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BioXcel Therapeutics, Inc. (BTAI-NASDAQ)

BTAI: Positive Results for BXCL501 in TRANQUILITY Trial; Raising Valuation to $140…

Based on our probability adjusted DCF model that takes into account potential future revenues of BXCL501 and BXCL701, BTAI is valued at $140.00/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 (01/07/21)	$47.74
Valuation	**$140.00**

OUTLOOK

On January 5, 2021, BioXcel Therapeutics, Inc. (BTAI) announced topline results for the Phase 1b/2 TRANQUILITY trial of BXCL501 in patients with agitation associated with dementia. The results showed that BXCL501 was well tolerated (no cases of syncope or fall) and resulted in a statistically significant reduction in agitation at two hours post-dose in the 60 μg cohort as measured by the PEC, PAS, and Mod-CMAI scales. Numerical separation was seen as soon as 30 minutes post-dose with the duration of response lasting eight hours. These data set the stage for a pivotal program for BXCL501 in agitation associated with dementia in which the company will eventually explore the use of BXCL501 across the agitation spectrum. Based on these results, we have increased our valuation to $140 per share.

SUMMARY DATA

52-Week High	**$64.63**
52-Week Low	**$12.26**
One-Year Return (%)	**263.79**
Beta	**1.31**
Average Daily Volume (sh)	**545,575**
Shares Outstanding (mil)	**24**
Market Capitalization ($mil)	**$1,183**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**49**
Insider Ownership (%)	**9**
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	**-12.5**
P/E using 2020 Estimate	**-26.6**

Risk Level	**Above Avg.**
Type of Stock	**Mid-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	0 A	0 A	0 A	0 A	0 A
2020	0 A	0 A	0 A	0 E	0 E
2021					0 E
2022					113 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$0.46 A	-$0.54 A	-$0.57 A	-$0.42 A	-$2.02 A
2020	-$0.79 A	-$1.06 A	-$1.07 A	-$0.56 E	-$3.45 E
2021					-$2.24 E
2022					$0.88 E

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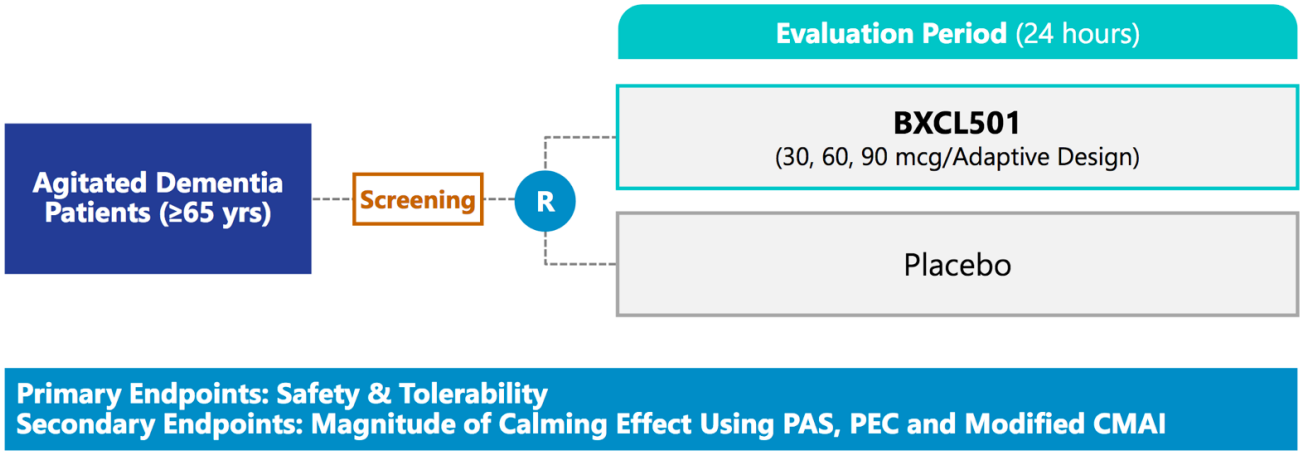
Business Update

Positive Topline Data for TRANQUILITY Trial

On January 5, 2021, BioXcel Therapeutics, Inc. (BTAI) announced positive topline results for the Phase 1b/2 TRANQUILITY trial of BXCL501 for the acute treatment of agitation in dementia patients, including those with Alzheimer's disease. The multicenter, randomized, double blind, placebo controlled, ascending dose trial was 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. An outline of the trial is given below.



Source: BioXcel Therapeutics, Inc.

A total of 54 patients were enrolled in the trial; 16 in the 30 mg BXCL501 cohort, 20 in the 60 mg BXCL501 cohort, 4 in the 90 mg BXCL501 cohort, and 14 in the placebo cohort. Approximately 87% of all trial participants had Alzheimer's disease. The following table shows that BXCL501 was well tolerated with no serious or severe adverse events reported, with the most common side effect being somnolence, which was seen in approximately 50% of patients administered BXCL501.

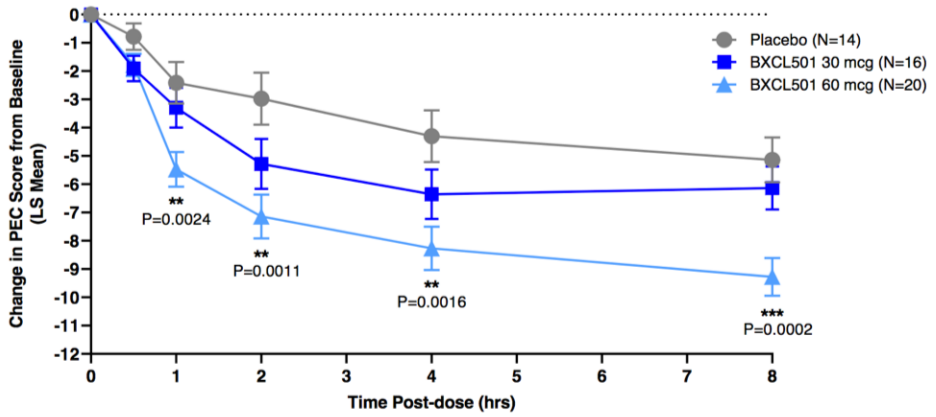
		BXCL501 30 mcg (N=16)	BXCL501 60 mcg (N=20)	Placebo (N=14)
Somnolence*	Mild	8 (50.0 %)	11 (55.0 %)	1 (7.1 %)
	Moderate	0	1 (5.0 %)	
Hypotension	Mild	0 (0)	1 (5 %)	0
	Moderate	0 (0)	1 (5 %)	0
Orthostatic hypotension	Mild	0 (0)	1 (5 %)	0
	Moderate	1 (6.3 %)	0 (0)	0
Dizziness	Mild	1 (6.3 %)	1 (5 %)	0
	Moderate	0 (0)	0 (0)	
Bradycardia		0	1 (5 %)	0
Dry mouth		0	1 (5 %)	0
Nausea		0	1 (5 %)	0
Headache		0	1 (5 %)	0

*Verbatim; drowsy or feeling sleepy

All subjects self-administered the sublingual film

Source: BioXcel Therapeutics, Inc.

The following chart shows a rapid, dose dependent decrease in PEC score from baseline that separates from placebo numerically by 30 minutes post-treatment and becomes statistically significantly different by 60 minutes. The decrease is seen up to eight hours post-treatment (the last time point examined in the trial). And 70% of patients in the 60 μg BXCL501 cohort were responders, which was defined as a ≥40% reduction in PEC score.

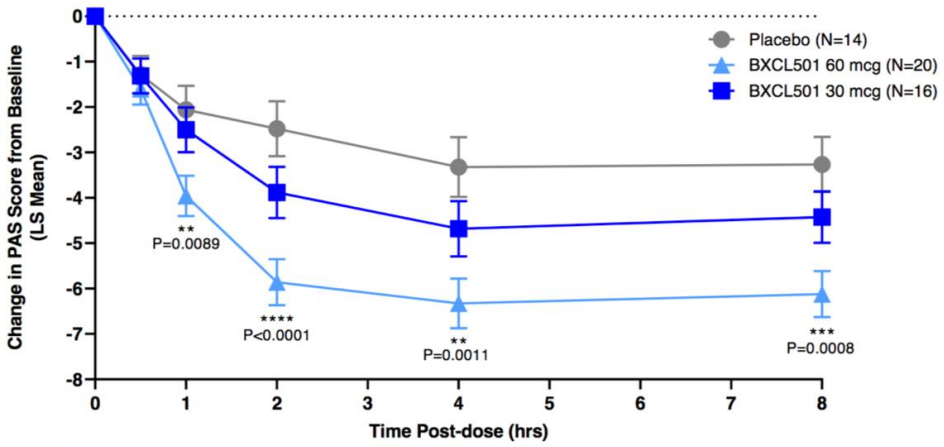


Efficacy Results at 120 mins	PEC Total Score	Placebo	BXCL501 30 mcg	BXCL501 60 mcg
	Change from Baseline (LS Mean)	-2.9	-5.4	-7.1 **
	Response °	7%	25%	70% **

PANSS-Excitatory Component (PEC) is a 5 items scale: Excitement, Hostility, Tension, Uncooperativeness, Poor Impulse Control, rated 1-Absent to 7-Extreme
ITT analysis, Least Square Means ± SEM
° Proportion achieving ≥ 40% PEC reduction

Source: BioXcel Therapeutics, Inc.

Similar results were seen in the PAS score, as treatment with 60 μg BXCL501 resulted in a statistically significant separation from placebo by one hour that continued out to eight hours post-treatment.



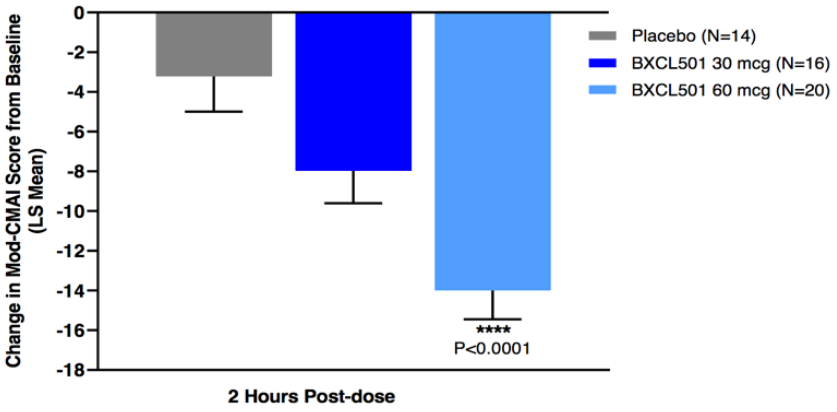
Efficacy Results at 120 mins	PAS Total Score	Placebo	BXCL501 30 mcg	BXCL501 60 mcg
	Change from Baseline (LS Mean)	-2.5	-3.9	-5.9 ****

Pittsburgh Agitation Scale (PAS) measures 4 behavior groups: aberrant vocalization, motor agitation, aggressiveness, and resisting to care rated 0- no agitation present to 4 – highest form of agitation.
ITT analysis, Least Square Means ± SEM

Source: BioXcel Therapeutics, Inc.

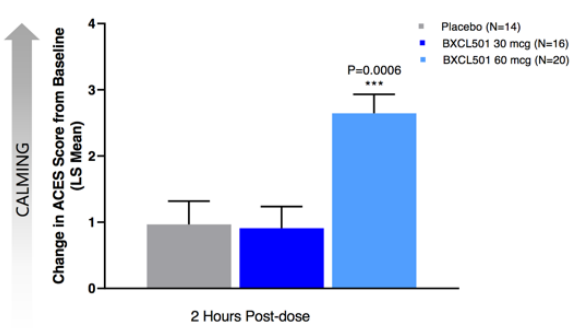
Lastly, the positive findings in PEC and PAS score reductions were further confirmed by the change in Mod-CMAI, the ACES, and the CGI-I. The following figure shows a robust decrease in the Mod-CAMI score for patients administered 60 μg BXCL501 (top graph), an increase in ACES score, which indicates increased calmness (lower left graph), and a statistically significant percentage of patients who were deemed

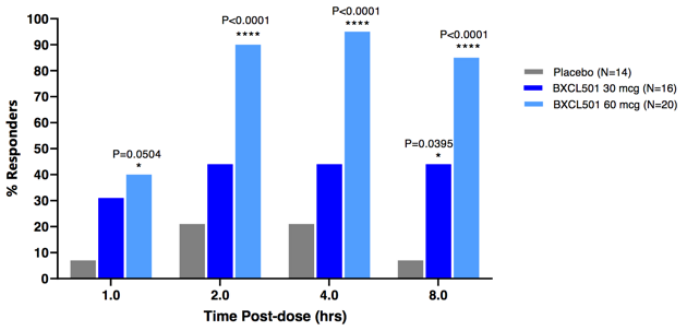
'responders' according to the CGI-I, defined as very much or much improved following treatment (lower right graph).



Efficacy Results at 120 mins	Mod-CMAI Total Score	Placebo	BXCL501 30 mcg	BXCL501 60 mcg
	Change from Baseline (LS Mean)	-3.2	-8.0	-14.0 ****

Modified Cohen-Mansfield Agitation (Mod-CMAI) is an inventory consisting of 29 behaviors, each rated on a 7-point scale of frequency: 1 – never to 7 – several times an hour. Only behaviors manifested by the subject at baseline were assessed throughout the study.
ITT analysis, Least Square Means ± SEM





The Clinical Global Impression scale – Improvement (CGI-I) is a 7-point scale.
Ratings of (1) Very Much, or (2) Much Improved were considered Responders.
ITT analysis

Source: BioXcel Therapeutics, Inc.

Background on Agitation Associated with Dementia

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 dementia patients, 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.

Conclusion

The data reported by BioXcel from the TRANQUILITY trial are better than we had anticipated and fully justify moving to a pivotal program as quickly as possible. The company will be meeting with the FDA to discuss trial design and efficacy endpoints and with the large treatment effect seen in the TRANQUILITY trial we anticipate a similar number of patients to be included in the Phase 3 program as was seen for the SERENITY trials. Based on these results we have increased our probability of approval for BXCL501 in treating agitation associated with dementia along with the potential market share, which has increased our valuation to $140 per share and we would be eager buyers of the stock at the current share price.

PROJECTED FINANCIALS

BioXcel Therapeutics, Inc.	2019 A	Q1 A	Q2 A	Q3 A	Q4 E	2020 E	2021 E	2022 E
BXCL501	$0	$0	$0	$0	$0	$0	$0	$113
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**	**$113**
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$4
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$25.8	$12.4	$17.9	$16.3	$11.0	$57.6	$45.0	$47.0
General & Administrative	$7.8	$2.6	$3.5	$8.5	$2.8	$17.4	$12.0	$40.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($33.6)	($15.0)	($21.4)	($24.8)	($13.8)	($75.0)	($57.0)	$22.0
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.6	$0.1	$0.0	$0.0	$0.1	$0.2	$1.0	$1.0
Pre-Tax Income	($33.0)	($15.0)	($21.5)	($24.8)	($13.7)	($74.8)	($56.0)	$23.0
Income Taxes	$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	**($33.0)**	**($15.0)**	**($21.5)**	**($24.8)**	**($13.7)**	**($74.8)**	**($56.0)**	**$23.0**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($2.02)**	**($0.79)**	**($1.06)**	**($1.07)**	**($0.56)**	**($3.45)**	**($2.24)**	**$0.88**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	16.3	19.0	20.3	23.1	24.4	21.7	25.0	26.0

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

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HISTORICAL STOCK PRICE



Source: Zacks SCR

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