Tiziana Life Sciences Plc (TLSA – $0.73*)
Buy; $3.00 PT; $77.6M Market Cap
Company Update
Friday, September 8, 2023

New Preclinical Data And Recent IND Clearance Expands Value Creation Roadmap to Alzheimer's; Reit. Buy, $3 PT

Mayank Mamtani
646-885-5463
mmamtani@brileyfin.com

William Wood, Ph.D.
703.312.1748
wwood@brileyfin.com

Yuan Zhi, Ph.D.
703-312-1776
yzhi@brileyfin.com

Brandon Carney, Ph.D.
646-885-5469
bcarney@brileyfin.com

Summary and Recommendation

We return to our Buy thesis for TLSA (Buy, $3 PT) following a new preclinical publication validating scientific rationale for testing lead program, intranasal foralumab, in Alzheimer's disease (AD). Recently published in the *Proceedings of the National Academy of Sciences* (PNAS) and titled, "Nasal administration of anti-CD3 monoclonal antibody ameliorates disease in a mouse model of Alzheimer disease" the new data highlights how intranasal anti-CD3 monoclonal antibody delivered 3 times per week for 5 months to 3xTg mice, a mouse model of AD, demonstrated, (1) improved cognition independent of amyloid beta (Aβ) reductions, (2) reduced AD symptoms, (3) reduced microglial activation, and (4) increased regulatory T cells in the periphery (Lopes et al. 2023). Recall this is the second publication pertaining to intranasal anti-CD3 monoclonal antibody to be published in PNAS this year, with the first, "Nasal administration of anti-CD3 mAb (foralumab) downregulates *NKG7* and increases *TGFB1* and *GIMAP7* expression in T cells in subjects with COVID-19" highlighting the immunological basis for intranasal foralumab's mechanism of action (MOA), aiding in defining the increasing overlap of potentially treatable disease states, as evidenced in new PNAS AD data, as well as ongoing MS study (Moreira et al. 2023; 5/5 Note).

Separately, recent FDA IND clearance allows TLSA to initiate a 3-month Ph. II, placebo-controlled trial in mild-to-moderate Alzheimer's disease patients at doses similar to current MS doses, i.e., 50 mg to 100 mg, to assess microglial activation. Expected to begin screening this year at Brigham and Women's Hospital, TLSA plans to report data in 2024. TLSA also anticipates disclosing additional 6-month MS data from expanded access patients 3-6 (EA3-6) imminently, with fulsome patient-level data disclosure planned for ECTRIMS'23 conference (10/11-13) including (1) disability scores, i.e., EDSS, 25 ft walk, and fatigue score; (2) biomarker data, i.e., CSF readouts on NFL, etc., interleukins and cytokines; and (3) QoL scores. Importantly, we view these data as aiding in the derisking of the upcoming 3-month Ph. IIa placebo-controlled study in MS, which is expected to begin enrolling this year, and readout 4Q24 (6/7 Note; Exhibit 1).

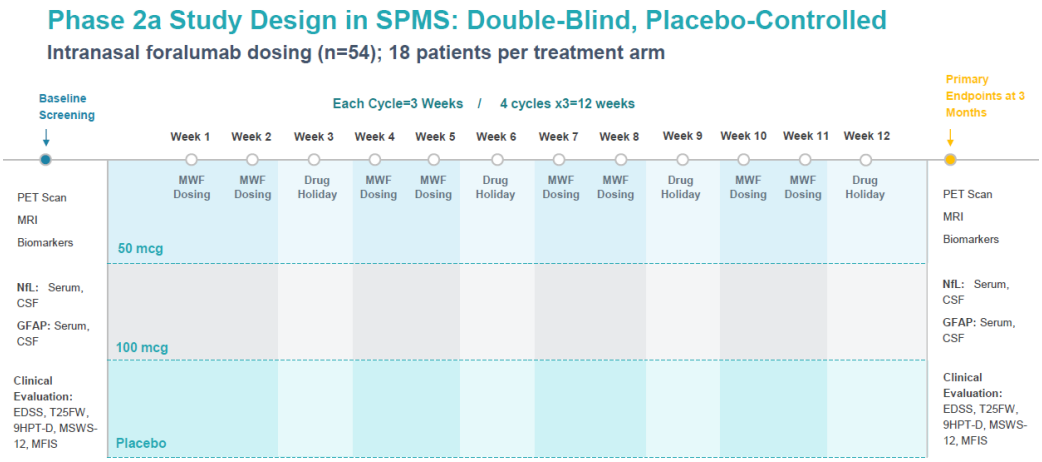
Key Points

- **Foralumab's novel anti-CD3 mediated T cell neuromodulatory effect mechanistically well-suited to thrive in fast-evolving Alzheimer's landscape.** Digging in deeper, newly presented data describes how following 1 µg/mouse intranasal anti-CD3 monoclonal antibody treatment 3X per week for five months in one-month-old 3xTg mice (Exhibit 2) ameliorates the disease phenotype compared to either isotype control (IC) or phosphate-buffered saline (PBS). Data here demonstrated that intranasal foralumab led to an upregulation of M0 related genes, representative of a resting phenotype, in both males and females, e.g., Nfkb1, Mertk, Jun, Cx3cr1, and Mafb, while control or isotype control led to increases in MGnD (neurodegenerative microglia) and inflammation related genes, e.g., Trem2, Apoe, Clec7a, Csf1, and Ccrl2 all associated with MGnD, and similar to DAM (disease-associated microglia) (Exhibit 3). Additionally, data also showed an expansion of CD4+IL10+ Tregs in the spleen in males and females and in the cervical lymph nodes in treated males but not females in the periphery (Exhibit 4). **(Continued on the next page...)**

(....continued from prior page)

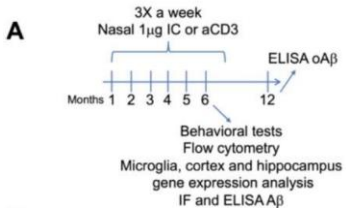
- An increased number of CD3+ T cells were found in the brain, represented by an increased number of CD4+ T cells, but with no meaningful change of CD8+ cells (Exhibit 5). Importantly, these changes led to improvements in cognition as demonstrated in significant improvements in males ($p=0.001$) and females ($p=0.04$) in the morris water maze (MWM), including reduced latency to target in both sexes ($p<0.05$) and increases number of transitions to platform, which reached significance in males ($p<0.05$; Females $p=0.248$) (Exhibit 6). Cognitive improvements were also found following the Y-maze test, with females demonstrating exploring similar to wildtype mice and significant improvements over isotype controls ($p<0.05$). Interestingly, cognitive improvements were found to be independent of amyloid clearance, highlighted by no changes in intracellular amyloid beta (Aβ) in the CA1 of the hippocampus, prefrontal cortex (PC), and retrosplenial cortex (RSC) (Exhibit 7), as well as in Aβ oligomers (Exhibit 8), collectively suggesting a therapeutic potential as a mono- or combo therapy approach.

Exhibit 1. Ph. II Multiple Sclerosis (MS) Design



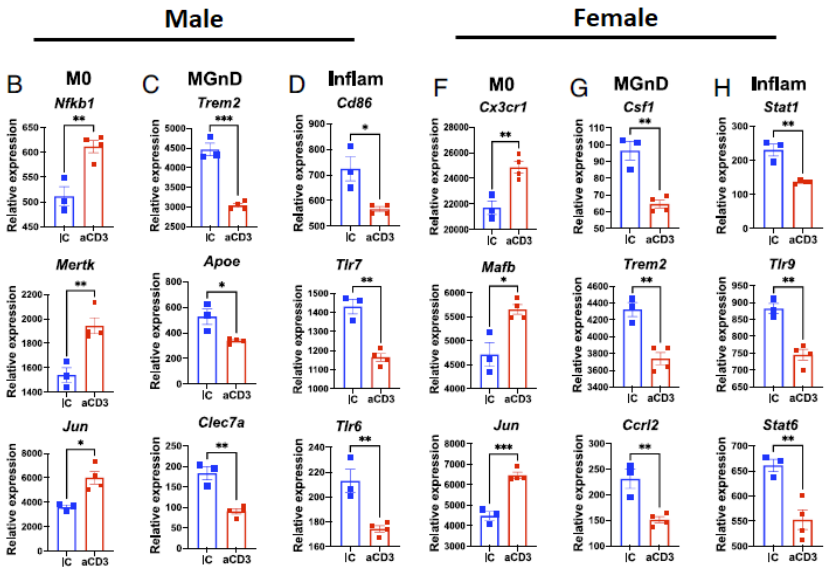
Source: Tiziana company filings.

Exhibit 2. Experiment Design of Preclinical Alzheimer's disease Mouse Study



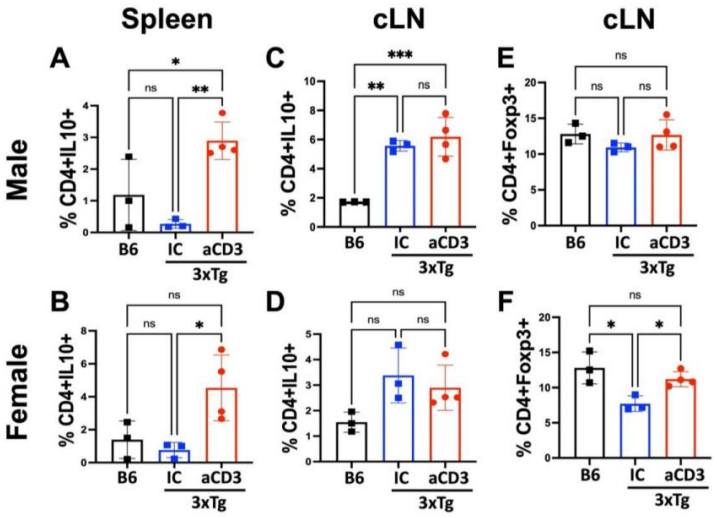
Source: Lopes et al. 2023. PNAS.

Exhibit 3. Increased "Resting" Microglia and Reduced Diseased Microglia following Anti-CD3 mAb Treatment



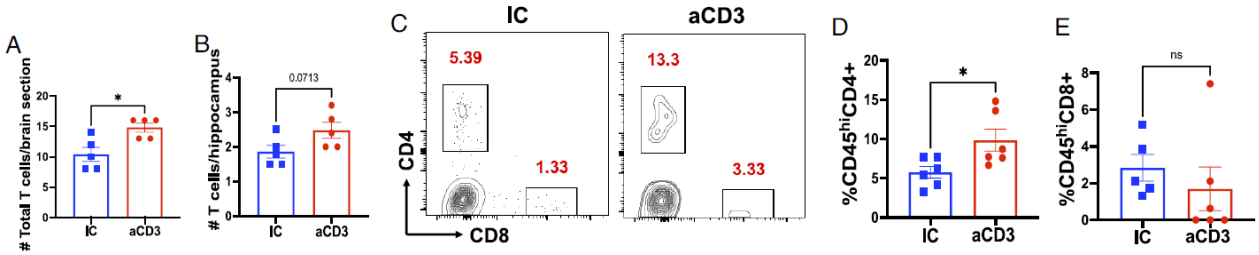
Source: Lopes et al. 2023. PNAS.

Exhibit 4. Anti-CD3 mAb Treatment Leads to Expanded Peripheral T cells



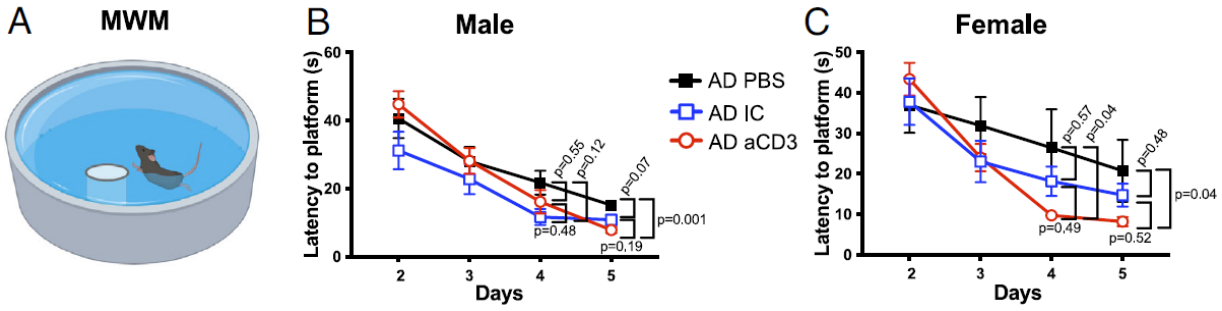
Source: Lopes et al. 2023. PNAS.

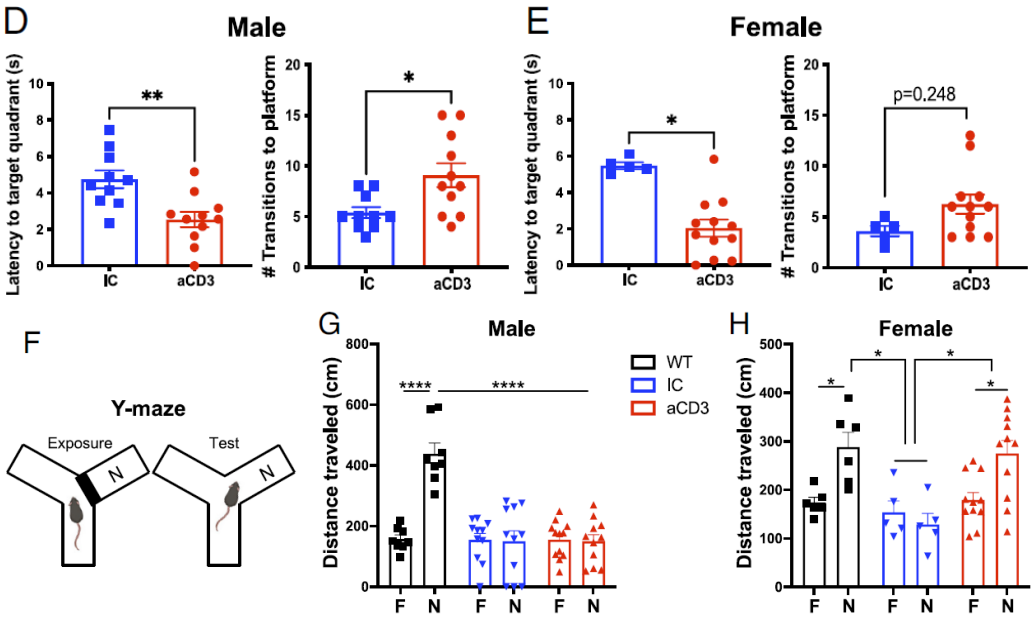
Exhibit 5. Anti-CD3 mAb Treatment Leads to Expanded CD4+ T cells in The Brain



Source: Lopes et al. 2023. PNAS.

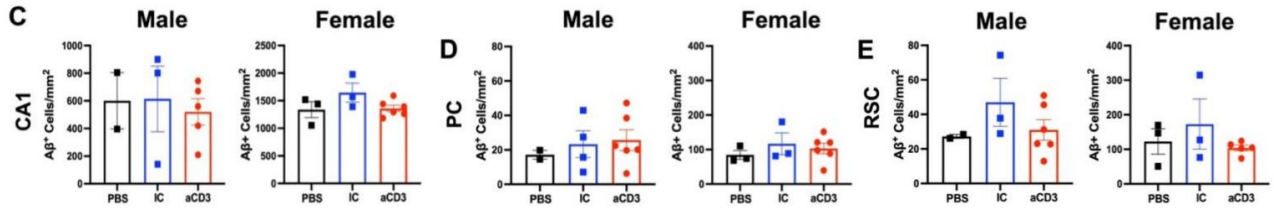
Exhibit 6. Cognitive Improvements Found in Mice Post Anti-CD3 mAb Treatment





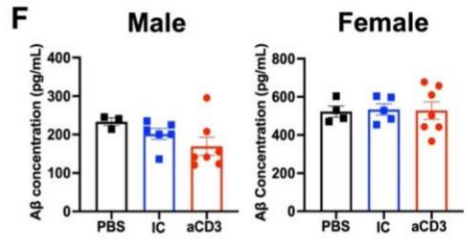
Source: Lopes et al. 2023. PNAS.

Exhibit 7. Anti-CD3 mAb Treatment Does not Impact Amyloid Beta Levels



Source: Lopes et al. 2023. PNAS.

Exhibit 8. Anti-CD3 mAb Treatment Does not Impact Oligomeric Amyloid Beta Levels



Source: Lopes et al. 2023. PNAS.

Valuation

We base our Buy rating and 12-month $3 PT per share on a discounted cash flow (DCF) analysis of revenue and cash flow projection through 2030. Our projections of free cash flow to the firm from sales of nasal foralumab for non-active SPMS are adjusted and weighted based on historical regulatory approval rates of similar treatments at similar stages of development. Our DCF analysis applies a WACC-calculated 14.5% discount rate and a 2% terminal growth rate, in line with other clinical-stage biotech companies, yielding an implied enterprise value of $63M. For 2030, the final projected year of our model, we forecast $173M in total risk-adjusted revenue, which assumes a 25% probability of clinical and regulatory success for nasal foralumab.

Risks

Clinical risks. It is uncertain whether the clinical benefit observed in the clinical studies for foralumab and future registrational trials will be sufficient to support regulatory approval in the U.S., Europe, and other countries. Negative safety and/or efficacy findings in these trials could lead to downward revisions to our price target.

Regulatory risks. The regulatory pathway for all of TLSA's programs in the U.S. is uncertain, and it is unclear whether positive data will be sufficient for a New Drug Application (NDA) submission for each program in the U.S. Additionally, there is no certainty that any of TLSA's drugs will be approved or reimbursed. If the regulatory path for TLSA's candidates is more complex and/or time-consuming than anticipated, there could be a materially negative impact to our estimates and price target, even with success in achieving clinical endpoints.

IP risks. The patent protection related to foralumab and other candidates may expire in the near term and be subject to litigations from competitors. For example, the methods of use patent, pertaining to autoimmune or Inflammatory disease and disorder, for foralumab is expected to expire in 2025.

Commercialization risks. The market potential of TLSA's therapies may not be as significant as projected. In addition, TLSA will need to establish a sales and medical affairs infrastructure in the U.S., Europe, and other geographies for foralumab and other pipeline candidates.

Financing risk. With approximately $18M in cash and cash equivalents, TLSA will likely need to raise additional capital for continued clinical and preclinical candidate development, perhaps via additional equity financing, before reaching profitability, likely resulting in equity share dilution.

Stock price volatility. Share price volatility is common for developmental biopharma firms like Tiziana Life Sciences.

*Closing price of last trading day immediately prior to the date of this publication unless otherwise indicated.

Important Information

This report has been prepared by B. Riley Securities, Inc. ("B. Riley Securities") and may be distributed by its affiliates and subsidiaries as third-party research pursuant to FINRA Rule 2241. B. Riley Wealth Management, Inc. ("B. Riley Wealth"). is a subsidiary of B. Riley Financial, Inc., which is the parent company to B. Riley Securities and B. Riley Wealth. As such, B. Riley Wealth may distribute B. Riley Securities research pursuant to Rule 2241 and by mutual agreement.

B. Riley Securities, B. Riley Wealth,is a broker-dealer registered with the SEC and are members of FINRA, SIPC, and the NASDAQ stock market.

The principal business address of B. Riley Securities is 11100 Santa Monica Blvd., Suite 800, Los Angeles, CA 90025.

Company-Specific Disclosures

B. Riley Securities, Inc. or any of its affiliates, expects to receive or intend to seek compensation for investment banking services from Tiziana Life Sciences Plc in the next 3 months.
Tiziana Life Sciences Plc currently is, or within the past 12 months was, a client of B. Riley Securities, Inc. The services provided were Investment Banking Services.

Tiziana Life Sciences Plc currently is, or within the past 12 months was, a client of B. Riley Securities, Inc., or any of its affiliates. B. Riley Securities, Inc, or any of its affiliates, has received compensation from this company for Non-Investment Banking services in the past 12 months.

For up-to-date B. Riley Securities, Inc. company disclosures, please click on the following link or paste the URL in a web browser: https://brileysecurities.bluematrix.com/sellside/Disclosures.action.

General Disclosures

Information about the Research Analyst Responsible for this report:

The primary analyst(s) covering the issuer(s), Mayank Mamtani, certifies (certify) that the views expressed herein accurately reflect the analyst's personal views as to the subject securities and issuers and further certifies that no part of such analyst's compensation was, is, or will be, directly or indirectly, related to the specific recommendations or views expressed by the analyst in the report. The analyst(s) responsible for this research report has received and is eligible to receive compensation, including bonus compensation, based on B. Riley Securities, Inc.'s overall operating revenues, including revenues generated by its investment banking activities.

Information about B. Riley Securities, Inc.'s Conflicts Management Policy:

B. Riley Securities, Inc.'s Research conflicts management policy is available at: https://brileyfin.com/conflicts-management-policy/.

Information about investment banking:

In the normal course of its business, B. Riley Securities, Inc. or any of their affiliates seek to perform investment banking and other services for various companies and to receive compensation in connection with such services. As such, investors should assume that B. Riley Securities, Inc., or any of their affiliates intend to seek investment banking or other business relationships with the companies covered in their research reports.

Information about our recommendations, holdings and investment decisions:

The information and rating(s) included in this report represent the long-term view as described more fully below. The analyst may have different views regarding short-term trading strategies with respect to the stocks covered by the rating(s), options on such stocks, and/or other securities or financial instruments issued by the company, and such views may be made available to all or some of our clients from time to time. Our brokers also may make recommendations to their clients, and our affiliates may

make investment decisions that are contrary to the recommendations contained in this research report. Such recommendations or investment decisions may be based on the particular investment strategies, risk tolerances, and other investment factors of that particular client or affiliate. From time to time, B. Riley Securities, Inc., its affiliated entities, or their respective directors, officers, employees, or members of their immediate families may have a long or short position in the securities or other financial instruments mentioned in this report.

We provide to certain customers on request specialized research products or services that focus on covered stocks from a particular perspective. These products or services include, but are not limited to, compilations, reviews, and analysis that may use different research methodologies or focus on the prospects for individual stocks as compared to other covered stocks or over differing time horizons or under assumed market events or conditions. Readers should be aware that we may issue investment research on the subject companies from a technical perspective and/or include in this report discussions about options on stocks covered in this report and/or other securities or financial instruments issued by the company. These analyses are different from fundamental analysis, and the conclusions reached may differ. Technical research and the discussions concerning options and other securities and financial instruments issued by the company do not represent a rating or coverage of any discussed issuer(s). The disclosures concerning distribution of ratings and price charts refer to fundamental research and do not include reference to technical recommendations or discussions concerning options and other securities and financial instruments issued by the company.

Our analysts' short-term views, recommendations by our brokers, views contained in products and services provided to customers on an individualized basis, and\or strategies, analysis, or decisions made by B. Riley Securities, Inc. or its affiliates and their respective directors, officers, employees, or members of their immediate families may be different from those published by the analyst in this report and could impact the price of the securities mentioned in this report.

Information about our rating system:

B. Riley Securities, Inc. uses the following three-tiered rating system for securities covered in their research reports:

- **Buy**: We generally expect "Buy" rated stocks to have an above-average risk-adjusted total return over the next 12 months. We recommend that investors buy the securities at the current valuation.
- **Neutral:** We generally believe "Neutral" rated stocks will have an average risk-adjusted total return over the next 12 months.
- **Sell:** We generally expect "Sell" rated stocks to have a below-average risk-adjusted total return over the next 12 months. We recommend that investors reduce their positions until the valuation or fundamentals become more compelling.

B. Riley & Co., LLC and FBR Capital Markets & Co. (before the merger of the broker dealers) adopted this rating system on August 9, 2017. A description of the prior ratings system for each Firm can be found at http://www.brileyfin.com/fbr-ratings-system-from-1072002-to-882017/.

Rating	B. Riley Securities, Inc. Research Distribution [1]	B. Riley Securities, Inc. Banking Services in the past 12 months[1]
BUY [Buy]	78.10%	41.77%
HOLD [Neutral]	21.90%	29.35%
SELL [Sell]	0.00%	0.00%

(1) As of midnight on the business day immediately prior to the date of this publication.

General Information about B. Riley Securities, Inc. Research:

Additional information on the securities mentioned in this report is available upon request. This report is based on data obtained from sources we believe to be reliable but is not guaranteed as to accuracy and does not purport to be complete. Opinions are as of the date of the report unless labeled otherwise and are subject to change without notice. Updates may be provided based on developments and events and as otherwise appropriate. Updates may be restricted based on regulatory requirements or other considerations. Consequently, there should be no assumption that updates will be made. B. Riley Securities, Inc. or any

of their affiliates disclaim any warranty of any kind, whether express or implied, as to any matter whatsoever relating to this research report and any analysis, discussion, or trade ideas contained herein. This research report is provided on an "as is" basis for use at your own risk, and B. Riley Securities, Inc. or any of their affiliates are not liable for any damages or injury resulting from use of this information. This report should not be construed as advice designed to meet the particular investment needs of any investor or as an offer or solicitation to buy or sell the securities or financial instruments mentioned herein, and any opinions expressed herein are subject to change. Some or all of the securities and financial instruments discussed in this report may be speculative, high risk, and unsuitable or inappropriate for many investors. B. Riley Securities, Inc. or any of their affiliates make no representation as to the suitability or appropriateness of these securities or financial instruments for individual investors. Investors must make their own determination, either alone or in consultation with their own advisors, as to the suitability or appropriateness of such investments based upon factors including their investment objectives, financial position, liquidity needs, tax status, and level of risk tolerance. These securities and financial instruments may be sold to or purchased from customers or others by B. Riley Securities, Inc. or any of their affiliates acting as principal or agent.

Securities and financial instruments issued by foreign companies and/or issued overseas may involve certain risks, including differences in accounting, reporting, and registration, as well as foreign currency, economic, and political risks.

This report and the securities and financial instruments discussed herein may not be eligible for distribution or sale in all jurisdictions and/or to all types of investors. This report is provided for information purposes only and does not represent an offer or solicitation in any jurisdiction where such offer would be prohibited. Commentary regarding the future direction of financial markets is illustrative and is not intended to predict actual results, which may differ substantially from the opinions expressed herein.

B. Riley Securities, Inc. utilizes a tiered approach to service its clients. The services provided by B. Riley Securities, Inc.'s research analysts to clients vary based upon a variety of factors, including, but not limited to, client preferences and the extent of a client's total relationship with the Firm. B. Riley Securities, Inc. does not provide any of the Firm's clients with access to unpublished research opinions. B. Riley Securities, Inc. provides clients across all tiers equal access to research reports.

Paired Trade Disclaimer

From time to time, B. Riley Securities, Inc. Research Analysts will offer short-term trading ideas, including identifying a paired trade. In a paired trade, an investor buys the securities of one company and sells the securities of another company. The idea to buy the securities of one company and sell the securities of the other company is based on the expected short-term price move or relative value between the two companies mentioned in the paired trade, not between the companies and any other companies. In contrast, the recommendations in a Research Analyst's published report reflect the Research Analyst's views on a company over the long term (i.e., the next 12 months) relative to other companies covered by the Research Analyst. The trade idea in a paired trade is unrelated to the Research Analyst's long-term view of the companies as expressed in the Research Analyst's most recently published research report. A paired trade idea to sell a company that is rated as Neutral or higher, or to buy a security that is rated Neutral or lower, is not inconsistent because the call to sell or buy the company is relative to the other company mentioned in the paired trade over the short term; it is not a long-term view relative to other companies covered by the Research Analyst.

Important information for B. Riley Securities, Inc. Clients with French Addresses and Potential Investors:

Addresses and potential investors based in France expressly acknowledge that they have not been subject to any kind of solicitation by B. Riley Securities, Inc. or its affiliates, as defined under Article L.341-1 and seq. of the French Monetary and Financial code.

The above analyses have not been prepared in the context of a public offering of financial instruments in France within the meaning of Article L.411-1 and seq. of the French Monetary and Financial code and shall not be deemed to be drawn up for the purpose of providing investment services as defined under Article L.321-1 and seq. of the French Monetary and Financial code. In this respect, the above analyses shall not be qualified as personalized investment advice related to financial instruments under French law and shall, therefore, not be deemed to be qualified as investment advice provided by B. Riley Securities, Inc. or its affiliates.

Addresses and potential investors based in France may initiate the first contact with B. Riley Securities, Inc. in order to get additional information on financial analyses and services provided by the latter. By doing so, addresses and potential investors

based in France expressly acknowledge that the banking and financial solicitation regime as defined under Article L.341-1 and seq. of the French Monetary and Financial code shall not be applicable.

Information for Clients of B. Riley Securities, Inc.:

This publication has been approved by B. Riley Securities, Inc. which accepts responsibility for its contents and its distribution to our clients. Any B. Riley Securities, Inc. client who receives this research and wishes to effect a transaction in the securities or financial instruments discussed should contact and place orders with a B. Riley Securities, Inc. Sales representative.