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Lipocine Inc. (LPCN: NASDAQ)

LPCN: 1154 Results Illuminate Accelerated Pathway

Our DCF model employs a 15% discount rate for Tlando royalty cash flows and a 20% discount rate and a 21% probability adjusted DCF valuation for LPCN 1144, LPCN 1148 and LPCN 1154. We model all of Lipocine's assets to eventually be developed by partners and Lipocine to receive upfronts, milestones and royalties.

Current Price (5/18/2023)	$3.67
Valuation	**$40.00**

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. Tlando, is being commercialized by partner Halozyme and royalties are expected. Lipocine is developing treatments for CNS disorders with its LPCN-1154, -1148 and -2101 assets. Other assets are intended for partnerships including those for the treatment of male hypogonadism; the prevention of pre-term birth, NASH and cirrhosis.

Tlando's US commercialization activities began in June 2022 while ex-US rights remain available. Lipocine's R&D is focused on several indications including -1154 (postpartum depression), -1148 (cirrhosis) & -2101 (epilepsy).

LPCN 1144 for pre-cirrhotic NASH has shown promise in a space with no other approved treatment. Phase II data demonstrated reduction in liver fat and favorable safety data making it a primary candidate for partnership. LPCN-1107, -1148 & -1154 have various PK and food effect studies required before beginning the next stage of studies.

SUMMARY DATA

52-Week High	**16.15**
52-Week Low	**3.30**
One-Year Return (%)	**-75.8**
Beta	**0.9**
Average Daily Volume (sh)	**20,956**
Shares Outstanding (mil)	**5.207**
Market Capitalization ($mil)	**19.1**
Short Interest Ratio (days)	**7.0**
Institutional Ownership (%)	**12.0**
Insider Ownership (%)	**2.6**
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 2023 Estimate	**N/A**
P/E using 2024 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of USD)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	$0.0 A	$0.5 A	$0.0 A	$0.0 A	$0.5 A
2023	$0.1 A	$0.0 E	$0.0 E	$0.0 E	$0.1 E
2024					$0.0 E
2025					$0.0 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2022	-$0.67 A	-$0.51 A	-$0.46 A	-$0.43 A	-$2.07 A
2023	-$0.74 A	-$0.64 E	-$0.57 E	-$0.53 E	-$2.48 E
2024					-$2.26 E
2025					-$2.41 E

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WHAT'S NEW

1Q:23 Financial and Operational Results

Efforts year to date for Lipocine Inc. (NASDAQ: LPCN) were dominated by the pharmacokinetic (PK) study for LPCN 1154, which is in development for postpartum depression (PPD). The underlying drug in LPCN 1154 is brexanolone, which is approved in an intravenous (IV) formulation for PPD. Results from the study were reported several days after first quarter financial and operational results were released. Lipocine's recent strategy change to focus on the development of treatments for central nervous system (CNS) disorders, particularly neuroactive steroids, has oriented the company's efforts towards a narrow portfolio of products and indications including the previously mentioned LPCN 1154 as well as LPCN 1148 and LPCN 2101.

On May 11, 2023 Lipocine (NASDAQ: LPCN) filed its 1Q:23 Form 10-Q and posted its earnings release for the quarter ending March 31, 2023.

Highlights for 2023 include:

- First subject dosed in LPCN 1154 PK trial – April 2023
- 1:17 reverse stock split – May 12, 2023
- Topline results from LPCN 1154 PK trial – May 2023

Lipocine generated revenues of $0.1 million during 1Q:23 and posted a net loss of ($3.9) million, or ($0.74) per share. These results are adjusted for the 1:17 reverse stock split that became effective following the filing of the 1Q:23 10-Q. Reported per share numbers do not adjust for the reverse split that took place on May 12, 2023.

For the quarter ending March 31, 2023 and versus the same period in the prior year:

- Revenues were $55,000 compared to nil. The amounts reflect a payment from Spiraso related to a licensing agreement for products in the cough and cold field;
- Research & Development expense totaled $3.1 million, rising 65% from $1.9 million. The increase was driven by CRO expense related to LPCN 1148 and LPCN 1154, personnel expense, lab supplies, small equipment and other R&D expenses. Offsets arose from lower LPCN 1111 scale up costs, LPCN 1144 CRO and outside consulting costs and amounts related to ancillary studies for LPCN 1107;
- General & Administrative expenses were $1.3 million, up 4% from $1.2 million primarily due to higher strategic advice and planning related legal fees, business development consulting fees, director fees and other professional fees. These amounts were offset by lower board recruitment fees and corporate insurance;
- Total other net income was $0.5 million related to interest and investment income and a gain on warrant liability;
- Net loss was ($3.9) million or ($0.74) per share compared with net loss of ($3.5) million or ($0.67) per share, respectively.

At quarter's end, marketable securities, cash and equivalents totaled $28.9 million. Cash burn for 1Q:23 was ($3.9) million, matching prior year period amounts. $6,000 of cash was used in financing related to the costs of the at the market (ATM) offering.

Product Candidates

Lipocine's primary research and development efforts in the CNS pipeline focus on lead candidate LPCN 1154 for post-partum depression (PPD), LPCN 2101 for women with epilepsy and LPCN 1148 for management of decompensated cirrhosis and hepatic encephalopathy.

LPCN 1154
LPCN 1154 recently completed a pilot pharmacokinetic (PK) bridge study and is the most advanced of the company's active assets. It is attractive as existing administration of the underlying molecule, brexanolone is burdensome and is administered as a continuous intravenous infusion over a period of 60 hours. It is mixed in a sterile solution and delivered through an intravenous catheter. The infusion is started at a low dose and gradually increased over the first 24 hours to the target dose, which is determined based on the patient's weight. During the infusion, the patient's vital signs are closely monitored, and any side effects or adverse reactions are addressed as needed. The

time needed to infuse and the requirement that the patient receive the infusion in the hospital create substantial burdens and costs that could be largely alleviated if an oral form is successfully developed.

Lipocine's PK bridge study results will inform a follow up meeting with the FDA where further discussions are planned to design a pivotal study in order to support a submission via the 505(b)(2) regulatory pathway. Based on input from management, we think that a pivotal study could cost from $4 to $5 million and be completed in a year.

Postpartum Depression

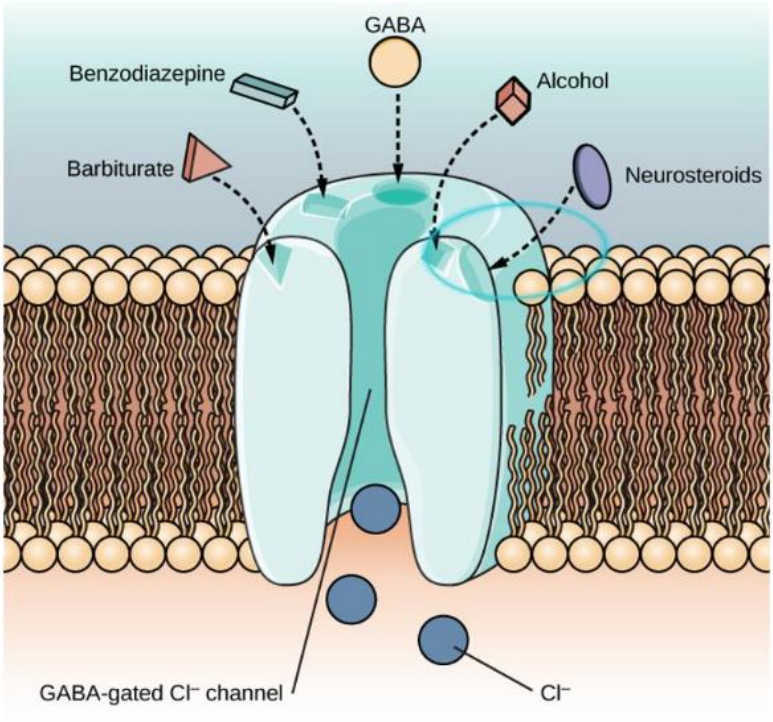
Postpartum depression (PPD) is a mood disorder that affects women after childbirth. Hormonal changes and neurotransmitter imbalances are believed to play a role. GABA (gamma-aminobutyric acid) is an inhibitory neurotransmitter in the brain that helps regulate mood and anxiety. GABA receptors are classified into different subtypes, including $GABA_A$ and $GABA_B$ receptors. These receptors have specific binding sites for GABA and are involved in different physiological processes.

The GABA receptors may be allosterically modulated, where a molecule binds to a specific receptor or enzyme at a site distinct from the active site, known as the allosteric site. There are both positive allosteric modulator (PAM) sites which augments the function of the primary receptor and negative allosteric modulator (NAM) sites which diminish the function of the primary receptor. When a PAM binds to the allosteric site, it induces a conformational change in the receptor or enzyme, leading to an increase in the affinity of the receptor for its natural ligand or enhancing the enzyme's catalytic activity. This positive modulation can result in an increase in the response or signaling produced by the receptor or enzyme, effectively amplifying its function.

Research suggests that $GABA_A$ receptors may be implicated in the development of postpartum depression. During pregnancy, the levels of certain hormones, such as progesterone and allopregnanolone (a neurosteroid), increase significantly. These hormones can enhance the activity of $GABA_A$ receptors, leading to increased GABAergic inhibition and a calming effect on the brain. However, after childbirth, there is a rapid decline in the levels of these hormones. This sudden hormonal shift can disrupt the balance of GABA receptor activation, leading to decreased GABAergic inhibition. This imbalance may contribute to the development of PPD symptoms, such as anxiety, irritability, and depressed mood.

Furthermore, alterations in GABA receptor function can affect the regulation of other neurotransmitters, such as serotonin and dopamine, which are also implicated in mood disorders. Imbalances in these neurotransmitter systems may further contribute to the development of PPD.

Exhibit I – GABA Receptor Substrates Binding[1]



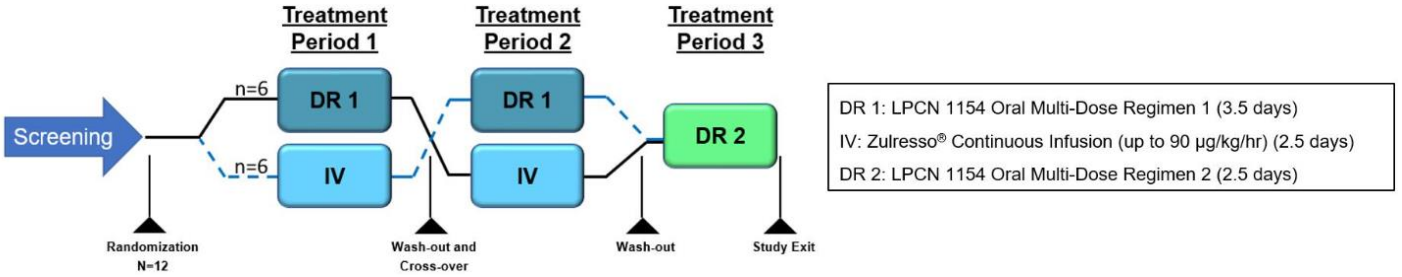
[1] Lipocine LPCN 1154 Presentation, May 16, 2023

Brexanolone is a positive allosteric modulator of the $GABA_A$ receptor. In its approved form, it is administered over a 60-hour period in the hospital with the patient under observation. Many of the adverse events are related to IV infusion errors and patients must contend with the cost and difficulty of overnight stays, cost and accessibility.

LPCN PK Study Results

In a May 16th press release, Lipocine provided a summary of the pharmacokinetic bridging study results. The study was designed as an open label, randomized, partial crossover study in healthy postmenopausal women. The primary objective of the study was to compare the pharmacokinetics (AUC_∞ and C_{max}) of two LPCN 1154 oral multi-dose regimens and a continuous IV infusion dosing regimen of brexanolone, to inform the dose selection for the planned confirmatory pivotal PK registration study. Details and duration of the 1:1 administration of brexanolone in 12 subjects is included in the following graphic.

Exhibit II – LPCN 1154 Pilot Pharmacokinetic Bridge Study Design[2]



The primary goal of this smaller PK study was to identify an appropriate dose. Results from the study were provided in a summary comparing Lipocine's oral version of brexanolone to the intravenous version of brexanolone branded Zulresso. While the FDA has final say regarding the specifics of this application, regulatory guidelines for pharmacokinetic parameters generally require the new formulation to fall within 80% to 125% for AUC and C_{max}. In the data provided below, oral brexanolone (LPCN 1154) was generally within the set parameters. The pilot study is intended to identify the optimal dose, so we anticipate that results from the follow-on study will fall more closely within required parameters. The pilot study data will be used to interact with the FDA and determine the design for a larger pivotal PK study that would be required for filing for marketing authorization.

Exhibit III – Ratios of Geometric Mean, LPCN 1154 vs. IV Brexanolone[3]

PK Parameter	DR 1 vs IV 60 µg*	DR 1 vs IV 90 µg	DR 2 vs IV 60 µg*	DR 2 vs IV 90 µg
AUC_∞	98%	77%	106%	83%
C_{max}	114%	68%	134%	79%

While explicit details of the safety parameters were not provided, the Lipocine team noted that, as in previous studies, LPCN 1154 appeared safe and well-tolerated in the study. Adverse events were mild or moderate in severity, and similar across trial arms. One of the primary concerns for Zulresso, hypoxia, was not observed in LPCN 1154 subjects, nor were any sedation related events.

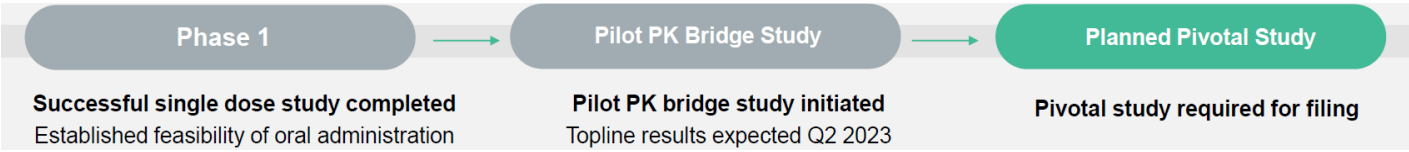
While LPCN 1154 appears to improve several significant hurdles faced by PPD patients that may benefit from brexanolone, there are other considerations. It is unclear whether or not LPCN 1154 would maintain the black box warning that appears in the label for Zulresso. The risk of excessive sedation and loss of consciousness requires that patients be monitored by a provider and have blood oxygen levels measured over the duration of treatment.

Next Steps

Next steps for Lipocine management for LPCN 1154 are to share data from the pilot PK study with the FDA and design the pivotal study. After FDA assent, the study will launch in 2H:23. Assuming supportive results, LPCN 1154 will pursue a 505(b)(2) pathway. Expected cost for the pivotal study is estimated at $4 to $5 million.

[2] Lipocine LPCN 1154 Presentation, May 16, 2023
[3] Lipocine LPCN 1154 Presentation, May 16, 2023

Exhibit IV – LPCN 1154 Clinical Pathway[4]



LPCN 1154 may address many of the shortcomings of Zulresso; however, there are potential competitors waiting in the wings. Zuranolone is an investigational medication which is under development by SAGE Therapeutics for the treatment of depressive disorders and a variety of other indications. The oral, $GABA_A$ positive allosteric modulator has been submitted to the FDA in a new drug application for major depressive disorder (MDD) and PPD. A target action date of August 5, 2023 has been assigned.

LPCN 1148 Phase II Study in Decompensated Cirrhosis

Lipocine is conducting a Phase II study in decompensated cirrhosis with its LPCN 1148 asset. LPCN 1148 is a novel prodrug of androgen receptor agonist for oral administration with multi modal action to improve liver and muscle function. The compound proposes to improve quality of life for patients awaiting liver transplant, decrease hospital admissions and prevent or reduce the occurrence and recurrence of decompensation events. The 24-week trial completed enrollment of the targeted 30 patients and is expected to announce results in mid-2023. The ongoing Phase II proof of concept trial employs a prospective, multi-center, randomized, placebo-controlled two-stage design. The primary endpoint is change in skeletal muscle index at week 24. Secondary endpoints include change in liver frailty index and myosteatosis,[5] rates of breakthrough hepatic encephalopathy and number of waitlist events including all-cause mortality. Total treatment duration which includes the placebo-controlled stage one and the single-active arm, open-label extension stage two is 52 weeks.

CNS Disorders

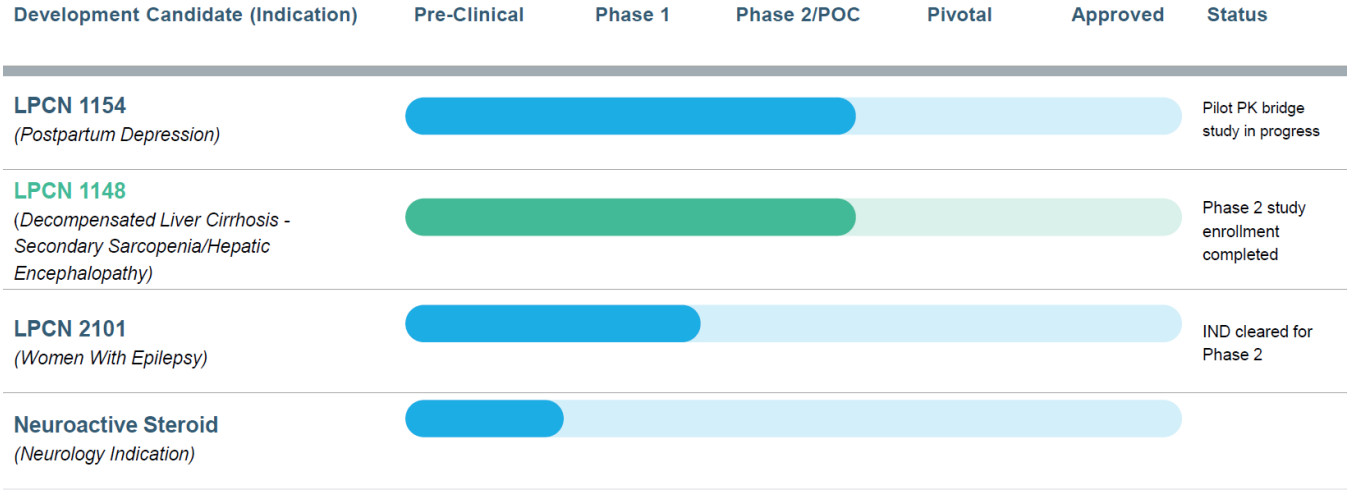
In late September, Lipocine announced that it had narrowed its research and development aims. It will apply the Lip'ral technology to creating new treatments for central nervous system (CNS) disorders. The company's initial focus will be on oral formulations of endogenous neuroactive steroids that are applicable to the CNS space. Lipocine anticipates that its approach can be applied to enable effective oral delivery of endogenous modulators of the $GABA_A$ receptor, which historically have been challenging to deliver orally due to poor aqueous solubility. The CNS development portfolio includes LPCN 1154, a fast-acting oral antidepressant for postpartum depression (PPD) with potential for outpatient use; LPCN 2101, with a novel mechanism of action, for women with epilepsy; and another undisclosed CNS-focused candidate. LPCN 1148 will also be considered to be in the active pipeline for its use in hepatic encephalopathy.

The shift towards a CNS-focused portfolio converts the non-core assets into partnership opportunities. In terms of priority for business development, Tlando ex-US is first, with 1107 for pre term birth, 1144 for non-alcoholic steatohepatitis (NASH), 1148 for cirrhosis and Tlando XR following in order of priority. No further material investment is expected by Lipocine in these assets and related indications.

To support its move toward CNS disorders, Lipocine has appointed several new leaders, as shared in a November press release. George Nomikos, M.D., Ph.D. joined the company as Chief Medical Officer (CMO) and Spyros Papapetropoulos, M.D., Ph.D. was elevated to lead director and Chairman of the Board. The new additions are expected to help guide the development portfolio forward leveraging backgrounds in neurology and psychiatry and experience leading CNS-focused companies. Dr. Nomikos is a biopharmaceutical R&D scientist who has held senior roles at Scholar Rock, Biogen, Sage, Takeda, Astellas Amgen and Eli Lilly. He was also an associate professor at the Karolinska Institutet in Stockholm, Sweden. Dr. Papapetropoulos has been a member of Lipocine's board since April 2022 and is CMO at Vigil Neuro. Former roles include senior positions at Acadia Pharmaceuticals, SwanBio Therapeutics, Cavion and a number of large pharmaceutical companies including Biogen and Pfizer.

[4] Lipocine January 2023 Corporate Presentation
[5] Myosteatosis, also known as "muscle fat infiltration," is a condition where fat accumulates in the skeletal muscle tissue, leading to decreased muscle quality and function. It is commonly observed in older adults and individuals with obesity, metabolic syndrome, or diabetes.

Exhibit V - Lipocine Active Pipeline[6]

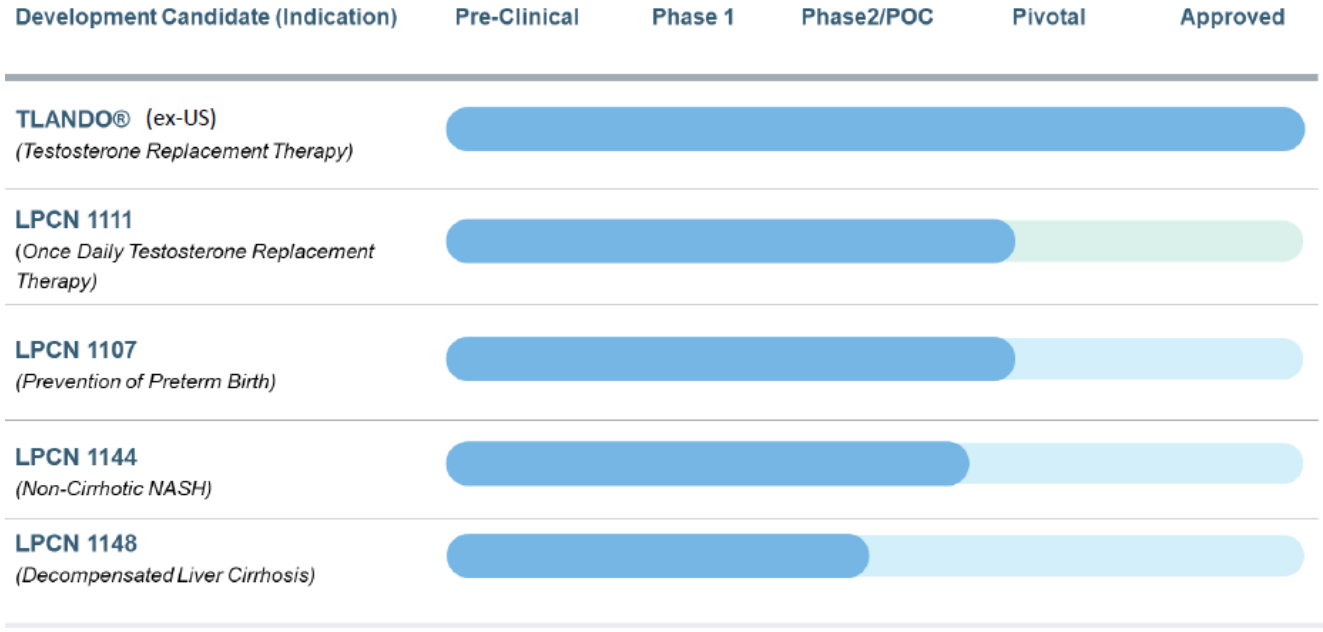


LPCN 1144

One of Lipocine's most important partnership assets is LPCN 1144 for the treatment of non-cirrhotic non-alcoholic steatohepatitis (NASH). Program 1144 has completed a Phase II study (LiFT) and management is exploring cooperation opportunities for this asset. The end of Phase II meeting that was held with the FDA identified a requirement to conduct a dose ranging study using Lipocine's proposed testosterone ester, testosterone dodecanoate (TD); however, Lipocine will not pay for or conduct the study. TD has several favorable characteristics compared with testosterone undecanoate including anti-infective properties and favorable pharmacokinetics.

The NASH space is still wide open, especially after the response by the FDA to Intercept (ICPT) application for Obeticholic acid (OCA) ahead of a Advisory Committee panel meeting. The agency identified numerous safety risks that did not appear to be counterbalanced by the product's efficacy profile. The target action date for the drug is still June 22, 2023.

Exhibit VI – Non-core Asset Pipeline[7]



[6] Lipocine January 2023 Corporate Presentation
[7] Lipocine January 2023 Corporate Presentation

Milestones

- LPCN 1154 multi-dose PoC study – 4Q:22
- LPCN 1148 (sarcopenia) Phase II enrollment complete – 4Q:22
- LPCN 1154 PK bridge study results – 2Q:23
- LPCN 1148 top-line 24-week results – mid-2023
- Partnering activities for LPCN 1111, 1144, 1107 & Tlando ex-US – 2023+
- LPCN 1148 Phase II topline data – mid-2023

For LPCN 1111, the asset that is in development to replace Tlando as a once-daily testosterone replacement is ready for a pivotal trial which will be conducted by a partner if one emerges. LPCN 1107 in pre-term birth is also available for partner development.

Valuation

We adjust our valuation to reflect the 1:17 reverse stock split and future anticipated capital needs. Our updated target is $40.00 per share.

Summary

The new CNS-focused strategy is coincident with the addition of new leadership with experience in the CNS space to advance the primary assets of LPCN 1154, 1148 and 2101. Sales of Tlando at Halozyme are expected to continue to grow and may provide additional cash flows to Lipocine if revenues exceed minimum thresholds. Other assets that have been developed to the point of proof of concept are available to partners who may elect to advance them further. Results from the LPCN 1154 PK study are promising and further illuminate the path forward to regulatory approval. The compound solves many of the shortcomings of the approved IV version of the underlying drug, in a space with few alternatives. While there are competitors on the horizon, LPCN 1154 would offer a product with a better-known profile and potentially faster mechanism of action for PPD. We will keep our eyes open for additional business development activities by Lipocine as it seeks partners to take the baton on programs for Tlando XR, pre-term birth and ex-US Tlando programs. We modify our valuation to reflect updated outstanding and anticipated outstanding shares to $40.00.

PROJECTED FINANCIALS

Lipocine Inc. - Income Statement

Lipocine Incorporated	2022 A	Q1 A	Q2 E	Q3 E	Q4 E	2023 E	2024 E	2025 E
Total Revenues ($MM)	**$0.5**	**$0.1**	**$0.0**	**$0.0**	**$0.0**	**$0.1**	**$0.0**	**$0.0**
R&D	$8.6	$3.1	$2.1	$2.1	$1.9	$9.2	$10.0	$10.0
G&A	$4.1	$1.3	$1.1	$0.9	$0.9	$4.2	$5.6	$6.0
Other expenses	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($12.1)	($4.3)	($3.2)	($3.0)	($2.8)	($13.3)	($15.6)	($17.0)
Operating Margin	-					-	-	-
Total Other Income	$1.4	$0.5	($0.1)	($0.1)	($0.1)	$0.1	($0.5)	($0.5)
Pre-Tax Income	($10.8)	($3.9)	($3.3)	($3.1)	($2.9)	($13.2)	($16.1)	($17.5)
Taxes & Other	$0.0	($0.0)				$0.0	$2.0	$3.0
Tax Rate	*0%*	*$0.0*	*0%*	*0%*	*0%*	*0%*	*-12%*	*-17%*
Net Income	($10.8)	($3.9)	($3.3)	($3.1)	($2.9)	($13.2)	($18.1)	($20.5)
Reported EPS	**($2.07)**	**($0.74)**	**($0.64)**	**($0.57)**	**($0.53)**	**($2.47)**	**($2.26)**	**($2.41)**
YOY Growth	-					-	-	-
Shares Outstanding	5.204	5.207	5.210	5.500	5.510	5.357	8.000	8.500

Source: Company Filing // Zacks Investment Research, Inc. Estimates

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HISTORICAL STOCK PRICE

Lipocine Inc. – Share Price Chart



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