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September 18, 2023
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CervoMed Inc.

(CRVO-NASDAQ)

CRVO: Publication in* Neurology *Highlights Correlation Between ptau181 Level and Response to Neflamapimod…

Based on our probability adjusted DCF model that takes into account potential future revenues for neflamapimod in DLB, CRVO is valued at $17.00/share. This model is highly dependent upon continued clinical success of neflamapimod and will be adjusted accordingly based upon future clinical results.

Current Price (09/18/23)	$5.33
Valuation	**$17.00**

OUTLOOK

On September 6, 2023, CervoMed Inc. (CRVO) announced the publication of additional pre-specified analyses of the AscenD-LB Phase 2a clinical trial in the journal *Neurology*. The results showed that patients with normal pre-treatment levels of plasma ptau181 showed a statistically significant benefit from neflamapimod treatment with a treatment effect size of at least 0.7 for each of the measures of dementia severity, attention, recognition memory, and functional mobility. The company is currently conducting a Phase 2b clinical trial of neflamapimod in patients with Dementia with lewy bodies (DLB) and are excluding those with abnormal levels of plasma ptau181. The results published in *Neurology* suggest that excluding patients with increased plasma ptau181 should increase the possibility of success in the Phase 2b clinical trial.

SUMMARY DATA

52-Week High	**$9.90**
52-Week Low	**$4.20**
One-Year Return (%)	**-43.60**
Beta	**1.72**
Average Daily Volume (sh)	**48,294**
Shares Outstanding (mil)	**1**
Market Capitalization ($mil)	**$7**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**13**
Insider Ownership (%)	**2**
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**

Risk Level	**High**
Type of Stock	**Small-Value**
Industry	**N/A**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	0 A	0 A	0 A	0 A	0 A
2023	0 A	0 A	0 E	0 E	0 E
2024					0 E
2025					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	-$2.22 A	-$2.06 A	-$1.37 A	-$2.00 A	-$7.65 A
2023	-$2.01 A	-$3.04 A	-$0.95 E	-$0.95 E	-$5.59 E
2024					-$2.67 E
2025					-$3.22 E

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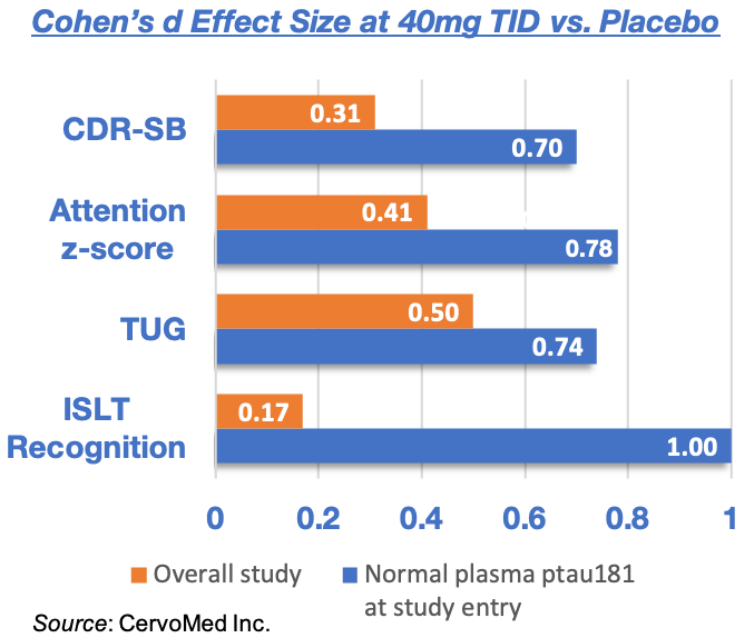
Business Update

New Analyses of AscenD-LB Phase 2a Trial

On September 6, 2023, CervoMed Inc. (CRVO) announced the publication of pre-specified analyses of the AscenD-LB Phase 2a clinical trial of neflamapimod in patients with Dementia with lewy bodies (DLB) in the journal *Neurology* (Alam *et al*., 2023). The results of the analyses show an association between plasma phosphorylated tau at position 181 (ptau181) levels at the beginning of the study and a patient's response to neflamapimod. Patients with ptau181 levels below a pre-determined cut-off (<2.2 pg/mL) showed significant improvement over placebo in an Attention Composite measure, the Clinical Dementia Rating Scale Sum of Boxes, the Timed Up and Go test, and International Shopping List Test-Recognition.

Pre-treatment plasma ptau181 levels were determined for 85 participants from the AscenD-LB trial, with a cutoff level of 2.2 pg/mL. This cutoff level was established prior to measuring the ptau181 levels in samples from the AscenD-LB trial based on a previous analysis of 40 Alzheimer's patients and 40 age- and sex-matched healthy controls (Bayoumy *et al*., 2021). Importantly, there were no baseline differences between patients in the AscenD-LB trial with a baseline ptau181 < 2.2 pg/mL and those with a baseline ptau181 > 2.2 pg/mL. The mean baseline ptau181 level was 1.6 (0.4) pg/mL in participants below the cut-off (n=45) and 3.4 (1.4) pg/mL in those above the cut-off (n=40).

Additional statistical analyses using Mixed Models for Repeated Measures (MMRM) were conducted for each sub-group (baseline ptau181 < and ≥2.2 pg/mL) for the following endpoints from the AscenD-LB trial: the NTB (cognitive test battery), Attention Composite, CDR-SB, and TUG test. For patients with baseline ptau181 < 2.2 pg/mL, there was significant improvement, compared with placebo, for the Attention Composite (*P*=0.023; Cohen's *d*=0.78), CDR-SB (*P*=0.031; *d*=0.70), and TUG test (*P*<0.001; *d*=0.74). This is summarized in the following slide, which shows the effect size for the endpoints for the overall study and for the participants with normal baseline plasma ptau181 level.



Source: CervoMed Inc.

In the past couple of years, a number of publications have reported an association between plasma tau phosphorylated at position 181 or 217 and amyloid plaque status, tau pathology, and/or cerebral (particularly medial temporal lobe) neurodegeneration and atrophy in DLB patients (Moscoso *et al*., 2021; Tissot *et al*., 2021; Wang *et al*., 2021). Following completion of the AscenD-LB trial, a publication reported that levels of ptau181 or ptau217 could be used to predict the presence of concomitant Alzheimer's disease (AD) pathology, assessed by either abnormal tau PET scan in the temporal cortex of abnormal levels of CSF Aβ42/Aβ40 ratio (Hall *et al*., 2021). Elevated levels of phosphorylated tau are associated with neurodegeneration and faster clinical decline in DLB patients (Abdelnour *et al*., 2020; Gonzalez *et al*., 2022). Other results using pathology and/or MRI data have demonstrated that DLB patients without AD co-pathology (cortical tau pathology and/or neuritic amyloid plaques) have minimal cortical atrophy, particularly in the medial temporal lobe (Hansen *et al*., 1998; Amin *et al*., 2020). Thus, the positive results reported by CervoMed for patients with ptau181 levels <2.2 pg/mL could be explained by the fact that patient population has less advanced disease, particularly in regards to neurodegeneration in the cortex, and is not impacted by AD co-pathology. The AD co-pathology itself is likely not directly impacting response to neflamapimod, but is instead representative of patients with more advanced disease, as it has been reported that AD co-pathology develops secondary to DLB and increases the rate of decline in DLB patients (Kantarci *et al*., 2022; Nedelska *et al*., 2019). Once a patient has advanced to where neuronal loss has occurred in the cortex (e.g., it's no longer reversible), there is unlikely to be any functional improvement over a 16-week treatment period. However, DLB patients without AD co-pathology are likely to have reversible deficits that could respond to an agent that acts on the cholinergic system such as neflamapimod.

Conclusion

In the main analysis of the Phase 2a study (Jiang *et al*., 2022) the results showed that at 40 mg TID there was a significant improvement over placebo on the CDR-SB, TUG test, and Attention. In the new analysis, after exclusion of patients with AD co-pathology (i.e., with elevated baseline plasma ptau181), the effects on those endpoints remained significant despite the smaller number of patients. In addition, there is now a significant improvement on recognition memory. Moreover, for all the endpoints, the magnitude of the treatment effect goes up (generally double or more) and is now substantial. As such, the results reported by CervoMed in *Neurology* are very encouraging and support the company's use of an exclusion criteria based on baseline ptau181 level in the ongoing Phase 2b clinical trial of neflamapimod in DLB, which we believe will increase the odds of success for the trial as the company is enriching for DLB patients without AD co-pathology. The use of blood-based biomarkers is a welcome advancement in the study of DLB and other neurodegenerative diseases, as it is a simple screening tool that may make it possible to intervene earlier in the course of disease when treatments are more likely to be effective. Enrollment continues in the Phase 2b trial of neflamapimod in DLB and we continue to anticipate the trial being fully enrolled in the first half of 2024 and topline results being announced in the second half of 2024. With no changes to our model our valuation remains at $17.00 per share.

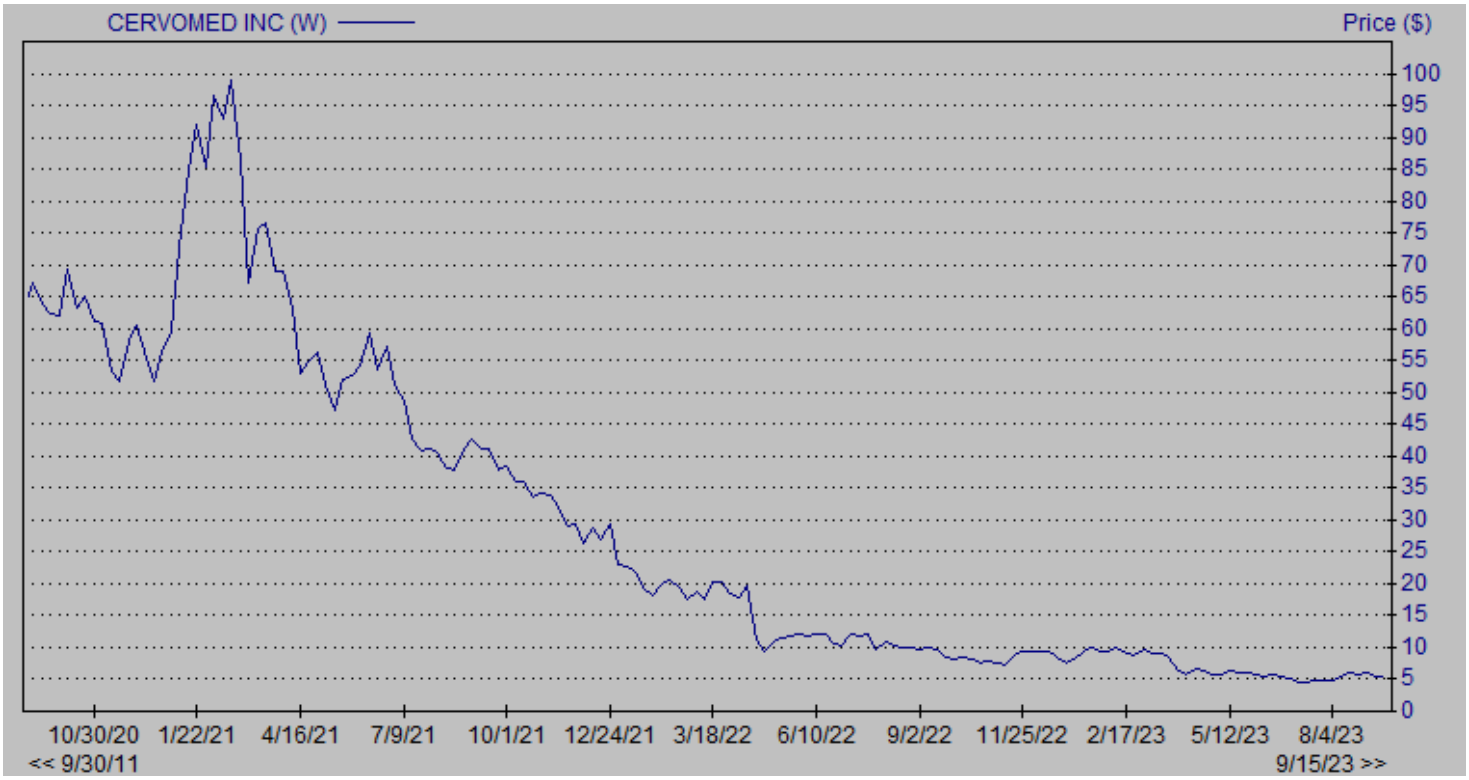
PROJECTED FINANCIALS

CervoMed, Inc.	2022 A	Q1 A	Q2 A	Q3 E	Q4 E	2023 E	2024 E	2025 E
Neflamapimod	$0	$0	$0	$0	$0	$0	$0	$0
Grants & Collaborative Revenue	$0	$0	$0	$0	$0	$0	$0	$0
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$7.2	$1.3	$1.4	$1.4	$1.4	$5.5	$6.0	$17.0
General & Administrative	$8.7	$3.0	$5.2	$4.0	$4.0	$16.1	$10.0	$12.0
Operating Income	($16.0)	($4.3)	($6.6)	($5.4)	($5.4)	($21.6)	($16.0)	($29.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.4	$0.2	$0.4	$0.0	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($15.6)	($4.09)	($6.2)	($5.4)	($5.4)	($21.6)	($16.0)	($29.0)
Income Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Net Income	**($15.6)**	**($4.1)**	**($6.2)**	**($5.4)**	**($5.4)**	**($21.6)**	**($16.0)**	**($29.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($7.65)**	**($2.01)**	**($3.04)**	**($0.95)**	**($0.95)**	**($5.59)**	**($2.67)**	**($3.22)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	2.0	2.0	2.0	5.7	5.7	3.9	6.0	9.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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HISTORICAL STOCK PRICE



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