Zacks Small-Cap Research
Sponsored – Impartial - Comprehensive

January 10, 2020
David Bautz, PhD
312-265-9471
dbautz@zacks.com

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

BioXcel Therapeutics, Inc. (BTAI-NASDAQ)

BTAI: Potentially Transformative Year Ahead for BioXcel…

Based on our probability adjusted DCF model that takes into account potential future revenues of BXCL501 and BXCL701, BTAI is valued at $24.00/share. This model is highly dependent upon continued clinical success of the company's pipeline and will be adjusted accordingly based on future clinical results.

Current Price (01/10/20)	$12.26
Valuation	**$24.00**

OUTLOOK

BioXcel Therapeutics, Inc. (BTAI) is set to have a potentially transformative year as the company has recently initiated two pivotal Phase 3 clinical trials for BXCL501 for the acute treatment of agitation in patients with schizophrenia and bipolar disorder as well as a Phase 1b/2 clinical trial of BXCL501 in the acute treatment of agitation associated with dementia. Positive results in the bipolar and schizophrenia trials could lead to an NDA filing by the end of 2020, while positive results in the dementia trial would support a greatly expanded potential market opportunity for BXCL501. We anticipate data readouts from both trials in mid-2020.

SUMMARY DATA

52-Week High	**$16.71**
52-Week Low	**$4.05**
One-Year Return (%)	**98.38**
Beta	**3.77**
Average Daily Volume (sh)	**365,787**
Shares Outstanding (mil)	**18**
Market Capitalization ($mil)	**$221**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**23**
Insider Ownership (%)	**65**
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 2019 Estimate	**-4.8**
P/E using 2020 Estimate	**-5.0**

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

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	0 A	0 A	0 A	0 A	0 A
2019	0 A	0 A	0 A	0 E	0 E
2020					0 E
2021					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	-$0.37 A	-$0.19 A	-$0.31 A	-$0.47 A	-$1.32 A
2019	-$0.46 A	-$0.54 A	-$0.57 A	-$0.50 E	-$2.12 E
2020					-$2.00 E
2021					-$2.10 E

© Copyright 2020, Zacks Investment Research. All Rights Reserved.

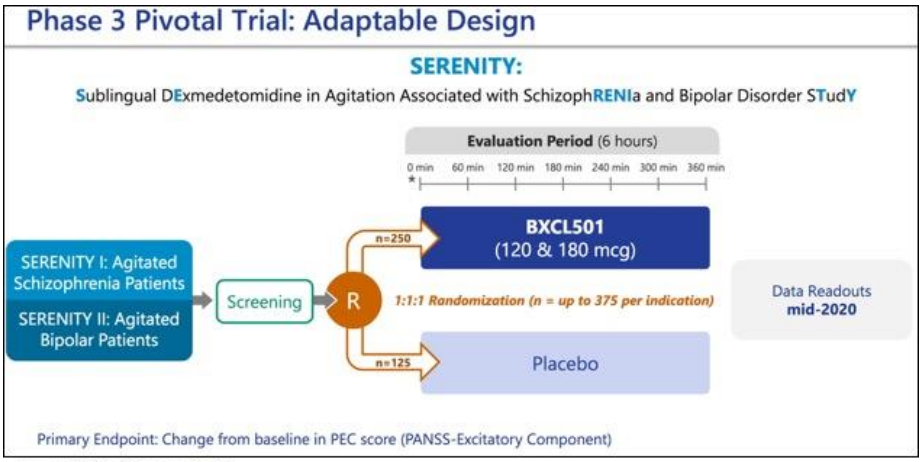
Business Update

BXCL501 Update

BioXcel Therapeutics, Inc. (BTAI) is a clinical stage biopharmaceutical company focused on two lead development programs: BXCL501 – a sublingual formulation of the α2a adrenergic receptor agonist dexmedetomidine (Dex) for the treatment of neurological and psychiatric disorders; and BXCL701 – an immuno-oncology agent for treatment of a rare form of prostate cancer and pancreatic cancer. BioXcel has recently initiated two Phase 3 clinical trials (acute agitation in schizophrenia and bipolar disorder) and a Phase 1b/2 clinical trial (acute agitation in dementia) for BXCL501. Each of those trials is expected to report topline data in mid-2020. Positive results from the schizophrenia and bipolar trials will likely lead to an NDA filing in late 2020, while positive results from the dementia trial would greatly expand the potential market opportunity for BXCL501.

Phase 3 Trials in Schizophrenia and Bipolar Disorder Underway

The company recently initiated the pivotal Phase 3 SERENITY (Sub-Lingual DExmedetomidine in Agitation Associated With SchizophRENIa and Bipolar Disorder STudY) trials of BXCL501 for acute treatment of agitation in patients with schizophrenia and bipolar disorder. The primary endpoint of both trials will be a reduction of symptoms of acute agitation using the Positive and Negative Syndrome Scale – Excitatory Component (PEC), a validated regulatory endpoint for quantifying agitation comprised of five elements associated with agitation scored from 1 (minimum) to 7 (maximum) (Montoya *et al*., 2011), as measured from baseline compared to placebo. A key secondary endpoint will be determining the earliest time where an effect on agitation is apparent by measuring the change in PEC score from baseline. An outline of the SERENITY program is shown below.



Source: BioXcel Therapeutics, Inc.

Phase 1b/2 Trial in Dementia Initiated

Just recently, the company announced the initiation of a Phase 1b/2 clinical trial of BXCL501 for the acute treatment of agitation in patients with dementia, including Alzheimer's disease (AD). The multicenter, randomized, double blind, placebo controlled, ascending dose trial is designed to evaluate the safety, efficacy, tolerability, and pharmacokinetics of BXCL501 in patients age 65 and older who exhibit acute agitation associated with all forms of dementia. It is an adaptive trial design and will evaluate multiple doses of BXCL501 or matching placebos. Following the completion of each dosing cohort, a safety and tolerability review will be conducted to determine the next tested dose.

Agitated behaviors (e.g., irritability, restlessness, aggression) are a significant issue in patients with dementia. Reports indicate that agitation occurs in up to 70% of AD patients and is a leading cause of institutionalization (Cohen *et al*., 1997). These behavioral disturbances have been linked with both cognitive decline (Teri *et al*., 1990) as well as increased caregiver burden, thus decreasing or eliminating them could be beneficial for both the patients and those taking care of them.

Agitation among dementia patients typically occurs in the late afternoon or evening and thus additional terms used to describe the condition include "sundown syndrome", "sundowning", and "nocturnal delirium". The terms all collectively refer to a set of neuropsychiatric symptoms that occur in elderly patients with dementia near sunset. The International Psychogeriatric Association defines agitation in those with dementia as excessive motor activity such as pacing and restlessness, verbal aggression such as screaming and shouting, or physical aggression such as grabbing, pushing, and hitting that 1) is frequently recurrent for at least two weeks and 2) results in excess disability (e.g., impairment in interpersonal relationships). Due to the lack of a clear definition until recently, some prior studies referring to "sundown syndrome" included behaviors only in late afternoon while some included behaviors occurring throughout the night, thus making it difficult to draw comparisons across different studies.

The symptoms of agitation are generally seen in alterations of three main areas: mood, anxiety, and psychosis.

- Mood refers to emotional states such as sadness, happiness, irritability, and lability. In dementia patients, mood is typically dysregulated and in addition to agitation this can also lead to depression.

- Anxiety is driven by an overactive "fight or flight" response, which is analogous to what is seen in patients with posttraumatic stress disorder (PTSD), particularly hyperarousal and hypervigilance.

- Psychosis, which results in disturbed perceptions, delusions, and disorganized thought processes, occurs in many dementia patients due to paranoid ideation.

There is no agreed upon theory as to the cause of agitation in AD, although there are a number of hypotheses, including:

- Unmet physical or psychological needs as a result of isolation at night (Cohen-Mansfield *et al*., 1990), fatigue (Cohen-Mansfield *et al*., 1995), or some other nonspecific unmet need (Evans, 1987).

- Disordered circadian rhythm manifested as increased nocturnal activity, later peak of daytime activity, and less correlation in body temperature with a 24-hour cycle (Volicer *et al*., 2001).

- Sleep disorders caused by the degradation of neuronal pathways that initiate and regulate sleep (Bliwise *et al*., 2004). Staedt *et al*. provide a comprehensive overview of the biological causes of sleep disruption in AD patients (Staedt *et al*., 2005). An additional factor affecting sleep may be restless leg syndrome, which was found to correlate with agitation in patients with AD (Rose *et al*., 2011).

Currently there are no FDA approved therapies for agitation in dementia and the treatments that are used are either not effective, have a number of potential serious side effects, or both. Treatment typically involves changes in the patient's environment and/or the off-label use of pharmaceutical agents.

For alterations in mood, mood stabilizers (valproic acid or carbamazepine) or antidepressants (typically selective serotonin reuptake inhibitors, SSRIs) are most commonly used. The FDA has not approved any drugs from either class for the treatment of agitation in dementia. There is evidence for efficacy of antidepressants, however their use is also associated with adverse side effects (Porsteinsson *et al*., 2014).

Anxiety is typically treated with benzodiazepines (e.g., lorazepam). While effective at calming patients, they have serious tolerability issues and can have a negative impact on memory, cognition, balance (potentially leading to falls), and potentially increase the risk of death (Saarelainen *et al*., 2017).

Antipsychotics are the most common medications prescribed to treat psychosis. While some atypical antipsychotics have shown superiority over placebo in treating agitation in AD (Ballard *et al*., 2009), in 2005

the FDA published a document regarding deaths related to the use of antipsychotics in elderly patients with behavioral disturbances (FDA, 2005) that led to a “black box” warning for this class of drugs in 2008.

Agitation Market Opportunity

Agitation treatment represents a sizeable market opportunity. The initial focus will be on agitation in emergency departments (ED). Total ED visits associated with mental health disorders increased 44% from 2006 to 2014 (Moore *et al*., 2017), and a sizeable percentage of mental health patients experience agitation during ED visits (Zun *et al*., 2008). In addition to EDs, there is the potential to expand treatment to different clinical environments, including urgent care centers, intensive care, medical and psychiatric inpatient units, psychiatric hospitals, and mental health clinics.

For the treatment of acute agitation in patient with dementia, while a large number of these patients are taken to the ED, a potential future opportunity exists in treating patients in a nursing home setting, thus offering a positive pharmacoeconomic benefit as well as easing the burden on the patient and caregiver. In addition, an effective treatment for ‘sundowning’ could obviate the need to move a dementia patient to an assisted living environment, as that condition is heavily burdensome on family members and can often times lead to moving a dementia patient out of the home and into an escalating level of supervision at an increased cost.

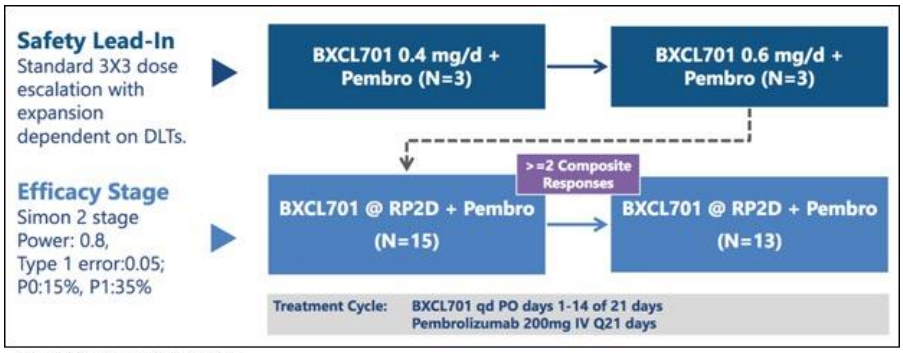
For the initial indications that BioXcel is targeting, we estimate there are approximately 3.5 million schizophrenics (SARDAA) and 5.7 million adults in the U.S. with bipolar disorder (DBSA). The company will also be targeting agitation in Alzheimer’s disease (5 million U.S. adults), delirium (3 million U.S. adults), and opioid withdrawal (2 million U.S. adults). Of those patients, we estimate that approximately 1.7 million schizophrenics, 2.3 million bipolar patients, 2.0 million Alzheimer’s disease patients, 1.0 million delirium patients, and 0.5 million opioid withdrawal patients will suffer from agitation, with approximately 60% of them having mild to moderate agitation that would be amenable to treatment. We estimate each patient is likely to have 12-24 episodes of agitation per year (1-2 per month), thus representing tens of millions of potential treatment opportunities. At an estimated launch price of $135 per treatment, the total market opportunity is over $1 billion.

BXCL701 Update

BXCL701 (talabostat) is an oral small molecule immunomodulator designed to activate the innate immune system through inhibition of dipeptidyl peptidase (DPP) 8/9 and fibroblast activation protein (FAP). The drug has been tested in over 700 patients through multiple clinical trials, thus there exists a large amount of data on its safety, tolerability, proof of mechanism, and single-agent anti-tumor activity. BioXcel is developing BXCL701 as a treatment for treatment-emergent neuroendocrine prostate cancer (tNEPC) and pancreatic cancer.

BXCL701 in tNEPC

BioXcel is currently conducting a Phase 1/2 clinical trial of BXCL701 in combination with Keytruda® (anti-PD-1 mAb) in patients with tNEPC (NCT03910660). It is a single arm, open label trial to examine the safety, pharmacokinetics, and anti-tumor activity of the combination of BXCL701 and Keytruda®. An outline of the trial is shown below.



Source: BioXcel Therapeutics, Inc.

The company presented interim safety and tolerability data from the Phase 1b portion of the study at the 26th Annual Prostate Cancer Foundation Scientific Retreat in Oct. 2019. A total of five patients were evaluable at the time of the presentation (three at 0.4 mg/day BXCL701 + Keytruda® and two at 0.6 mg/day BXCL701 + Keytruda®). Results showed that the combination of BXCL701 and Keytruda® was safe with no serious adverse events (SAEs) or dose limiting toxicities (DLTs). We anticipate additional data being reported in the first half of 2020.

BXCL701 in Pancreatic Cancer

BioXcel is conducting a Phase 1/2 clinical trial of BXCL701 in combination with NKTR-214 and avelumab (anti-PD-L1 mAb). The company has entered into a collaboration agreement with both Nektar Therapeutics, in which Nektar will supply NKTR-214 and share in the costs of the combination trial, and Merck KGaA, which will supply avelumab.

A safety run-in study of NKTR-214 and avelumab is currently being conducted, as those two agents had not previously been studied together. Once the safety of those two agents in combination is established, then additional patients can be treated with all three agents. We anticipate the safety run-in study of NKTR-214 and avelumab to complete in the first half of 2020 and safety data for the triplet combination to be available in the second half of 2020.

BXCL701 in Solid Tumors

On Dec. 11, 2019, BioXcel announced the initiation of a single center, open label Phase 2 trial to evaluate BXCL701 in combination with a checkpoint inhibitor in multiple advanced solid tumors (NCT04171219). The trial is taking place at MD Anderson Cancer Center with the goal of identifying tumor types that are amenable to combination therapy with Keytruda® and BXCL701. Outcomes being evaluated include overall response rate, progression-free survival, and duration of response along with the safety of the combination therapy.

Conclusion

With a Phase 3 data readout in mid-2020 we believe that BioXcel should be on all biotech investor's radar screens, as the opportunity exists for a significant revaluation of the company on positive results. A good precedent for such an event was set in 2019 by Karuna Therapeutics (KRTX), a biopharmaceutical company developing KarXT, which is a proprietary formulation of two compounds: xanomeline, a muscarinic receptor agonist, and trospium, an FDA approved muscarinic antagonist. Following the announcement of positive results for a Phase 2 clinical trial of KarXT for the treatment of acute psychosis in schizophrenia patients the stock increased >500%, and while it has pulled back some it is still up >300% from where it was prior to the release of the data. KarXT has a number of similarities with BXCL501, including the fact it is a reformulation of an already FDA approved compound, it is targeting the same patient population, and it is being evaluated through a rapid development pathway, thus we believe it provides an excellent case study for how a company's valuation can dramatically change following positive results for a CNS-targeted therapy.

We have slightly increased our valuation to $24 based on modeling a per dose price of $135 for BXCL501 (up from $130) and moving the DCF model forward a year. While the stock has been on a great run since the beginning of November 2019, we believe there is still a lot of upside left, particularly if the company reports positive Phase 3 data later in the year.

PROJECTED FINANCIALS

BioXcel Therapeutics, Inc.	2018 A	Q1 A	Q2 A	Q3 A	Q4 E	2019 E	2020 E	2021 E
BXCL501	$0	$0	$0	$0	$0	$0	$0	$0
BXCL701	$0	$0	$0	$0	$0	$0	$0	$0
Other Income	$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	$14.6	$5.7	$6.5	$7.1	$6.7	$26.0	$27.0	$30.0
General & Administrative	$5.4	$1.7	$2.1	$2.0	$2.3	$8.2	$10.0	$12.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($19.9)	($7.4)	($8.6)	($9.1)	($9.0)	($34.2)	($37.0)	($42.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.7	($0.2)	($0.2)	$0.1	($0.1)	($0.4)	$0.0	$0.0
Pre-Tax Income	($19.2)	($7.2)	($8.5)	($9.0)	($9.1)	($34.6)	($37.0)	($42.0)
Income Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($19.2)**	**($7.2)**	**($8.5)**	**($9.0)**	**($9.1)**	**($34.6)**	**($37.0)**	**($42.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.32)**	**($0.46)**	**($0.54)**	**($0.57)**	**($0.50)**	**($2.12)**	**($2.00)**	**($2.10)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	14.6	15.7	15.7	15.8	18.1	16.3	18.5	20.0

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

© Copyright 2020, Zacks Investment Research. All Rights Reserved.

HISTORICAL STOCK PRICE



Source: Zacks SCR

© Copyright 2020, Zacks Investment Research. All Rights Reserved.

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, David Bautz, PhD, 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.
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.

CANADIAN COVERAGE

This research report is a product of Zacks SCR and prepared by a research analyst who is employed by or is a consultant to Zacks SCR. The research analyst preparing the research report is resident outside of Canada, and is not an associated person of any Canadian registered adviser and/or dealer. Therefore, the analyst is not subject to supervision by a Canadian registered adviser and/or dealer, and is not required to satisfy the regulatory licensing requirements of any Canadian provincial securities regulators, the Investment Industry Regulatory Organization of Canada and is not required to otherwise comply with Canadian rules or regulations.