Zacks Small-Cap Research

Sponsored – Impartial - Comprehensive

scr.zacks.com

August 26, 2021
John D. Vandermosten, CFA
312-265-9588 / jvandermosten@zacks.com

10 S. Riverside Plaza, Chicago, IL 60606

Lipocine Inc. (LPCN-NASDAQ)

Liver Biopsy Results

Based on our DCF model and a 20% discount rate, LPCN is valued at approximately $10.00 per share. We include a valuation component for tentatively approved TLANDO (95% probability) and Phase II asset LPCN 1144 (15% probability). Despite a cleared investigational new drug application (IND), no valuation is given to LPCN 1148 or LPCN 1154 prior to entry in the clinic.

Current Price (8/25/21)	$1.40
Valuation	**$10.00**

OUTLOOK

Lipocine uses its proprietary Lip'ral technology to improve bioavailability and convenience of previously approved compounds using the 505(b)(2) regulatory pathway. Lip'ral's favorable pharmacokinetic profile facilitates lower dosing, reduces side effects and eliminates gastrointestinal interactions that limit absorption. Six drugs are in development that employ the Lip'ral technology; two are for the treatment of male hypogonadism; one is for the prevention of pre-term birth, one for post-partum depression and two candidates target NASH and cirrhosis.

The lead product, Tlando, was tentatively approved in December 2020 with full approval anticipated March 2022. LPCN's other candidates, Tlando XR and LPCN 1107 are on hold. LPCN 1144 is in development for pre-cirrhotic NASH and is now exploring next steps after positive Phase II biopsy data. LPCN 1148's IND was cleared in March 2020 and will launch a Phase II after additional funding is obtained.

SUMMARY DATA

52-Week High	**$2.42**
52-Week Low	**$1.09**
One-Year Return (%)	**-2.77**
Beta	**0.38**
Average Daily Volume (sh)	**977,641**
Shares Outstanding (mil)	**88.3**
Market Capitalization ($mil)	**$124**
Short Interest Ratio (days)	**4.16**
Institutional Ownership (%)	**10.6**
Insider Ownership (%)	**2.51**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2020 Estimate	**N/A**
P/E using 2021 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $US)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	$0.0 A	$0.0 A	$0.0 A	$0.0 A	$0.0 A
2021	$0.0 A	$0.0 A	$0.0 E	$0.0 E	$0.0 E
2022					$116.9 E
2023					$134.0 E

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	-$0.14 A	-$0.13 A	-$0.07 A	-$0.07 A	-$0.38 A
2021	-$0.04 A	-$0.08 A	-$0.05 E	-$0.06 E	-$0.23 E
2022					$1.09 E
2023					$1.29 E

WHAT'S NEW

LiFT Liver Biopsy Results

On August 25th, 2021 Lipocine (NASDAQ: LPCN) released liver biopsy results for its Phase II LiFT study in NASH. LiFT, or Liver Fat Intervention with Oral Testosterone, is a Phase II clinical study designed to evaluate LPCN 1144 oral testosterone in men with biopsy-confirmed NASH. Primary endpoint 12-week data for the trial was released in January of this year and demonstrated a statistically significant improvement in hepatic fat fraction.

As a long-term follow up to the results in January, August's biopsy results focused on the 36-week assessment of histological change for NASH resolution and no worsening of fibrosis and body composition and liver injury markers. These are the secondary endpoints. After the post-biopsy two week follow up, subjects will have the option to join the open label extension study which will take a further look at safety. In total, 56 patients enrolled in the safety set, 44 provided both baseline and 36 week biopsy and 37 produced a baseline NAS of greater than or equal to 4, with improvement in at least 1 point for both inflammation and ballooning, measures of NASH resolution.

Liver biopsies were taken at baseline and at 36 weeks to measure NASH resolution and fibrosis. NASH resolution results were favorable with very good statistical significance. The FDA requires resolution of steatohepatitis on overall histopathological reading and no worsening of liver fibrosis on NASH CRN fibrosis score.[1] We see that with this small sample of data, both treatment arms were able to produce substantially more responders than the placebo group, even with the added constraint of no worsening of fibrosis.

Scoring

A standard scoring system was used for the LiFT study evaluation. The same system has been used in other trials and is the standard accepted by the FDA to evaluate results. Below, we summarize the components of the scoring system which includes measurements of steatosis grade, inflammation, ballooning and fibrosis.

Exhibit I – NASH CRN Scoring System[2]

Steatosis Grade		Lobular Inflammation		Hepatocellular Ballooning		Fibrosis Score	
Degree	Description (%)	Degree	Description	Degree	Description	Degree	Description
0	<5	0	None	0	None	0	None
1	5–33	1	<2 foci/20× optical field	1	Mild, few	1a	Mild (delicate) zone 3 perisinusoidal fibrosis
						1b	Moderate (dense) zone 3 perisinusoidal fibrosis
2	34–66	2	2–4 foci/20× optical field	2	Moderate/marked, many	1c	Portal/periportal fibrosis only
						2	Zone 3 perisinusoidal fibrosis with portal/periportal fibrosis
3	>66	3	>4 foci/20× optical field			3	Bridging fibrosis
						4	Cirrhosis

LPCN 1144 36-Week Biopsy Results

When evaluated using CRN, LPCN 1144 was superior to placebo at p-values of 5% for Treatment arm A, and 1% and 0.1% level in Treatment B, respectively.

Exhibit II – NASH CRN Scoring Outcomes[3]

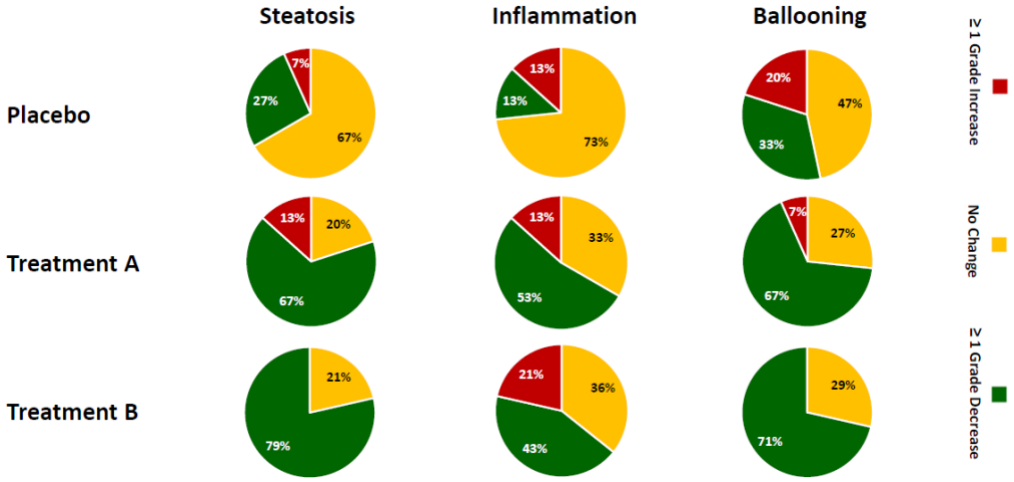
Histology NASH CRN **Scoring Outcomes**	**Placebo (n=11)**	**Treatment A (n=13)**	**Treatment B (n=13)**
NASH Resolution Responders	1 (9%)	7 (54%)*	9 (69%)**
NASH Resolution with No Worsening of Fibrosis Responders	0 (0%)	6 (46%)*	9 (69%)***

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

[1] FDA Draft Guidance. Noncirrhotic Nonalcoholic Steatohepatitis With Liver Fibrosis: Developing Drugs for Treatment. December 2018.
[2] Puri, P, Sanyal, A, Nonalcoholic Fatty Liver Disease: Definitions, Risk Factors, and Workup. Clinical Liver Disease, Vol. 1, No. 4, August 2012
[3] Source: Company press releases and Zacks analyst work.

For approval, the FDA requires histologic support of resolution of NASH with no worsening of fibrosis and/or resolution of fibrosis with no worsening in NASH and surrogate markers of efficacy. To score fibrotic development, NASH CRN is used as a surrogate, comparing to baseline. Each of the readings were performed on the same slides and pathologists were blinded as to the timing of the reads (baseline and end of study) and treatment group to reduce bias.

Exhibit III – Histological Changes in NASH CRN Scoring[4]



Other approaches to assess resolution of NASH include paired read analysis, where the baseline biopsy vs. the 36 week biopsy slides are evaluated side by side. The paired read results concurred with the NASH CRN findings.

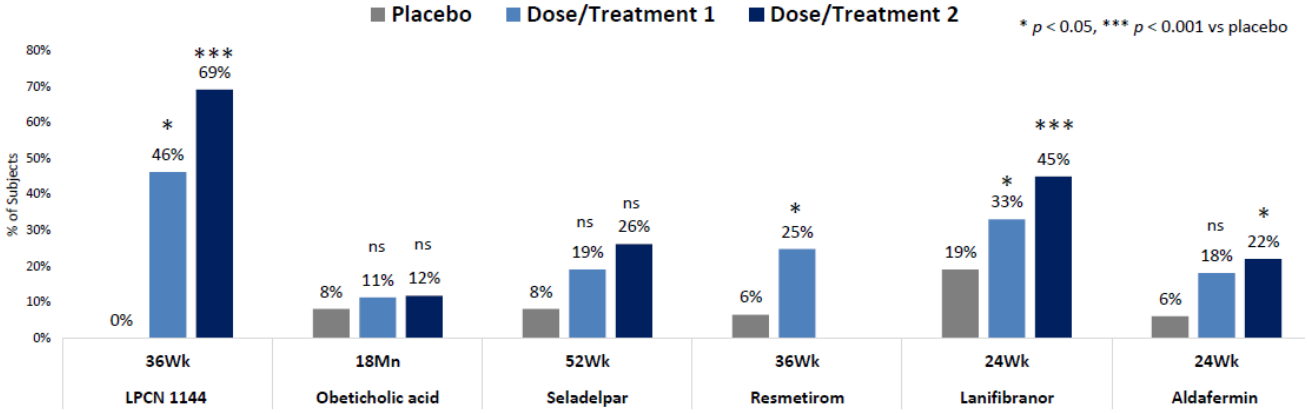
Exhibit IV – Paired Read Analysis[5]

NASH Biopsy Paired Read	Placebo (n=11)	Treatment A (n=13)	Treatment B (n=13)
Improvement in NASH Responders	2 (13%)	9 (60%)*	8 (57%)*
Improvement in NASH with No Worsening of Fibrosis Responders	2 (13%)	9 (60%)*	8 (57%)*

* p < 0.05 ** p < 0.01 *** p < 0.001

Lipocine compiled a comparison of results from other clinical trials and the proportion of the population in the treatment arm that was able to resolve NASH. The comparator trials are different in terms of trial design, size and patient populations and that there have been no head to head trials among the NASH candidates. Results from the comparison are very favorable for LPCN 1144, and demonstrate a substantial improvement over placebo.

Exhibit V – LPCN 1144 Comparison with Other NASH Drug Candidates[6]



[4] Source: Lipocine August 25 LiFT Key Topline Results Corporate Presentation
[5] Source: Lipocine August 25 LiFT Key Topline Results Corporate Presentation
[6] Source: Lipocine August 25 LiFT Key Topline Results Corporate Presentation

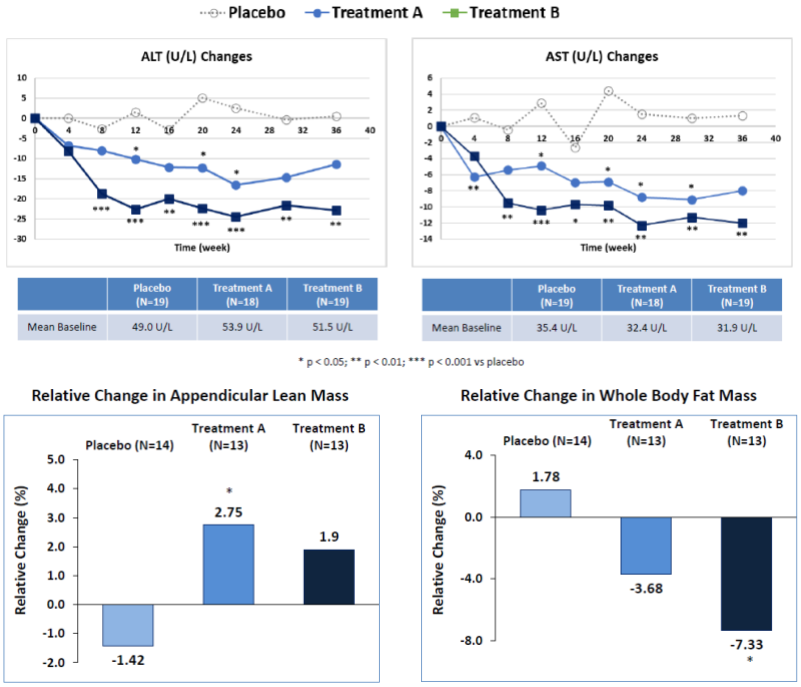
In summary, the combination of NASH measures in the restricted patient population warrant confirmation in a larger study. We note an anomalous result: placebo appeared to outperform the treated arms on a measure of fibrosis improvement of > 1 Stage with no NASH worsening on number of responders.

Exhibit VI – Fibrosis Outcomes Across Biopsy Assessment Techniques[7]

Histopathological Assessment Techniques	Placebo (n=11)	Treatment A (n=13)	Treatment B (n=13)
NASH CRN: Fibrosis improvement > 1 Stage, No NASH Worsening, Responders	6 (40%)	4 (27%)	2 (14%)
Paired Technique: Fibrosis Improvement with No NASH Worsening, Responders	3 (20%)	6 (40%)	8 (57%)
Digital Technique-FibroNext: Fibrosis Improvement, Responders	5 (33%)	12 (80%)	6 (43%)

The follow up also assessed changes in liver injury markers, ALT and AST, and body composition, that were directionally favorable, but with varying degrees of statistical significance.

Exhibit VII - Changes in Liver Markers and Body Composition[8]



Safety results from the trial through week 36 were favorable with frequency and severity of treatment emergent adverse effects (TEAEs) for both treatment arms comparable with placebo. Drug related TEAEs were mild to moderate. Four subjects discontinued participation from the trial in the placebo arm and one discontinued in the treatment arms. Cardiovascular events were balanced among the groups and there were no reported cases of hepatocellular carcinoma or drug induced liver injury. Other measures were also mild to moderate with little difference between the control and active groups.

[7] Source: Lipocine August 25 LiFT Key Topline Results Corporate Presentation
[8] Source: Lipocine August 25 LiFT Key Topline Results Corporate Presentation

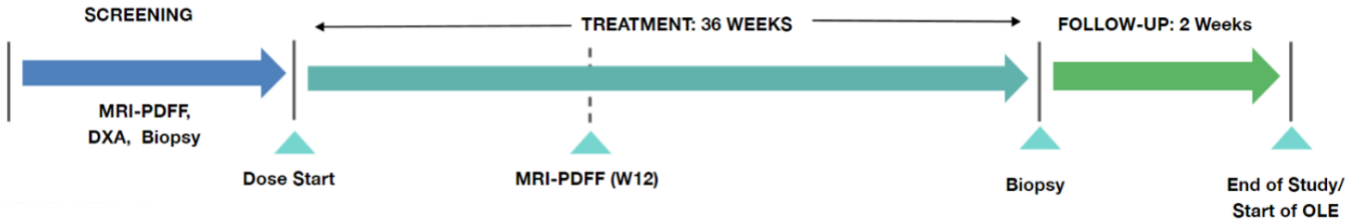
January 2021 Topline Results from LiFT Study

Lipocine announced positive 12-week topline data from its LiFT study in January 2021. LiFT is a Phase II evaluation of its candidate LPCN 1144, an oral pro-drug of endogenous testosterone, in biopsy-confirmed, non-cirrhotic male NASH patients with F1-F3 fibrosis. Results were positive and show statistical significance in the primary endpoint of change in hepatic fat fraction, quantified via MRI-PDFF[9] at week 12. Lipocine's LPCN 1144 demonstrated robust, statistically significant efficacy in not only its primary endpoint of reduction of hepatic fat fraction, but secondary endpoints as well, which were published in the most recent release.

LiFT Study Design

LiFT (Liver Fat intervention with oral Testosterone) is a Phase II trial designed to evaluate LPCN 1144 oral testosterone in men with biopsy-confirmed NASH. It enrolled 56 men with confirmed NASH, randomized 1:1:1 in three arms. The arms included Treatment A, 142 mg testosterone equivalent twice daily, Treatment B, which was the same as Treatment A but with the addition of 217 mg of d-alpha tocopherol equivalent twice daily and a placebo arm with twice-daily administration. Excluding the open label extension, LiFT had a duration of 36 weeks.

Exhibit VIII – LiFT Trial Timeline[10]



The primary endpoint for LiFT was change in hepatic fat fraction, evaluated using MRI-PDFF at week 12, topline results for which were released in January 2021. Secondary endpoints included change in NASH activity and fibrosis via liver biopsy scoring at week 36, change in hepatic fat fraction via MRI-PDFF at week 36, change in liver injury markers, anthropomorphic measurements, lipids, insulin resistance and inflammatory/fibrosis markers, and Patient Reported Outcomes (PROs) including quality of life and global impression scores (PGI). In the latest update, Lipocine obtained biopsy samples to evaluate the four markers used in NASH CRN scoring.

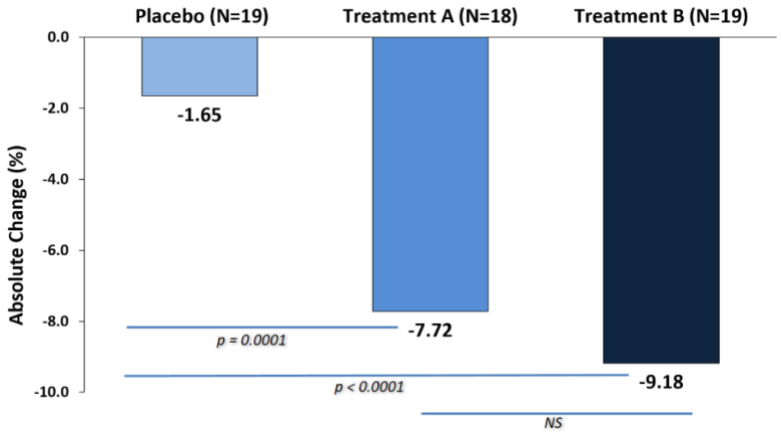
Patients will be offered access to LPCN 1144 through an open label extension study, announced December 30, 2020. This option for patients will enable the collection of additional data for up to 72 weeks total. The open label enrollment is ongoing with data reporting expected in mid-2022.

[9] Magnetic Resonance imaging Proton Density Fat Fraction
[10] Source: Lipocine August 25 LiFT Key Topline Results Corporate Presentation

Topline Results for Primary Endpoint

Baseline characteristics were presented that recounted the participants, completion, age, BMI, diabetes and hypertension, as well as baseline measurements of endpoint factors.

Exhibit IX – Absolute Change in Liver Fat (%)[11]



The primary endpoint for LiFT was change in hepatic fat fraction. As reported, there was a statistically significant decrease in hepatic fat, significant at the 0.01% level ($p < 1\%$) for both Treatment A and Treatment B arms. The percentage of subjects with greater than 30% reduction in liver fat was statistically significant in excess of 1% in both arms vs placebo. Absolute and relative change in liver fat percentage in subjects with baseline liver fat in excess of 5% was statistically significant at 0.01% for both arms vs placebo.

In evaluation of liver injury markers, d-alpha tocopherol's potentiation of LPCN 1144 was quantifiably apparent. With respect to alanine aminotransferase (ALT), both treatment arms were statistically differentiable from placebo at 1.6% and 0.01% for A and B arms, respectively. Here, Treatment B was statistically distinguishable from Treatment A arm at the 0.5% level. Evaluation of change in aspartate aminotransferase (AST) was again statistically significant for both arms at 2% and 0.01% levels for A and B arms, respectively, but here A and B arms were not statistically different, although directionally consistent. ALT and AST reduction in absolute terms were up to 22.4 U/L and 10.4 U/L, respectively. Results including d-alpha tocopherol generated substantially reduced liver injury markers ALT and AST compared with LPCN 1144 alone. The difference between the two arms was less dramatic in other measures such as hepatic fat fraction reduction. Lipocine proposed antioxidant activity of d-alpha tocopherol as a possible mechanism that impacted ALT and AST, although the exact mechanism was not understood.

Finally, longitudinal analysis of changes in the two liver injury markers showed that as early as week four, for AST, and week eight for both ALT and AST, combination LPCN 1144 and d-alpha tocopherol showed statistically significant changes. The treatment was not only successful where other NASH therapies have struggled, but also conveniently orally administered and timely in its efficacy.

Adverse events were comparable to the placebo arm with no observed tolerability issues. Three subjects in the placebo group and one in a treatment arm discontinued study due to treatment emergent adverse events (TEAE).

36-week biopsy data are now available as discussed above. Enrollment for the open label extension to the LiFT study has begun, which will allow the collection of additional data for up to 72 weeks of therapy.

Next Steps

Now that selected 36-week biopsy data has been presented to investors, Lipocine's next steps are to schedule an end-of-Phase II meeting with the FDA, prepare a presentation for a scientific and medical conference, and complete the extension study. Results from the Phase II study are positive and can lead down several pathways depending upon the FDA's guidance following the anticipated meeting. A Phase IIb study may be launched, or if data appears to provide sufficient proof of concept, a Phase III may be launched. We think it is likely that Lipocine will seek a partner to advance LPCN 1144 into a registrational study.

[11] Lipocine March 2021 corporate presentation

Milestones

- NDA filed for Tlando – February 2020
- IND clearance for Phase II study of LPCN 1148 – May 2020
- Tentative approval of Tlando – December 2020
- LiFT Study
    - Primary endpoint – January 2021
    - Last patient, last visit for biopsy data – June 2021
    - Presentation of 36-week, biopsy data to investors – August 2021
    - End of Phase II meeting with FDA – 2H:21
    - Presentation of study data at conference – 4Q:21
- Abstract presentation at EASL – June 2021
- Male cirrhosis trial first subject dosed for LPCN 1148 – 4Q:21
- Topline announcement for PK study for LPCN 1154 – 3Q:21
- Launch of Phase IIa proof of concept PPD trial – 4Q:21
- Results from LiFT Extension Study – Mid-2022
- Tlando eligible for final approval – 2Q:22

Summary

Lipocine's Phase II biopsy data for LPCN 1144 yielded positive results, with agreement across multiple measures of NASH, with statistical significance in a small patient group, as well as positive liver marker, body composition and safety results. While fibrosis improved more in the placebo arm vs. the treatment group under the NASH CRN guidelines, other techniques for measuring fibrosis showed conflicting conclusions, indicating that a larger study is needed to validate the results. A trial in a larger patient population is expected, which will be under consideration as Lipocine prepares to meet with the FDA. We also expect the launch of a Phase IIa trial in PPD and first subject dosed in the LPCN 1148 trial before year end. See our previous report for details. The primary valuation driver for the company is Tlando, which must wait for full approval and first sales until the expiration of its competitor's exclusivity. In the interim between now and anticipated full approval, Lipocine will be meeting with prospects to identify a path forward for commercialization. We maintain our target price of $10.00.

PROJECTED FINANCIALS

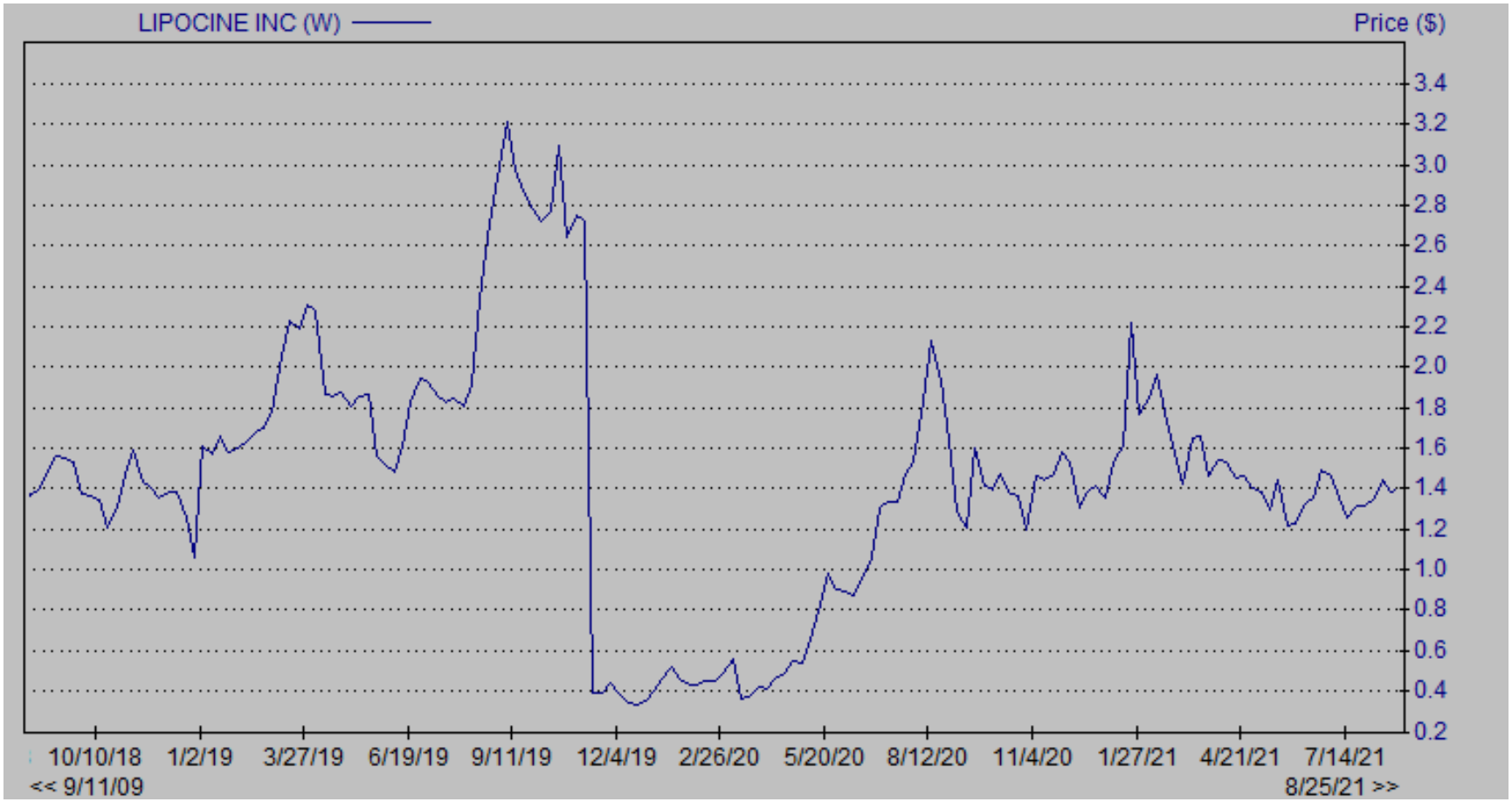
Lipocine Inc. - Income Statement

Lipocine Incorporated	2020 A	Q1 A	Q2 A	Q3 E	Q4 E	2021 E	2022 E	2023 E
Total Revenues ($MM)	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$116.9**	**$134.0**
R&D	$9.7	$1.6	$1.5	$2.5	$2.8	$8.3	$10.0	$10.0
G&A	$8.2	$1.5	$1.5	$2.1	$2.3	$7.5	$8.3	$6.0
Other expenses	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$1.1
Operating Income	($18.0)	($3.1)	($3.0)	($4.6)	($5.1)	($15.8)	$98.6	$116.9
Operating Margin	-					-	-	-
Total Other Income	($3.0)	($0.3)	($3.8)	($0.1)	($0.1)	($4.3)	($0.5)	($0.5)
Pre-Tax Income	($21.0)	($3.4)	($6.8)	($4.7)	($5.2)	($20.1)	$98.1	$116.4
Taxes & Other	$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%*
Net Income	($21.0)	($3.4)	($6.8)	($4.7)	($5.2)	($20.1)	$98.1	$116.4
Reported EPS	**($0.38)**	**($0.04)**	**($0.08)**	**($0.05)**	**($0.06)**	**($0.23)**	**$1.09**	**$1.29**
YOY Growth	-					-	-	-
Shares Outstanding	55.7	81.9	88.3	88.5	88.7	86.8	90.0	90.0

Source: Company Filing // Zacks Investment R

HISTORICAL STOCK PRICE

Lipocine Inc. – Share Price Chart



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, John Vandermosten, hereby certify that the views 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.
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.