DURECT CORPORATION

Corporate Factsheet, September 2023

DURECT is pioneering the development of epigenetic therapies that target dysregulated DNA methylation to transform the treatment of serious and life-threatening conditions, including acute organ injury and cancer.

PIPELINE OVERVIEW

	Indication	Pre-clinical / Ph 1 / Ph 2 / Ph 3	Marketed	Status
Larsucosterol	Alcohol-Associated Hepatitis (AH)			Enrollment completed in Phase 2b AHFIRM trial; Topline data expected in Q4 2023
Larsucosterol	Non-Alcoholic Steatohepatitis (NASH)			Positive Phase 1b topline results
New Chemical Entities (NCE)	Hematology/ Oncology			Molecule selection targeted for Q4 2023
POSIMIR® (bupivacaine solution)				Sold by Innocoll in the U.S.; DURECT maintains ex-U.S. rights

FAST FACTS

NASDAQ: DRRX (Common Stock)	
Cash & investments[1]:	$48.7 M
Debt[2]:	$20.7 M
Market Cap[3]:	$84.5 M
Shares outstanding[4]:	27.6 M

[1]As of 6/30/23. Pro forma for receipt of $13.8M of net proceeds from July 2023 registered direct offering
[2]As of 6/30/23
[3]As of 8/31/23
[4]As of 8/7/23.

LARSUCOSTEROL

Larsucosterol is an endogenous sulfated oxysterol and an epigenetic modulator. It binds to and inhibits the activity of DNA methyltransferases (DNMTs), epigenetic enzymes associated with hypermethylation, found to be elevated in severe alcohol-associated hepatitis (AH) patients. By decreasing DNA hypermethylation, larsucosterol modulates the expression of genes important in maintaining cellular functions, thereby reducing cell death, lipotoxicity and inflammation in AH.

Larsucosterol is investigational and has not been approved by the FDA for marketing in the U.S. for any indication.

PROGRAM HIGHLIGHTS

LARSUCOSTEROL FOR AH: Compelling Opportunity in Underserved Market

- AH: life-threatening acute liver disease caused by chronic misuse of alcohol, frequently after increased consumption, with no approved therapies and a 90-day overall mortality rate of 29% following hospital admission; ~158K U.S. hospitalizations/y
- Positive Phase 2a data: 100% survival rate at 28 days; showed improvement in key biomarkers and prognostic indicators
- Potential pivotal data expected in Q4 2023; successful trial may support NDA filing; FDA Fast Track Designation

LARSUCOSTEROL FOR NASH: Novel Approach via Epigenetic Modulation

- Non-alcoholic steatohepatitis (NASH): advanced form of non-alcoholic fatty liver disease; no approved drugs
- Positive topline Phase 1b data: improvements in liver enzymes, liver stiffness, biomarkers and serum lipids

POSIMIR® (bupivacaine solution)

- U.S. rights exclusively licensed to Innocoll Pharmaceuticals. DURECT is eligible to receive up to $122 million in future milestone payments as well as low double-digit to mid-teens royalties on net product sales
- Commercially available in the U.S. - Indicated for post-surgical analgesia for up to 72 hours following arthroscopic subacromial decompression

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LARSUCOSTEROL FOR AH – COMPELLING PHASE 2a RESULTS[1]

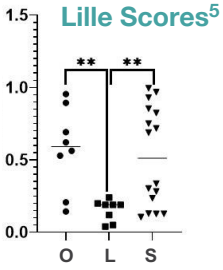
Survival	**100% of patients** treated with larsucosterol (n=19) survived the 28-day follow-up period in contrast to 26% historical 28-day mortality rate
Time to Discharge	**74% of patients treated with larsucosterol discharged within 4 days** of treatment after 1 dose
Bilirubin	**Significant reduction** compared to baseline at days 7 and 28
Prognostic Indicators of Mortality for AH	**MELD** (Model for End-Stage Liver Disease): significant reduction at day 28 compared to baseline **LILLE SCORE:** AH patients with Lille score <0.45 have an 85% 6-month survival rate vs. 25% survival rate when Lille score >0.45[2] **Lille score in severe AH patients:** All 8 severe AH patients in the 30 or 90 mg dose cohorts were treatment responders[3] (Lille score <0.45) and their Lille scores were statistically lower than those of well-matched patients from an Observational Arm and Study-Steroid Arm of the DASH Consortium trial in a cross-study comparison[4] (shown below)[5]

[1] Hassanein, T et al. 2023. Am J Gastroenterol, DOI: 10.14309/ajg.0000000000002275; [2] Louvet A et al. 2007, Hepatology, 45: 1348-54; [3] Lille score <0.45 is considered a "responder." [4] Patients from both comparative arms were diagnosed with AH, screened for inclusion and exclusion criteria similar to the larsucosterol trial, and treated with standard-of-care, including corticosteroids. In addition, they were matched by MELD score to the 8 severe AH patients who received 30 or 90 mg of larsucosterol.

Arm	Median Baseline MELD
Observational (O)*	24.5
Larsucosterol (L)	24.5
Study-Steroid (S)*	24

* Patients who did not survive at 28 days were censored

Lille Scores[5]



LARSUCOSTEROL FOR NASH: POSITIVE PHASE 1B TOPLINE DATA

(N=65) ** Indicates p-value <0.05; ** indicates p < 0.01; *** indicates p <0.001; Data at 28-days*

Liver Enzymes	Significant median **reduction** from baseline of serum **ALT** (-17%***), **AST** (-18%**) and **GGT** (-8%*) in the high dose group
Liver Imaging	At day 28, **43% of patients** showed **≥10% liver fat reduction** from baseline. **Significant reduction in liver stiffness** as measured by FibroScan (-10%**) in the low dose group
Serum Lipids & Biomarkers	Median **reduction in triglycerides** (-24%**) in patients with elevated baseline (≥200 mg/dL; n=16) across all dose groups; **Reduction in LDL-C** (-11%*) in the mid dose group and **CK-18**s in those with reduced liver fat

MANAGEMENT TEAM

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