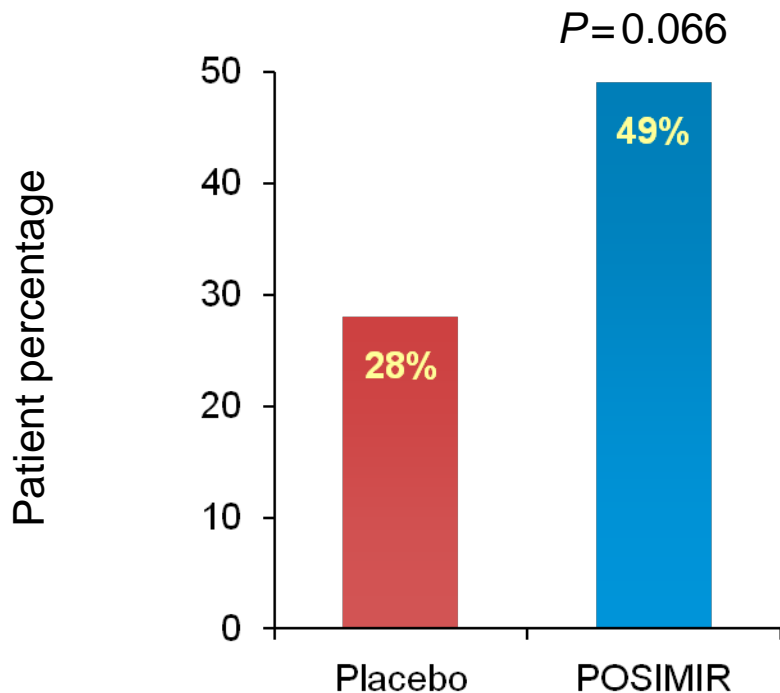


P-values derived from nonparametric Wilcoxon Rank Sum test.

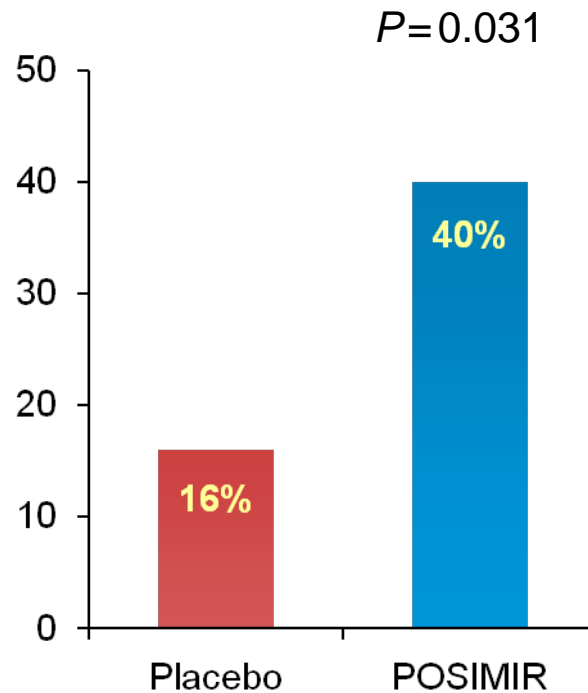
POSIMIR®

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

POSIMIR®

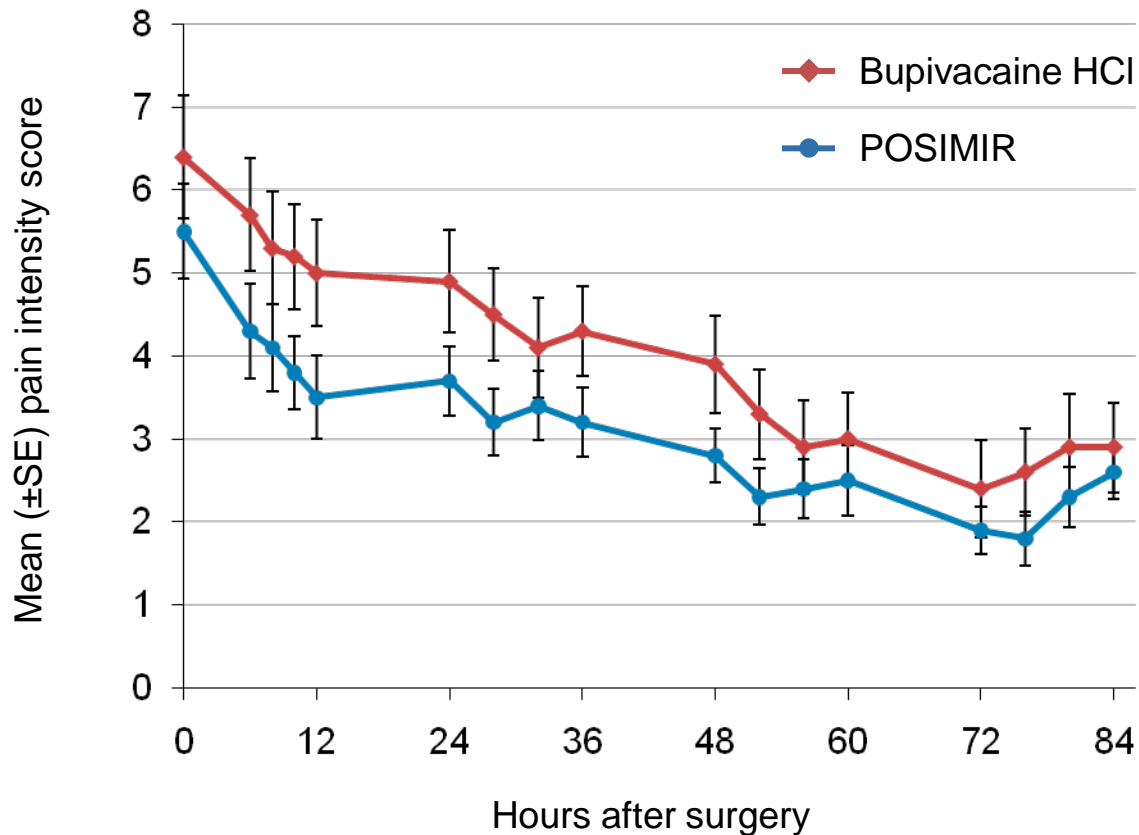
Phase 3 Pivotal Trial

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
 - Key secondary endpoint: pain intensity on movement during first 72 hours after surgery
 - Other secondary endpoints: cumulative use of opioids, etc
- Positive previous experience with this surgery

BESST Trial

Pain intensity on movement
Laparoscopic cholecystectomy (Cohort 2, N=50)



~25% Pain Reduction

$P=0.0198$, 2 days

$P=0.0235$, 3 days

POSIMIR®

Differentiating Features

- NDA to include efficacy data from 3 common surgical models
 - Hernia, shoulder, gall bladder removal
 - Aiming to be first product to demonstrate efficacy in laparoscopic procedures
- Extended duration of action (3 days)
 - SABER® formulation allows dosing 660 mg — 2½ times more than any other bupivacaine product
- Simple and rapid administration into the wound under visual supervision
 - Puts more drug closer to affected nerves
 - Facilitates use in laparoscopic procedures with multiple ports



Why Sandoz is the right partner

- Formidable resources to commit to a successful launch
 - Regulatory assistance, KOL development, Med Affairs, Phase 4 studies, etc.
- Extensive U.S. hospital presence to be leveraged
 - Dedicated sales and marketing organization focused on the hospital market
 - Contracting experience, formulary expertise and relationships to ensure access
- POSIMIR strategically fits with Sandoz and we view them as a motivated, committed partner

POSIMIR®

Collaboration with Sandoz



- DURECT:
 - \$20.0MM Up-front
 - 43.0MM Development & Regulatory Milestones
 - 230.0MM Sales Milestones
 - \$293.0MM Total
- + Double digit royalties on net sales
- + DURECT retains commercial rights to other territories
- Sandoz:
 - + Commercialization rights in U.S.
 - + Responsible for sales, marketing & launch costs in U.S.
- DURECT controls development / funds through approval



POSIMIR®

Commercial Opportunity

- >70 million surgeries per year in the U.S.
- ~30 million procedures as a potential available market
- U.S. commercial strategy to be driven by Sandoz
 - Strong POSIMIR pharmacoeconomics driven by reduction in opioid use
 - Competing product currently priced at ~\$300 / procedure

- 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

Indivior PLC



- Spun-out of Reckitt Benckiser in December 2014
- Indivior is traded on the London Stock Exchange (INDV), market cap of ~\$3.3 billion¹
- 2016 revenue of ~\$1.1 billion and adjusted net profit of ~\$254 million

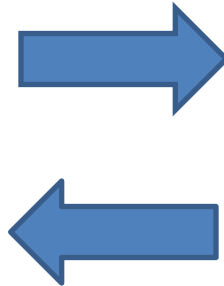
¹ As of September 29, 2017

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

➤ Indivior recently submitted an NDA for RBP-7000, implying potential approval in late 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 recently submitted the NDA for RBP-7000**

RBP-7000

PHASE III & HEOR DATA SUMMARY: RBP-7000¹

- 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

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

RBP-7000

Schizophrenia

- A devastating chronic relapsing illness characterized by adolescent onset and abnormalities of perception, thought, volition, cognition
- >21 million people are affected world-wide¹, ~2.4 million adult Americans²
- A top 10 cause of disability in the Western world³
- No known cure but effective treatments to control symptoms are available³
- Economic burden estimated at \$156B in direct and indirect costs in the US⁴
- Long Acting Injectables (LAI) have been shown to increase adherence and lower rates of relapse & psychiatric hospitalizations compared to oral therapy⁵
- LAI U.S. Sales exceeded ~ \$2.4B in 2016⁵

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 GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*, 2016, 388: 1545-602

⁴ *J Clin Psychiatry* 2016; 77(6): 764-771

⁵ *JAMA Psychiatry*. 2015 August ; 72(8): 822-829.

⁶ IMS Sales, factored for schizophrenia

DURECT Corporation

Company Financials

Shares Outstanding (August 4, 2017)	146.9
Recent Share Price (September 26, 2017)	\$ 1.74
Market Value	\$ 255.7 MM

<u>June 30, 2017</u>	
Cash and Investments	\$ 33.6 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

Potential Key Drivers Next 12-24 Months

Next 12 months

- Patient data, start of Phase 2 (DUR-928), initial Phase 2 data
- Complete Phase 3 (POSIMIR®), top-line data, NDA resubmission
- Potential RBP-7000 approval
- REMOXY® ER data generated by Pain Therapeutics to support resubmission in Q1 2018

Next 24 months

- Phase 2 data in one or more indications (DUR-928)
- POSIMIR® approval and launch by Sandoz
- Potential RBP-7000 launch
- Potential REMOXY® ER approval
- At least 1 new collaboration