November 16, 2018

Zacks Small-Cap Research

Sponsored – Impartial - Comprehensive

Brian Marckx, CFA
bmarckx@zacks.com
Ph (312) 265-9474

scr.zacks.com
10 S. Riverside Plaza, Chicago, IL 60606

Durect Corp (DRRX-NASDAQ)

DRRX: Protocol Amendment Should Speed DUR-928 Ph2 AH Trial. PERSERIS FDA Approval Triggers $5M Milestone, Adds New Revenue Stream

We value DRRX using sum-of-the-parts, with most of the value related to DUR-928 based on pricing of recent NASH-targeted M&A transactions as a proxy. Our methodology also includes DCF of DRRX's current cash-generating products and earn-outs.

Current Price (11/16/18)	$0.92
Valuation	**$6.00**

OUTLOOK

Last week DRRX reported results for their third quarter and provided a business update. Revenue of $8.0M benefited from a $5.0M milestone from Indivior related to FDA approval of PERSERIS (risperidone), a once-monthly subcutaneous long-acting injection for the treatment of adults with schizophrenia. DRRX is also eligible for single-digit % earn-outs based on U.S. sales. Indivior indicated that they expect to have initial quantities available in Q4'18 and, based on the outcome of an appeal by Dr. Reddy's lab (DRL) challenging the U.S. District Court of New Jersey's preliminary injunction (PI) prohibiting DRL from importing or selling its generic buprenorphine/naloxone sublingual film product, expect to commence a full product launch. A favorable outcome (i.e. appeals court upholding the PI) would be a significant positive for DRRX given the sizeable U.S. market opportunity for PERSERIS.
Recent progress on DUR-928 includes protocol amendment that has the potential to speed timeline of Ph2a alcoholic hepatitis clinical trial.
We value DRRX using sum-of-the-parts, with most of the value related to DUR-928 based on pricing of recent NASH-targeted M&A transactions as a proxy. Our methodology also includes discounted cash flow of DRRX's current cash-generating products and earn-outs. Maintaining $6/share price target.

SUMMARY DATA

52-Week High	**$2.55**
52-Week Low	**$0.84**
One-Year Return (%)	**-3.39**
Beta	**0.91**
Average Daily Volume (sh)	**287,322**
Shares Outstanding (mil)	**162**
Market Capitalization ($mil)	**$150**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**47**
Insider Ownership (%)	**10**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**20.1**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2018 Estimate	**N/A**
P/E using 2019 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Avg.,**
Type of Stock	**Small-Growth**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2016	3.6 A	3.2 A	3.7 A	3.5 A	14.0 A
2017	4.6 A	4.3 A	20.8 A	19.5 A	49.2 A
2018	3.5 A	3.4 A	8.0 A	3.6 E	18.5 E
2019					14.5 E

Price/Sales Ratio (Industry = 2.5x)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2016	-$0.06 A	-$0.07 A	-$0.06 A	-$0.06 A	-$0.26 A
2017	-$0.06 A	-$0.07 A	$0.04 A	$0.05 A	-$0.03 A
2018	-$0.05 A	-$0.04 A	-$0.02 A	-$0.05 E	-$0.16 E
2019					-$0.22 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

© Copyright 2018, Zacks Investment Research. All Rights Reserved.

WHAT'S NEW

Q3 Financial Results and Operational Update
Last week Durect reported financial results for their third quarter ending September 30th and provided a business update. Relative to the financials, revenue of $8.0M benefited from a $5.0M milestone payment from Indivior related to FDA approval (July 27th) of PERSERIS (risperidone), a once-monthly subcutaneous long-acting injection for the treatment of adults with schizophrenia.

DRRX is also eligible for single-digit percentage earn-outs based on U.S. sales of PERSERIS. Indivior indicated that they expect to have initial quantities available in Q4 '18 and, based on the outcome of an appeal by Dr. Reddy's lab (DRL) challenging the U.S. District Court of New Jersey's preliminary injunction (PI) prohibiting DRL from importing or selling its generic buprenorphine/naloxone sublingual film product, expect to commence a full product launch. A favorable outcome (i.e. appeals court upholding the PI) would be a significant positive for DRRX given the sizeable U.S. market opportunity for PERSERIS. Indivior estimates annual peak sales could be as much as $200M - $300M, which could translate into earn-outs in the several millions of dollars of incremental annual revenue to DRRX.

Meanwhile, product sales, which primarily consists of DRRX's ALZET mini pumps and LACTEL biodegradable polymer products, was $2.3M in Q3, down 15% sequentially and about 11% lower than the prior-year period. The yoy decline was attributed mostly to lower LACTEL unit sales. Product sales remain a cash cow, with gross margin at the 61% level for the second straight consecutive quarter. Product gross margin averaged 58% through the first nine months of 2018, compared to 43% in the comparable prior-year period and 49% in all of fiscal 2017. As earn-outs and sales royalties essentially represent 100% margin, both product sales and margins will further benefit from;

- the impending commencement of PERSERIS-related commercialization earn-outs (which represent 100% margin)
- Methydur sustained release capsules (for ADHD), Taiwan regulatory approval of which Orient Pharma received in September. Orient anticipates launching ORADUR-ADHD in that country in 2019 and is also seeking regulatory clearance and commercialization partners in other Asian countries, including in China. As a reminder, DRRX receives a royalty on sales of the product by Orient and retains rights to it in North America, Europe, Japan and all other countries not specifically licensed to Orient Pharma

Operating expenses fell nearly 18% from the year earlier period to $9.4M, which is up about 6% from Q2'18. The yoy decline reflects lower R&D spend related to certain programs, such as POSIMIR, ORADUR-ADHD and REMOXY ER, partially offset by an increase in costs associated with development progress of DUR-928. Management is guiding for flattish SG&A in Q4'18 and R&D expense to tick up as compared to Q3, again reflective of further progress of the DUR-928 program.

Cash
Financial position remains very healthy and with a recent amendment to terms of the $20M term loan, which pushes back the initial principal repayment and final maturity dates by 18 months (to June 2020) and 27 months (to Nov 2022), respectively, DRRX's cash runway is further extended. Cash balance was $41.3M at close of Q3. Operating ($4.6M/qtr) plus capex ($2.3M/qtr) burn averaged approximately $6.9M per quarter through the first nine months of 2018. We think that run-rate likely steps up into (at least) Q4, however, given the lack of significant near-term development milestones to offset operating cash usage as well as accelerating activities of the DUR-928 program.

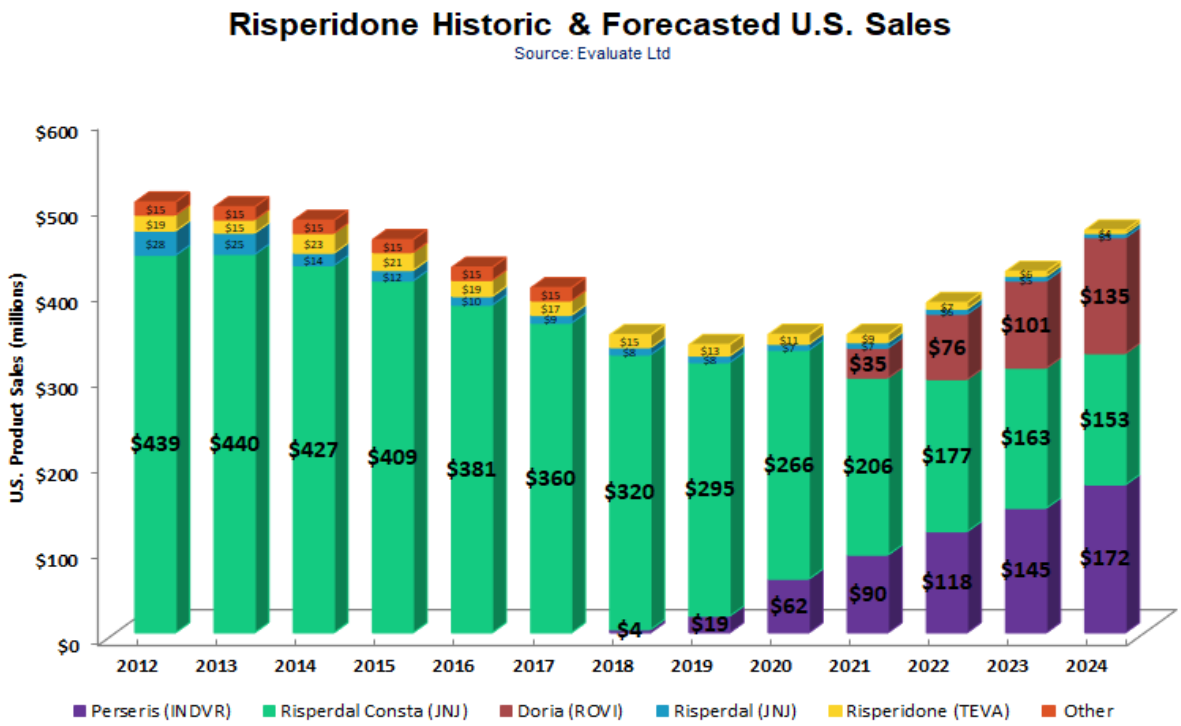
As it relates to the operational front…

There were several highlights in Q3 including;

- **FDA approval of PERSERIS**. On July 30th Indivior announced that FDA approved their NDA for PERSERIS (risperidone), the first once-monthly subcutaneous risperidone-containing, long-acting injectable for the treatment of schizophrenia in adults. That triggered a $5M milestone payment to DRRX. DRRX will also receive single-digit royalties on sales by Indivior. Risperidone (branded and unbranded) remains one of the most widely used anti-psychotics. PERSERIS addresses low compliance rates among individuals prescribed oral risperidone (taken daily), which has been shown to be a significant risk factor related to inadequate treatment of schizophrenia. As PERSERIS is the only long-acting risperidone-containing injectable, it represents the only available option that directly addresses lack of dosing adherence – which is particularly

problematic among individuals with psychosis given their cognitive handicaps.[1] This long-acting benefit could draw significant interest upon launch and drive early adoption, particularly for those patients that struggle with adherence to oral risperidone therapy. Indivior expects to have initial product available in Q4'18 and, assuming favorable outcomes of Dr. Reddy's legal action (i.e. PI is upheld on appeal), Indivior noted that they expect a full launch in 2019 supported with a sales force of between 40 and 60 U.S. reps. We currently model initial royalty revenue from sales of PERSERIS to DRRX commencing in 1H'19.

According to prescription data aggregated by Evaluate Pharma, U.S. and WW sales of risperidone in 2017 were approximately $380M and $1.0B, respectively. While forecasts suggest U.S. market contraction into 2019, the introduction of PERSERIS is expected to push total U.S. risperidone sales back to positive growth beginning in 2020. In fact, PERSERIS is expected to be the majority driver of U.S. risperidone sales as soon as next year (see chart below). Average analyst estimates forecast PERSERIS (purple bar) U.S. sales of $19M in 2019 and growing to $172M in 2024. While this implies a healthy 55% CAGR over that period, it may still be slightly more conservative than that anticipated by Indivior, which is guiding for peak annual sales of $200M - $300M. We base our PERSERIS sales related earn-out estimates on analysts' forecasted U.S. sales of the therapy (and apply an assumed 4% royalty rate) and currently look for DRRX to recognize ~$760k and $2.5M of PERSERIS earn-outs in 2019 and 2020, respectively.



- **Regulatory approval of Methydur sustained release capsules (for ADHD) in Taiwan**. Orient Pharma received notice of regulatory approval in Taiwan in September. DRRX receives a royalty on sales of the product by Orient and retains rights to it in North America, Europe, Japan and all other countries not specifically licensed to Orient Pharma. While we do not expect significant royalty-related revenue from sales in Taiwan (population ~24M), we do view this as meaningful as it may be a harbinger for accelerated development and regulatory activities in other, more meaningful markets, such as China

- **DUR-928** is where we continue to believe most of the upside value lies in DRRX, particularly following the latest CRL received (August 2018) for Pain Therapeutics' NDA for REMOXY ER. As a reminder, DUR-928 could have platform-like utility and is being investigated in several formulations and potential applications including oral, intravenous and topical formulas and in indications such NASH, alcoholic hepatitis (AH), primary sclerosing cholangitis (PSC) and psoriasis. Recent progress on these programs include (also see our detailed description of DUR-928 programs later in this report);

[1] Nielsen J., et al. Comparative Effectiveness of Risperidone Long-Acting Injectable vs FirstGeneration Antipsychotic Long-Acting Injectables in Schizophrenia: Results From a Nationwide, Retrospective Inception Cohort Study. Schizophrenia Bulletin vol. 41 no. 3 pp. 627–636, 2015

- **AH Phase 2a study with IV DUR-928**
  - Low-dose (30mg) cohort (n=4) completed among Part A (i.e. moderate AH) patients. Following safety and PK review, high-dose (90mg) will begin in Part A
  - Protocol amended with the goal of speeding trial completion. Protocol now allows for Part B (i.e. severe AH) to commence enrollment (initially with low-dose) following review by trial oversight committee, while simultaneously continuing to enroll Part A. Management noted that the trial sites have screened many AH patients that would have been eligible for enrollment for Part B but were too severe for Part A. This protocol modification, once effective, will allow investigators to immediately enroll these higher MELD-score patients. That should speed overall completion time of the trial

- **Primary Sclerosing Cholangitis Phase 2a study with oral DUR-928**: five patients have been enrolled of an expected total of 30 to 40 (i.e. two arms, n=15 - 20 per arm). DRRX noted that this trial is enrolling at a rate similar to that of other PSC studies sponsored by Shire, Gilead and others. DRRX expects to report data when a sufficient number of patients have been dosed

- **NASH study with oral DUR-928**
  - Anticipate commencing initial NASH clinical trial in 1H'19
  - DRRX expects to announce additional details of the study design as initiation nears

- **Psoriasis with topical DUR-928**
  - Plans underway for a Phase2a proof-of-concept study with topical DUR-928 in patients with mild-to-moderate plaque psoriasis
  - Anticipate dosing starting in Q1'19
  - Targeting enrollment of 20 in order to obtain data on at least 15 patients

Pipeline Refresher

PERSERIS (long-acting injectable risperidone)
In October 2017, Durect reached a $17.5 million patent purchase agreement with **Indivior UK Limited**, an affiliate of Indivior PLC (INDV.L). The deal assigned certain of Durect U.S. patent rights to Indivior for RBP-7000, Indivior's recently FDA-approved **once-monthly injectable risperidone product** for the treatment of schizophrenia. Per the agreement, Indivior made an upfront payment to Durect of $12.5 million. Then, in late-July, Indivior announced that FDA approved their NDA for PERSERIS, which triggered a $5M milestone payment to DRRX (received in Q3'18). DRRX will also receive quarterly earn-out payments based on a single-digit percentage of U.S. net sales of PERSERIS (as well as other products covered by the patent rights).

REMOXY
On August 6, 2018, Durect's partner Pain Therapeutics reported that it received a Complete Response Letter (CRL) from the FDA relative to their NDA REMOXY ER (oxycodone), extended-release capsules. The CRL concluded that, "The data submitted in [the] NDA do not support the conclusion that the benefits of [REMOXY] Extended-Release Capsules outweigh the risks." Following the CRL, Pain Therapeutics further announced a strategic reorganization to align its resources on advancing its drug and diagnostic assets in Alzheimer's disease.

While our assumptions will be updated if warranted, we have removed REMOXY from our model as we think it is more likely than not that the development program will be either completely discontinued or at least significantly delayed. We do note that there may be hope that REMOXY could be salvaged, however – or at least it appears that Pain Therapeutics believes that might be the case.

On November 12th, they announced a meeting on January 31st with FDA to discuss their appeal of the latest CRL. The PR also lays out their case supporting the appeal, noting that they believe there were calculation errors, "material mistakes and misrepresentations made by FDA during a June 2018 Advisory Committee" and that when corrected for these, "REMOXY has properties that may deter against common methods of abuse, such as injection abuse". The PR goes on, making the case for REMOXY as less abusable than ER oxycodone, associated with lower health risks and meeting all evidentiary standards for FDA approval.

So while we do not hold out much hope for a reversal by FDA, we may know more following the Jan 31st meeting with FDA – and, if warranted, our assumptions will be updated.

POSIMIR
POSIMIR is the company's investigational post-operative pain relief depot that utilizes the company's patented SABER technology and is intended to deliver bupivacaine to provide three days of pain relief after surgery.

In May 2017, Durect announced a development and commercialization agreement with Sandoz AG, a division of Novartis (NVS), to develop and market POSIMIR (SABER-Bupivacaine) in the U.S. Terms of that initial agreement called for Sandoz to make an upfront payment to DURECT of $20 million. DRRX was also eligible to receive up to $43 million in development and regulatory milestones, up to $230 million in sales-based milestones and a tiered double-digit royalty on product sales in the United States. The agreement was amended in May 2018 whereby Durect is now eligible for up to $30 million in milestone payments based on NDA approval. They continue to be eligible for up to an additional $230 million in sales-based milestones. Each party is also permitted to develop or commercialize competing products.

In June 2017 patient enrollment completed in PERSIST, a Phase 3 clinical trial evaluating POSIMIR for post-operative pain in patients undergoing laparoscopic cholecystectomy (gallbladder removal) surgery.
In a previous clinical trial of 50 patients in the same surgical model (laparoscopic cholecystectomy), POSIMIR was compared with the active control bupivacaine HCl. In a post-hoc analysis, POSIMIR demonstrated an approximate 25% reduction in pain intensity on movement for the first 3 days after surgery (p=0.024) and for the first 2 days after surgery (p=0.0198), using the same statistical methodology specified for the most recent trial.

On Oct. 19, 2017, DURECT reported that PERSIST, the **Phase 3** clinical trial for POSIMIR **did not** meet its primary efficacy endpoint of reduction in pain on movement over the first 48 hours after surgery as compared to standard bupivacaine HCl. While results trended in favor of POSIMIR versus the comparator, they did not achieve statistical significance. Management noted on the Q3'18 call that they "continue to evaluate and considered the potential next steps for the program and we will provide an update when a decision has been made and the future of the program is set."

Focus Is on DUR-928
With the CRL for Remoxy and the failure of the Phase 3 trial for POSIMIR, we believe the focus is squarely on the company's epigenetic program **DUR-928.**

Update on Phase II of Injectable DUR-928 for AH
In late-April 2018, Durect commenced patient dosing in a **Phase IIa** clinical trial of DUR-928 in patients with **alcoholic hepatitis (AH).**

This is an open label, dose escalation study conducted in two parts.

- **Part A** includes patients with moderate alcoholic hepatitis, and
- **Part B** will include patients with severe alcoholic hepatitis.

The study is being conducted using **three dose levels** (30, 90 and 150 mg) in Part A, with sequential dose escalation following review of safety and PK results of the prior dose level. Patients will receive DUR-928 by intravenous infusion, and the dose may be adjusted in Part B based on the findings from Part A. Patients will be enrolled at multiple clinical sites in the U.S. and the target number of participants to complete the study is **24-36**. The objectives of this study include safety, PK and PD signals, as determined by improvement in liver biochemistry, MELD and Lille scores, and other biomarkers.

As of early-November 2018, low-dose (30mg) cohort (n=4) completed among Part A (i.e. moderate AH) patients. Following safety and PK review, high-dose (90mg) will begin in Part A. The study protocol was recently updated with the goal of speeding trial completion. Protocol now allows for Part B (i.e. severe AH) to commence enrollment (initially with low-dose) following review by trial oversight committee, while simultaneously continuing to enroll Part A. Management noted on the Q3'18 call in November that the trial sites have screened many AH patients that would have been eligible for enrollment for Part B but were too severe for Part A. This protocol modification, once effective, will allow investigators to immediately enroll these higher MELD-score patients. That should speed overall completion time of the trial.

Update on Phase 1b Oral Study of DUR-928 for NASH

In January 2016, Durect initiated a single-ascending-dose **Phase 1b** clinical trial with oral DUR-928 in patients with nonalcoholic steatohepatitis **(NASH)** in **Australia.**

This Phase 1b trial of DUR-928 was a dose ranging (50 mg and 200 mg), single-ascending-dose safety and pharmacokinetic (PK) study of **oral DUR-928** in subjects with NASH and matched control subjects (MCS). This study was conducted in successive cohorts evaluating single-dose levels (first a low dose and then a high dose) of oral DUR-928. Both cohorts consisted of 10 NASH patients and 6 MCS.

Table 1. Patient Demographics (mean ±SD)

	Cohort 1 (50 mg)		Cohort 2 (200 mg)	
Demographics	NASH	MCS	NASH	MCS
# of Patients	10	6	10	6
Age (yrs)	53.4 (10.7)	56.8 (6.5)	53.2 (12.9)	54.7 (6.0)
BMI (kg/m2)	34.7 (6.2)	31.2 (2.4)	36.6 (6.4)	33.2 (4.4)
Gender (M/F)	5/5	5/1	5/5	3/3
Baseline ALT (U/L)	66.7 (18.9)	19.3 (6.5)	78.9 (45.5)	20.8 (4.8)
Cirrhotic Patients	2	--	3	--
Non-Cirrhotic Patients	6	--	5	--
Undetermined	2	--	2	--

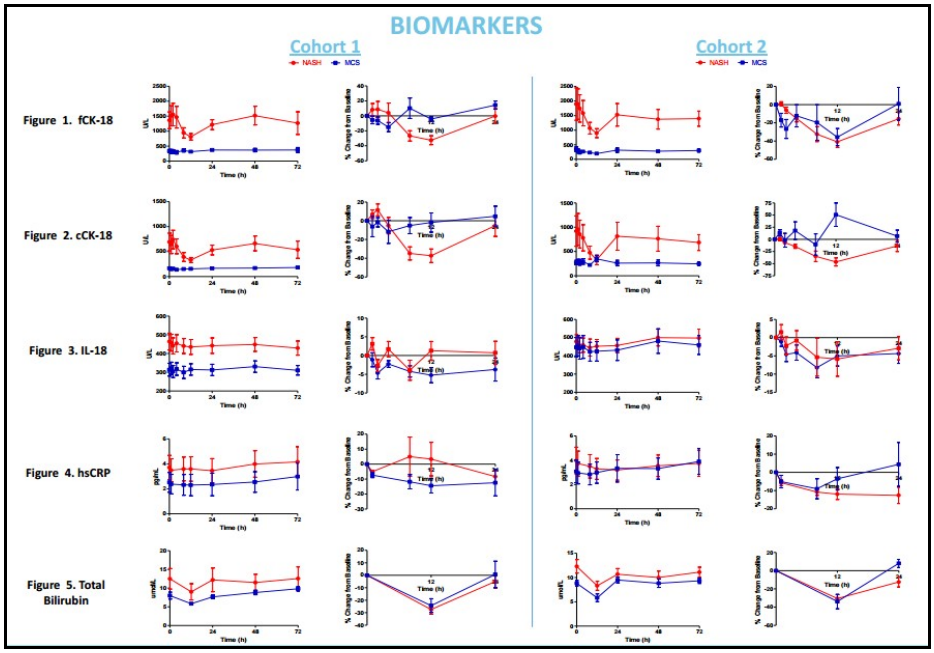
In April 2017 Durect presented the updated **Phase 1b** data at the International Liver Congress (EASL) in Amsterdam. In both cohorts, DUR-928 was **well tolerated overall**. There was an approximate 10-30% increase in DUR-928 exposure in NASH patients compared to MCS. A single serious adverse event (shortness of breath), designated as possibly related to study drug, was reported in cohort 2 in a NASH patient with a prior history of arrhythmia and an ongoing viral infection; no unusual abnormal biochemistry was observed and the symptom spontaneously resolved.

Table 2. Pharmacokinetic Parameters (mean ±SEM)

	Cohort 1		Cohort 2	
PK Parameters	NASH	MCS	NASH	MCS
Cmax (ng/mL)	113.2 (36.3)	94.0 (27.4)	332.7 (99.5)	260.5 (54.8)
Tmax (hr)	2.4 (0.8)	3.0 (1.1)	2.9 (1.2)	2.7 (1.0)
T½ (hr)	1.6 (0.2)	1.7 (0.3)	1.9 (0.4)	1.7 (0.4)
AUClast (ng*hr/mL)	512.7 (219.1)	476.5 (187.6)	1723.7 (470.9)	1316.9 (203.4)
AUCinf (ng*hr/mL)	528.1 (216.4)	487.9 (190.2)	1732.6 (470.5)	1325.5 (202.9)

Exploratory biomarker analysis indicated that a single oral dose of DUR-928 resulted in reductions from baseline in the levels of both full-length and cleaved cytokeratin-18 (CK-18), bilirubin, hsCRP and IL-18 in NASH patients.

- The decrease of full-length CK-18 (a generalized cell death marker) at 12 hours was approximately 33% in the NASH patients in the low dose cohort and approximately 41% in the high dose cohort. The decrease of cleaved CK-18 (a cell apoptosis marker) at 12 hours was approximately 37% in the NASH patients in the low dose cohort and approximately 47% in the high dose cohort.
- The decrease in total bilirubin (a liver function marker for which a decrease would be seen as positive) at 12 hours in the NASH patients was approximately 27% in the low dose cohort and approximately 31% in the high dose cohort.
- High sensitivity C-Reactive Protein (hsCRP), a marker of inflammation, trended higher at 12 hours in the NASH patients by approximately 3% in the low dose cohort but trended lower by approximately 12% in the high dose cohort.
- IL-18, an inflammatory mediator implicated in both liver and kidney diseases, trended lower at 12 hours by approximately 5% in both the low dose cohort and in the high dose cohort.



Update on Phase 1b Injectable DUR-928 for Kidney Disease

This trial was also conducted in **Australia**. This **Phase Ib** trial of DUR-928 is an open-label single-ascending-dose safety and pharmacokinetic study in patients **with impaired kidney function** (stage 3 and 4 chronic kidney disease) and matched control subjects. It was conducted in successive cohorts (first a low dose and then a high dose) evaluating single-dose levels of DUR-928 administered **by injection.**

The low dose cohort enrolled 6 kidney function impaired patients and 3 matched control subjects, and the high dose cohort enrolled 5 kidney function impaired patients and 3 matched control subjects. Results showed DUR-928 was well tolerated among all subjects and the PK parameters between the kidney function impaired patients and the matched control subjects were comparable.

In addition, Durect has held a pre-IND meeting with the Cardiovascular and Renal Products Division of the FDA, and the company is utilizing feedback from that meeting as well as from its clinical advisors to prepare an IND which is required to enable a future kidney disease clinical trial **in the United States**.

Topical Formulation for Psoriasis

Psoriasis effects between 7M and 32M Americans. Traditional first-line prescription therapy includes steroids to address inflammation and redness. DRRX is investigating topical DUR-928 for plaque psoriasis. Durect **completed** an initial **exploratory Phase 1b** trial in **psoriasis** patients (n = 9 evaluable patients) in Australia. The decision to proceed with clinical testing in psoriasis was based on the anti-inflammatory and cell survival properties of DUR-928, including the downregulation of IL-17, full length CK-18, cleaved CK-18, as well as the results of a psoriasis study with DUR-928 in mice.

The **Phase 1b** trial was conducted with intradermal micro injections of DUR-928, and the company thinks the results warrant further investigation. As a result, the company has developed several topical formulations of DUR-928 that the company is evaluating for a topical application microplaque trial. There is a large unmet medical need for new topical drugs for psoriasis for use prior to systemic biologic treatments which often have significant associated side effects.

Plans underway for a Phase2a proof-of-concept study with topical DUR-928 in patients with mild-to-moderate plaque psoriasis. Expected to commence in Q2'19, this will be a U.S.-based multi-site, randomized, double-blind, controlled study with targeted enrollment of ~20 anticipated, which is expected to yield ~15 evaluable patients.

Topical application will occur 1x daily for four weeks. Each patient will serve as their own control arm with DUR-928 and vehicle-control applied to separate plaques on each patient throughout the four-week duration of the study. Follow-up will occur during weeks five through eight (i.e. four weeks subsequent to treatment duration). Primary

efficacy endpoint will be improvement in local psoriasis scores in the DUR-928-treated plaque compared to the vehicle-treated plaque.

Update on Phase 2a Study of Oral DUR-928 for PSC

As a reminder, Durect received orphan drug designation for DUR-928 to treat patients with PSC. PSC is a chronic liver disease characterized by a progressive cause of cholestasis (decrease in bile flow) with inflammation and fibrosis of bile ducts. It is an orphan medical condition for which there is no established medical treatment.

On February 26, 2018, Durect announced commencement of patient dosing in a **Phase 2a** study of DUR-928 in patients with primary sclerosing cholangitis **(PSC).** As of early November 2018 (i.e. date of the Q3 earnings call), five patients have enrolled. DRRX noted that this trial is enrolling at a rate similar to that of other PSC studies sponsored by Shire, Gilead and others. DRRX expects to report data when a sufficient number of patients have been dosed

- This Phase 2a trial is a randomized, open label study with two cohorts (a low dose cohort of 10 mg and a high dose cohort of 50 mg), in which patients (n = 20 per cohort) will receive **oral dosing** of DUR-928 for 4-weeks with follow-up for an additional four-weeks.

- The objectives of this study include safety, pharmacokinetic (PK) and pharmacodynamic (PD) markers, including the percent change from baseline of serum alkaline phosphatase (ALP) and other biomarkers.

VALUATION

Large Market Opportunity for DUR-928

Although DUR-928 may have broad applications in many indications, we believe most of the underlying value resides in NAFLD/NASH and acute kidney injury.

Non-alcoholic fatty liver disease (NAFLD) is the build-up of extra fat in liver cells that is not caused by alcohol. It is normal for the liver to contain some fat. However, if more than 5% - 10% percent of the liver's weight is fat, then it is called a fatty liver (steatosis). The more severe form of NAFLD is called non-alcoholic steatohepatitis (NASH). NASH causes the liver to swell and become damaged.

NAFLD affects about 30% of adults and 10% of children in the US, among which 10-30% will develop NASH. 25-40% NASH patients will develop progressive liver fibrosis, while 20-30% NASH patients with advanced fibrosis will develop cirrhosis, which could lead to liver cancer. Currently there are no FDA approved medicines for the treatment of NAFLD/NASH.

Acute kidney injury (AKI) is defined as an abrupt or rapid decline in renal filtration function. This condition is usually marked by a rise in serum creatinine concentration or by azotemia (a rise in blood urea nitrogen [BUN] concentration).

Per Medscape, in the United States, approximately 1% of patients admitted to hospitals have AKI at the time of admission. The estimated incidence rate of AKI during hospitalization is 2-5%. AKI develops within 30 days postoperatively in approximately 1% of general surgery cases and arises in up to 67% of intensive care unit (ICU) patients. Approximately 95% of consultations with nephrologists are related to AKI. The appropriate nephrologist referral rate is approximately 70 cases per million populations.

The current treatment for AKI is mainly supportive in nature. No therapeutic modalities to date have shown efficacy in treating the condition. Therapeutic agents (eg, dopamine, nesiritide, fenoldopam, mannitol) are not indicated in the management of AKI and may be harmful for the patient.

Certainly, there are highly unmet medical needs in the NAFLD/NASH and acute kidney injury fields. The unique mechanism of action and the compelling animal and human data so far make DUR-928 a highly promising candidate for the management of NAFLD/NASH and kidney injury.

We value DRRX using sum-of-the-parts, with most of the value related to DUR-928 based on pricing of recent NASH-targeted M&A transactions as a proxy. Our methodology also includes discounted cash flow of DRRX's current cash-generating products and earn-outs.

DUR-928 valued at between $750M and $1B

Examples of some of the higher-profile NASH-related acquisitions include Allergan's (AGN) September 2016 purchase of Tobira Therapeutics. The deal, valued at $1.7B (inclusive of potential development and commercial milestones), brought two NASH candidates; Cenicriviroc, an oral CCR2/5 inhibitor in phase 2 and Evogliptin, an oral DPP-4 inhibitor in phase 1.

Earlier in 2018 Gilead bought Nimbus Therapeutics for $400M upfront and $800M in potential development milestones. NDI-0107976, an ACC inhibitor in phase 1 for the treatment of NASH was the main attraction for Gilead. Other recent NASH-related acquisitions are in the table below which was constructed by Evercore ISI. Preclinical and phase 1 candidates have commanded as much as $450M and $1B+, respectively, in buyouts.

We think frothiness of the NASH space coupled with the potential versatility of DUR-928 as it relates to formulations (oral, IV and topical) as well as its applicability in various conditions, including NASH, acute liver disease, PCS and even psoriasis warrants potential premium pricing. Initial human proof-of-concept in phase 1 studies for various formulations demonstrating a strong safety and drug interaction profile, in addition to compelling efficacy signals, further supports the relative value of DUR-928. Based on recent M&A transactions, DUR-928 has a relative value of between $750k and $1B. Further positive clinical trial progression would likely move valuation closer to the $1B mark.

Activity in the NASH space is high, with a number of recent acquisitions and partnerships.

Acquirer/Partner	Target	Type of Deal	Date Announced	Names of Programs	Phase of Development (at acquisition)	Total Value of Acquisition	Additional Details
Novartis	Conatus	Collaboration; NVS acquired worldwide rights to emricasan	December 2016	Emricasan	Phase 2b	Total potential value of at least $700 million	Conatus also eligible for tiered double digit royalties and option to co-commercialize
Allergan	Tobira	Acquisition	September 2016	Cenicriviroc (CVC), Evogliptin	CVC: Phase 3, Evogliptin: Phase 1	Total potential value of $1.695 billion	Upfront payment of $28.35 per share, in cash, and up to $49.84 per share in Contingent Value Rights
Allergan	Akarna	Acquisition	September 2016	AKN-083	Preclinical	>$50 million	$50 million upfront, with other milestones
Gilead	Nimbus	Acquisition	April 2016	NDI-010976 and other preclinical assets	Phase 1	Total potential value of $1.2 billion	Upfront payment of $400 million, with potential to receive $800 million in addition
Boehringer Ingelheim	Pharmaxis	Acquisition of PXS4728A program	May 2015	PXS4728A	Phase 1	Total potential value of ~$250 million for NASH	$31 million upfront, $222 million in milestone payments; in addition, royalties on sales
Merck	NGM Biopharma	Collaboration; MRK acquired 15% stake in the company	February 2015	Multiple including NP201	Preclinical	Total potential value of $450 million	$94 million upfront, 15% equity stake, up to $250 million to fund collaboration
Gilead	Phenex	Acquired NASH programs	January 2015	Multiple including Px-104	Phase 2	Total potential value of $470 million	Undisclosed upfront sum and milestones

Source: Company Press Releases

EVERCORE ISI

Current cash-generating products and earn-outs worth ~$90M

We estimate cash flow of DRRX's legacy products (Actel and Lactel) and PERSERIS earn-outs of approximately $85M over the next seven years. Discounting back to present at 12%, results in NPV of approximately $60M. We assign a 50% premium to the NPV value to reflect the likelihood of additional licensing, collaboration and earn-out opportunities materializing over the same period. We also note that this NPV value ($60M x 1.5 = $90M) may be conservative as it does not consider any assumed contribution from POSIMIR andy only minimal contribution from ORADUR. Upside to either of those programs (such as ORADUR launch in, and meaningful revenue from, China or a viable development strategy for POSIMIR), could result in relative upside to our NPV calculation.

Our sum-of-the-parts methodology values DRRX at approximately $965M, or $6.00/share

PROJECTED INCOME STATEMENT

Durect Corporation

DURECT Corp	Q1	Q2	Q3	Q4	2017A	Q1	Q2	Q3	Q4	2018 E	2019 E	2020 E
PERSERIS Earn-outs (US)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.8	$2.5
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	226.3%
PERSERIS (Ex-US)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-
ORADUR-ADHD (DRRX rights)	$0	$0	$0	$0	$0	$0	$0	$0	$0.0	$0.0	$0.0	$0.0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-
ORADUR-ADHD (Orient Pharma) Rylty	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.2	$0.4
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	100.0%
DUR-928	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-
Alzet Pumps & Lactel Polymers	$4.1	$3.1	$2.6	$3.3	$13.1	$2.4	$2.8	$2.3	$2.5	$10.0	$11.0	$12.0
YOY Growth	29.6%	9.5%	-22.0%	17.5%	7.8%	-42.1%	-9.3%	-11.3%	-23.4%	-23.6%	9.9%	9.1%
Total Product Sales	$4.1	$3.1	$2.6	$3.3	$13.1	$2.4	$2.8	$2.3	$2.5	$10.0	$12.0	$14.9
YOY Growth	29.6%	9.5%	-22.0%	17.5%	7.8%	-42.1%	-9.3%	-11.3%	-23.4%	-23.6%	19.5%	24.4%
Collaborative Revenue	$0.4	$1.3	$5.6	$16.3	$23.6	$1.1	$0.6	$5.7	$1.1	$3.1	$2.5	$2.5
YOY Growth	3.6%	241.8%	1491.5%	2105.0%	1154.1%	152.5%	-49.1%	1.6%	-93.2%	-86.7%	-20.0%	0.0%
Revenue from sale of IP rights			$12.5		$12.5	$0.0	$0.0	$0.0	$0.0	0.0%	0.0%	0.0%
Total Revenues	$4.6	$4.3	$20.75	$19.5	$49.17	$3.49	$3.41	$8.04	$3.60	$18.5	$14.5	$17.4
YOY Growth	26.6%	36.8%	454.3%	455.5%	250.6%	-23.6%	-21.0%	-61.3%	-81.6%	-62.3%	-22.0%	20.2%
Cost of Goods Sold	$1.5	$0.9	$3.1	$1.1	$6.6	$1.2	$1.1	$0.9	$1.0	$4.2	$4.2	$5.2
Product Gross Margin	62.7%	69.7%	-17.4%	67.5%	49.3%	50.9%	60.8%	61.1%	60.0%	62.0%	65.0%	65.0%
SG&A	$3.0	$3.7	$3.1	$3.3	$13.2	$3.2	$2.8	$2.9	$2.9	$11.8	$14.5	$17.2
% SG&A	66.6%	85.2%	15.1%	16.9%	26.8%	91.6%	82.5%	35.7%	80.6%	63.5%	100.3%	99.0%
R&D	$7.5	$9.1	$8.4	$6.6	$31.6	$7.0	$6.1	$6.5	$7.3	$26.9	$32.4	$36.8
% R&D	165.3%	210.2%	40.4%	33.8%	64.3%	199.3%	179.3%	81.4%	202.8%	145.2%	224.3%	211.7%
Operating Income	($7.6)	($9.4)	$6.1	$8.6	($2.2)	($7.8)	($6.6)	($2.3)	($7.6)	($24.3)	($36.7)	($41.8)
Operating Margin	-	-	-	-	-	-	-	-	-	-	-	-240.7%
Interest & Other Net	($0.5)	($0.6)	($0.0)	($0.3)	($1.5)	($0.5)	($0.4)	($0.4)	($0.6)	($1.9)	($2.6)	($2.4)
Pre-Tax Income	($8.1)	($9.9)	$6.1	$8.2	($3.7)	($8.3)	($7.0)	($2.7)	($8.2)	($26.2)	($39.3)	($44.2)
Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Net Income	($8.1)	($9.9)	$6.1	$8.2	($3.7)	($8.3)	($7.0)	($2.7)	($8.2)	($26.2)	($39.3)	($44.2)
YOY Growth	-	-	-	-	-					-	49.7%	12.6%
Reported EPS	($0.06)	($0.07)	$0.04	$0.05	($0.03)	($0.05)	($0.04)	($0.02)	($0.05)	($0.16)	($0.22)	($0.23)
YOY Growth					-					-	-	-
Shares Outstanding	141.8	142.5	147.2	150.8	145.6	153.6	161.6	162.0	164.0	160.3	175.0	190.0

Brian Marckx, CFA. Zacks Investment Research

© Copyright 2018, Zacks Investment Research. All Rights Reserved.

HISTORICAL STOCK PRICE



DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, Brian Marckx, CFA, hereby certify that the view expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.
Zacks SCR has received compensation from the issuer directly or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted. Fees typically range between ten thousand and fifty thousand dollars per annum. Details of fees paid by this issuer are available upon request.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.

© Copyright 2018, Zacks Investment Research. All Rights Reserved.

SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover. SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.