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 Company Highlights

<table>
<thead>
<tr>
<th></th>
<th>DURECT Company Highlights</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01</strong></td>
<td><strong>DUR-928 in Alcoholic Hepatitis</strong>&lt;br&gt;Phase 2a: 100% survival at 28 days in patients with 26% historical mortality rate&lt;br&gt;<strong>Next step:</strong> Initiate Phase 2b efficacy trial in 2H 2020 with survival primary endpoint</td>
</tr>
<tr>
<td><strong>02</strong></td>
<td><strong>DUR-928 in COVID-19 with Acute Liver or Kidney Injury</strong>&lt;br&gt;Recruiting patients in Phase 2 safety and efficacy trial</td>
</tr>
<tr>
<td><strong>03</strong></td>
<td><strong>DUR-928 in NASH</strong>&lt;br&gt;Positive topline Phase 1b data: Significant reductions in liver enzymes, imaging and serum lipids</td>
</tr>
<tr>
<td><strong>04</strong></td>
<td><strong>POSIMIR® in Post-Surgical Pain</strong>&lt;br&gt;<strong>FDA review of NDA ongoing</strong></td>
</tr>
</tbody>
</table>

*Multiple Potential Value-Creating Catalysts in 2020 & 2021*
DUR-928: Lead Compound in DURECT’s Epigenetic Regulator Program

1. **Sulfated oxysterol**, a new class of therapeutics & unique mechanism of action
   - Endogenous, small molecule, highly conserved across 7 mammals

2. Epigenetically modulates expression of multiple clusters of master genes involved in many important cell signaling pathways

3. Broad activity
   - Stabilizes mitochondria, reduces lipotoxicity, regulates inflammatory or stress responses, and promotes cell survival

4. Proprietary program - DURECT holds exclusive worldwide rights

5. Clinical Safety
   - Well tolerated in nearly 300 subjects, both healthy volunteers and patients, in multiple Phase 1 & 2 studies at all doses tested via oral, IM and IV administration
DUR-928
Potential in Alcoholic Hepatitis (AH)
Alcoholic Hepatitis (AH)

Symptoms, Characteristics & Diagnosis

• **Acute** form of alcoholic liver disease (ALD)

• **AH is characterized by:**
  - Long-term heavy intake of alcohol:
    - ~3 (female) or ~4 (male) standard drinks/day
    - for ≥6 months
  - Recent period of increased alcohol consumption (binge)
  - Onset of **jaundice** within prior 8 weeks
  - <6 weeks of abstinence prior to onset of jaundice
  - Fever, fatigue, weakness, nausea/vomiting, loss of appetite, negative mental state
  - Worsening liver enzymes and **bilirubin ≥3.0 mg/dL**

[Sources: ALD Graphic - The Surgeons Collective; Standard Drink Graphic: National Institute on Alcohol - NIH]
Alcoholic Hepatitis (AH)

Disease Burden Remains High With No Approved Therapy

Large Potential Pharmacoeconomic Impact

- No approved treatment for AH
- **26% mortality rate at 28 days** in large AH meta analysis (77 studies; n=8184) ¹
- **117,000** hospitalizations in 2016 with AH diagnosis ²
- Hospitalization cost of **>$50,000 per patient** in the first year ³
- ALD is a leading cause of liver transplants in the US ⁴
  - The cost of a *liver transplant exceeds $800,000* ⁵
- 89% of hospitalized AH patients are insured ⁶
Alcoholic Hepatitis (AH) Current Standard of Care

Current Treatment of AH is Limited and Fails to Address Unmet Need

- No approved treatment for AH
- Supportive care: primarily abstinence, nutrition and hydration
- Steroids are used off label, per AASLD Guidelines, but
  - Minimal benefit shown in landmark study with >1000 subjects (STOPAH trial)¹
  - Steroids increase infection rate: 13% with steroids vs 7% without steroids¹
- Only 25-45% of severe AH patients are eligible for steroid use²
  - Reasons for steroid ineligibility include: uncontrolled infection, AKI, GI bleeding, certain concomitant disease, multi-organ failure or shock
- Patients are discharged only when there are no critical conditions requiring inpatient care

“There’s a clear lack of treatment options out there – prednisolone doesn’t work; we’re still giving it because that’s what we’ve been taught to do … I’d want to see something that works that isn’t a steroid, doesn’t cause infection, and doesn’t need to be taken every day” — Gastroenterologist³

¹ STOPAH Trial: n engl j med 372;17 nejm.org April 23, 2015
² Journal of Hepatology 2018 vol. 69 j 534–543
³ Proprietary market research
DUR-928
Alcoholic Hepatitis (AH) Clinical Data
DUR-928 AH Phase 2a Trial Results Presented at The Liver Meeting® November 2019

- Oral Late-Breaking Presentation
- ‘Best of The Liver Meeting’ summary slide presentation in the alcohol-related liver disease category
- Poster presentation comparing to U. of Louisville historical control
Trial subjects received up to 2 doses of DUR-928:
- 1st dose on Day 1; 2nd dose on Day 4, if still hospitalized
- 28-day follow up
- Key endpoints: safety, PK, PD (liver biochemistry, biomarkers, prognostic scores (e.g., Lille, MELD)

Part A
- Moderate AH (MELD 11–20)
  - Cohort 1A: DUR-928 30 mg (n=4)
  - Cohort 2A: DUR-928 90 mg (n=3)

Part B
- Severe AH (MELD 21–30)
  - Cohort 1B: DUR-928 30 mg (n=4)
  - Cohort 2B: DUR-928 90 mg (n=4)
  - Cohort 3B: DUR-928 150 mg (n=4)
DUR-928 Alcoholic Hepatitis (AH) Phase 2a: Dosing and hospitalization

DUR-928 Resulted in Potential Pharmacoeconomic Benefit as Measured by Time to Discharge

<table>
<thead>
<tr>
<th></th>
<th>% of patients who received a single dose of DUR-928 and were discharged in ≤ 4 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n=19)</td>
<td>14/19 (74%)</td>
</tr>
<tr>
<td>Severe patients (MELD 21-30) (n=12)</td>
<td>8/12 (67%)</td>
</tr>
</tbody>
</table>
DUR-928 Alcoholic Hepatitis (AH) Phase 2a: Bilirubin

DUR-928 Reduces Bilirubin Across Patient Categories, Especially Those with Higher Bilirubin

One of 19 patients did not return for the follow-up visits on Day 7 and Day 28, all data were analyzed based on those who completed visits.
Lille Model

Composite score used to determine how a therapy is working after 7 days; prognostic indicator of mortality

Lille Model Score
Calculated based on:
- Age
- baseline albumin
- baseline sCr
- baseline prothrombin (s)
- baseline bilirubin
- (Day7-Day1) bilirubin

% Survival (6-month) with a Lille score of ≥ 0.45 vs. < 0.45

(Louvet A et al. Hepatology 2007; 45: 1348-54)
DUR-928 AH Phase 2a: Lille Score

DUR-928 treatment resulted in 89% (16/18) Response Rate (Lille <0.45) Across all patients
DUR-928 AH Phase 2a: Lille Score Comparison to UL Historical Control

DUR-928 treatment Led to a 4x lower median Lille score vs. a historical control group

UL Supportive Care ± Corticosteroids

<table>
<thead>
<tr>
<th>BASELINE MELD Day 0</th>
<th>Median Lille</th>
</tr>
</thead>
<tbody>
<tr>
<td>UL Supportive Care</td>
<td>0.41</td>
</tr>
<tr>
<td>DUR-928 0.3 mg</td>
<td>0.10</td>
</tr>
<tr>
<td>DUR-928 0.9 mg</td>
<td>0.10</td>
</tr>
<tr>
<td>DUR-928 1.5 mg</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*16/18 patients or 89% response rate with patients with Lille <0.45*

(1) Anonymized data provided by Dr. Craig McClain from the University of Louisville (UL) from his separate Trial, in which 15 AH patients with initial MELD scores ranging from 15-30 received either supportive care alone (n=8) or supportive care with corticosteroids (n=7). Provided as historical control data

(2) n=18, one patient did not return for the day 7 visit
DUR-928 Alcoholic Hepatitis (AH) Phase 2a: MELD

DUR-928 reduced MELD by Day 28, especially those with higher baseline bilirubin

![MELD Score Change by Time graph]

<table>
<thead>
<tr>
<th>Category</th>
<th>P-value on Day 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>0.005</td>
</tr>
<tr>
<td>DF ≥32</td>
<td>0.014</td>
</tr>
<tr>
<td>MELD 21-30</td>
<td>0.051</td>
</tr>
<tr>
<td>Bilirubin &gt;8</td>
<td>0.039</td>
</tr>
</tbody>
</table>
DUR-928 Alcoholic Hepatitis (AH) Phase 2a: **Subgroup Analysis vs Historical Control**

DUR-928 treated **Severe AH Patients** had Significantly lower Lille Scores than those treated w/ corticosteroids

Well-matched **severe AH patients** in the two treatment arms

- U. of Louisville AH patients in a contemporaneous trial who received corticosteroids for 28 days (n=13)
- DUR-928 treated severe AH patients (either 30mg or 90mg of DUR-928) (n=8)

<table>
<thead>
<tr>
<th>Baseline AH Severity</th>
<th>DUR-928</th>
<th>Steroid (UL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Baseline MELD (Severe AH ≥ 21)</td>
<td>24.5</td>
<td>24.5</td>
</tr>
<tr>
<td>Mean Baseline Maddrey’s Discriminant Function (Severe AH ≥ 32)</td>
<td>61.3</td>
<td>63.0</td>
</tr>
</tbody>
</table>

Source: McClain, et. al., “DUR-928 Therapy for Acute Alcoholic Hepatitis: A Pilot Trial” AASLD The Liver Meeting poster presentation, 11/10/2019. The steroid group in the above graph includes the 7 severe AH patients treated with steroids from the UL group shown in the MELD vs Lille graph plus an additional 6 severe AH patients subsequently treated in the UL study.
DUR-928 Alcoholic Hepatitis (AH) Phase 2a: Safety

DUR-928 Was Well Tolerated Across All Doses

- No Serious Adverse Events observed related to trial drug
- No discontinuations, early withdrawal or termination of trial drug or trial participation due to AEs
- Adverse events possibly related to DUR-928:
  - 1 occurrence each of moderate generalized pruritus, mild rash & grade 2 ALP
- 74% of patients (14/19) discharged in ≤ 4 days after receiving a single dose
- 100% of patients (n=19) survived through 28-day follow-up period
  - Historical mortality rate of 26% at 28 days

DUR-928
Next Steps in Alcoholic Hepatitis (AH)
Planned Phase 2b Clinical Trial of DUR-928 in Severe AH Patients

- Double-blind, randomized, placebo controlled, multi-center, international Phase 2b clinical trial
- Severe AH patients: MELD 21-30 and Maddrey’s Discriminant Function ≥ 32
- 3 arms:
  - 30 mg DUR-928
  - 90 mg DUR-928
  - Placebo
- Primary endpoint: Survival
- Initiation planned for the second half of 2020
  - Robust survival benefit may support NDA filing
DUR-928 in Alcoholic Hepatitis (AH)

Potential to be first approved therapy for AH

<table>
<thead>
<tr>
<th>Market Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 117,000 hospitalizations per year in the US&lt;br&gt;1</td>
</tr>
<tr>
<td>• No approved therapies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DUR-928’s Robust Phase 2a Data and Next Steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>100% survival at day 28</strong> in Phase 2a trial; compared to 26% historical 28-day mortality rate</td>
</tr>
<tr>
<td>• Phase 2b placebo-controlled efficacy trial planned for initiation in 2H 2020</td>
</tr>
<tr>
<td>• <strong>Survival primary endpoint</strong> – survival benefit could enable accelerated regulatory pathway</td>
</tr>
<tr>
<td>• Potential NDA filing after Phase 2b if robust survival benefit shown</td>
</tr>
<tr>
<td>• 37% of new drug approvals between 2005 and 2012 were based on a single pivotal trial&lt;br&gt;2</td>
</tr>
<tr>
<td>• 42% of new drugs launched in the US in 2018 were approved based on a single trial&lt;br&gt;3</td>
</tr>
</tbody>
</table>

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DUR-928
Potential in
COVID-19 Patients with Acute Liver or Kidney Injury
Phase 2 of DUR-928 in COVID-19 Patients with Acute Liver or Kidney Injury

Clinical and Pre-clinical data in acute organ injury support testing DUR-928 in COVID-19 patients

- As in AH patients, COVID-19 patients, especially those with acute liver or kidney injury, are at risk of septic shock and eventually multi-organ failure (62% have acute liver injury and 36% have AKI), and death
- DUR-928 stabilizes mitochondria, reduces lipotoxicity, regulates inflammatory or stress responses, and promotes cell survival
- DUR-928 reduced the absolute mortality rate by 80% in two pre-clinical multi-organ injury models
  - Protected multiple organs: including kidneys, liver, and lungs
  - Additional supportive data in AKI, sepsis, pancreatitis, cholestatic liver injury models and other preclinical acute models

---

Phase 2 of DUR-928 in COVID-19 Patients with Acute Liver or Kidney Injury

Patient Recruitment Ongoing

**Trial Design:**
- Randomized, double-blind, placebo-controlled, multi-center U.S. Phase 2 trial
- To evaluate the safety and efficacy of DUR-928 in COVID-19 patients with acute liver or kidney injury
- N=80 randomized at 3:1 ratio (150 mg DUR-928 : placebo)
  - I.V. infusion on days 1 and 4
- Primary efficacy endpoint is a composite of survival and being free of acute organ failure at day 28
DUR-928
Potential in NASH
DUR-928 NASH Phase 1b: Trial Design

1. U.S., open-label, Phase 1b trial
2. Orally-administered DUR-928 for 28 days in patients with NASH (fibrosis stage 1-3)
3. N=65
4. Key endpoints include:
   - Safety / PK
   - Clinical chemistry and biomarkers (e.g., ALT, AST, GGT, triglycerides, Non-HDL-C, CK-18s, inflammatory cytokines)
   - Imaging (e.g., MRI-PDFF, FibroScan®)

**Timeline**

- **Screening**
- **Run-in 2 weeks (baseline data)**
- **28-day dosing**
- **28-day follow-up**

**Dosage Groups**

- **Group 1:** DUR-928 50 mg PO QD
- **Group 2:** DUR-928 150 mg PO QD
- **Group 3:** DUR-928 300 mg PO BID

**Notes:**

- Screening Run-in 2 weeks (baseline data)
- Randomization
# DUR-928 NASH Phase 1b Topline Data

Improvements in Liver Enzymes, Imaging & Serum Lipids

<table>
<thead>
<tr>
<th>Liver Enzymes</th>
<th>All Subjects</th>
<th>Patients with ≥ 10% Reduction in MRI-PDFF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50 mg QD</td>
<td>150 mg QD</td>
</tr>
<tr>
<td></td>
<td>(n=21-23)</td>
<td>(n=20-21)</td>
</tr>
<tr>
<td>ALT</td>
<td>-16%*</td>
<td>-10%</td>
</tr>
<tr>
<td>AST</td>
<td>-14%</td>
<td>-9%</td>
</tr>
<tr>
<td>GGT</td>
<td>-6%</td>
<td>-1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Imaging</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI-PDFF</td>
<td>-7%</td>
<td>-7%</td>
<td>-4%</td>
<td>-18%***</td>
<td>-19%***</td>
<td>-23%***</td>
</tr>
<tr>
<td>FibroScan</td>
<td>-10%**</td>
<td>-9%</td>
<td>-1%</td>
<td>-7%</td>
<td>-9%**</td>
<td>-9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Serum Lipids</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>-6%</td>
<td>-11%*</td>
<td>-7%</td>
<td>-7%</td>
<td>-11%</td>
<td>-8%*</td>
</tr>
<tr>
<td>Non-HDL-C</td>
<td>-8%</td>
<td>-5%</td>
<td>-1%</td>
<td>-10%</td>
<td>-8%*</td>
<td>-12%*</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-13%*</td>
<td>-3%</td>
<td>-2%</td>
<td>-9%</td>
<td>0%</td>
<td>-8%</td>
</tr>
</tbody>
</table>

* 24% reduction in serum triglycerides in patients with elevated baseline triglycerides (≥200 mg/dL; n=16) across all dose groups at day 28 from baseline (p < 0.01)

ALT (alanine aminotransferase); AST (aspartate aminotransferase); GGT (gamma-glutamyl transferase); LDL-C (Low-Density Lipoprotein – Cholesterol); Non-HDL-C (Total cholesterol excluding High-Density Lipoprotein-Cholesterol); QD (once a day); BID (twice a day); MRI-PDFF (Magnetic Resonance Imaging - Proton Density Fat Fraction) is a non-invasive measure of the proportion of liver tissue which is composed of fat; FibroScan is a specialized ultrasound machine that measures the stiffness of liver tissue.

*p < 0.05; **p < 0.01; ***p < 0.001
# DUR-928 Summary

## 01
- Positive Phase 2a AH trial, 100% survival at 28 days
- 74% were discharged in \( \leq 4 \) days after receiving only one dose of DUR-928
- No drug-related serious adverse events

## 02
- Planned Phase 2b AH trial with survival as primary endpoint
- Initiation second half of 2020
- Robust survival benefit could support NDA filing

## 03
- Phase 2 trial in COVID-19 patients
- Could lead to an accelerated regulatory path

## 04
- Positive topline data from Phase 1b NASH trial
- Significant reductions in liver enzymes, liver stiffness & serum lipids
POSIMIR®
Potential in Post-Operative Pain
POSIMIR® (bupivacaine extended-release solution) Summary
Post-Operative Pain Control Utilizing SABER® Technology

1. Non-Narcotic, designed to provide up to 3 days of post-op pain control
2. Over 30 million annual potential procedures in the US
3. NDA resubmission filed, 6-6 vote at FDA Advisory Committee meeting January 16, 2020
4. DURECT holds worldwide rights

POSIMIR has not been approved by the FDA for marketing in the U.S. for any indication. POSIMIR and SABER are trademarks of DURECT Corp.
POSIMIR® Reduced Pain, Opioid Use and Proportion of Patients Taking Opioids

Hernia Surgery

- LS mean pain intensity score (time-normalized AUC; 1-72 hrs)
  - Placebo: 8, POSIMIR: 5.5, P = 0.003

- Median opioid consumption (IV morphine mg equiv; 0-72 hrs)
  - Placebo: 14, POSIMIR: 4, P = 0.009

- % of Patients Not Taking Opioids (0-72 hrs)
  - Placebo: 28%, POSIMIR: 49%, P = 0.066

Shoulder Surgery

- LS mean pain intensity score (time-normalized AUC; 1-72 hrs)
  - Placebo: 8, POSIMIR: 6.5, P = 0.012

- Median opioid consumption (IV morphine mg equiv; 0-72 hrs)
  - Placebo: 14, POSIMIR: 4, P = 0.013

- % of Patients Not Taking Opioids (0-72 hrs)
  - Placebo: 16%, POSIMIR: 40%, P = 0.031

P-values derived from ANOVA.
P-values derived from nonparametric Wilcoxon Rank Sum test.
P-values derived from CMH Chi-Square test adjusted by Trial sites.
<table>
<thead>
<tr>
<th>Financial Overview</th>
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<tr>
<td><strong>Nasdaq</strong></td>
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<td><strong>DRRX</strong></td>
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<tr>
<td>Recent Price</td>
</tr>
<tr>
<td>Shares O/S</td>
</tr>
<tr>
<td>Market Cap</td>
</tr>
<tr>
<td>Average 50-Day Trading Volume</td>
</tr>
<tr>
<td>Cash &amp; Investments</td>
</tr>
<tr>
<td>Debt</td>
</tr>
<tr>
<td>Federal NOL’s</td>
</tr>
</tbody>
</table>

<sup>1</sup> As of August 17, 2020  
<sup>2</sup> As of July 31, 2020  
<sup>3</sup> As of June 30, 2020  
<sup>4</sup> As of December 31, 2019
Alcoholic Hepatitis (AH): Positive Phase 2a: 100% survival at 28 days. 74% discharged ≤4 days after single dose of DUR-928. No drug-related SAEs. Phase 2b May support NDA filing if robust survival benefit shown.

DUR-928 in COVID-19 with Acute Liver or Kidney Injury
Phase 2 safety and efficacy trial.

DUR-928 Phase 1b NASH: Positive topline Phase 1b data, n=65: Significant improvements in liver enzymes, liver imaging, serum lipids.

POSIMIR®: Potential FDA approval and commercial partnership.
TRANSFORMING MEDICINE
RESTORING WELLBEING
DURECT Corporation
A Biopharmaceutical Company