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BioXcel Therapeutics, Inc. (BTAI-NASDAQ)

BTAI: Rolling NDA Submission Underway for BXCL501…

Based on our probability adjusted DCF model that takes into account potential future revenues of BXCL501 and BXCL701, BTAI is valued at $118.00/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 (11/16/20)	$54.28
Valuation	**$118.00**

OUTLOOK

On November 12, 2020, BioXcel Therapeutics, Inc. (BTAI) announced financial results for the third quarter of 2020 and provided a business update. The company recently announced the completion of a pre-NDA meeting with the FDA for BXCL501 for the treatment of acute agitation in schizophrenia and bipolar patients. The FDA agreed to a rolling review of the NDA and BioXcel has already submitted part of it, with plans to finish submitting all portions of the NDA in the first quarter of 2021.

BioXcel also recently presented two posters on BXCL701 clinical data at the Society for Immunotherapy of Cancer (SITC) 35th Annual Meeting. Early signs of efficacy and a reasonable safety profile were seen for both the Phase 1b/2 trial in advanced prostate cancer and the MD Anderson trial in patients with solid tumors.

SUMMARY DATA

52-Week High	**$64.63**
52-Week Low	**$4.36**
One-Year Return (%)	**953.98**
Beta	**1.64**
Average Daily Volume (sh)	**455,881**
Shares Outstanding (mil)	**24**
Market Capitalization ($mil)	**$1,323**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**41**
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	**-14.7**
P/E using 2020 Estimate	**-16.5**

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

WHAT'S NEW

Business Update

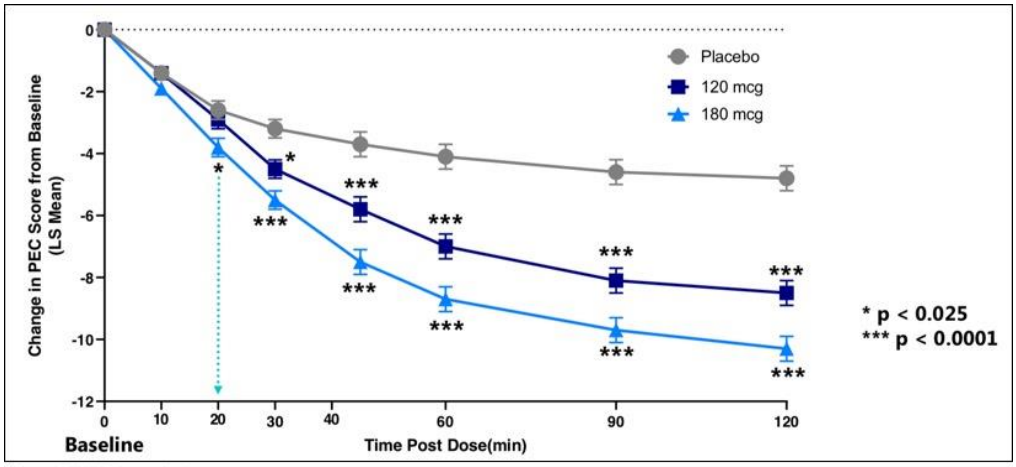
NDA Submission Underway for BXCL501 in Acute Agitation in Schizophrenia and Bipolar Disorder

On November 11, 2020, BioXcel Therapeutics, Inc. (BTAI) announced the initiation of a rolling submission of a New Drug Application (NDA) with the U.S. FDA for BXCL501 for treating acute agitation in schizophrenia and bipolar disorder patients. The initiation of the NDA submission comes following a pre-NDA meeting recently conducted by BioXcel and the FDA at which time the agency provided feedback on the regulatory data package, including clinical safety and efficacy data, non-clinical results, CMC, and other elements of the NDA. We anticipate the NDA filing to be completed in the first quarter of 2021. The FDA then has 60 days to decide whether to accept the NDA, and following acceptance of the NDA the review time is 10 months (or 6 months if the application is granted priority review).

The NDA filing for BXCL501 is based in part on the positive results from the Phase 3 SERENITY I and SERENITY II clinical trials, which the company disclosed in July 2020. The SERENITY I trial was a randomized, double blind, placebo controlled parallel group adaptive trial in patients with schizophrenia or schizoaffective disorder (n=381) that were randomized to receive 120 μg BXCL501, 180 μg BXCL501, or placebo. The SERENITY II trial was a randomized, double blind, placebo controlled parallel group adaptive trial in patients with bipolar disorders (n=378) that were randomized to receive 120 μg BXCL501, 180 μg BXCL501, or placebo.

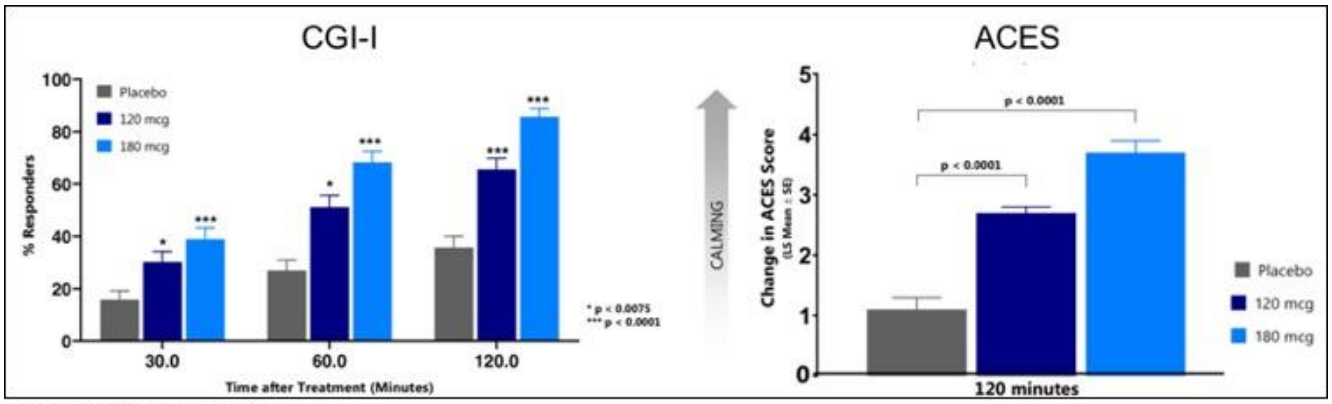
SERENITY I

The following graph shows the robust response seen in decreasing PEC scores in schizophrenia patients treated with BXCL501 compared to placebo. The results for the 180 μg arm became significant starting at 20 minutes after dosing and the separation from placebo continued to increase out to 120 minutes.



Source: BioXcel Therapeutics, Inc.

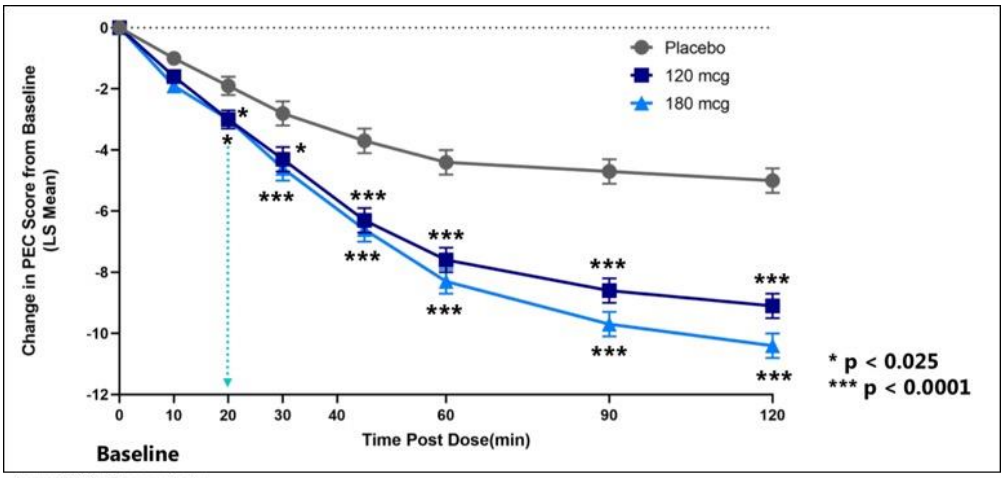
Clinically meaningful responses were also seen in the clinical global impression improvement scale (CGI-I) and the agitation and calmness evaluation scale (ACES), as shown in the following figures. The results from these secondary endpoints lend further support to the clinically meaningful effect that BXCL501 has on agitated patients.



Source: BioXcel Therapeutics, Inc.

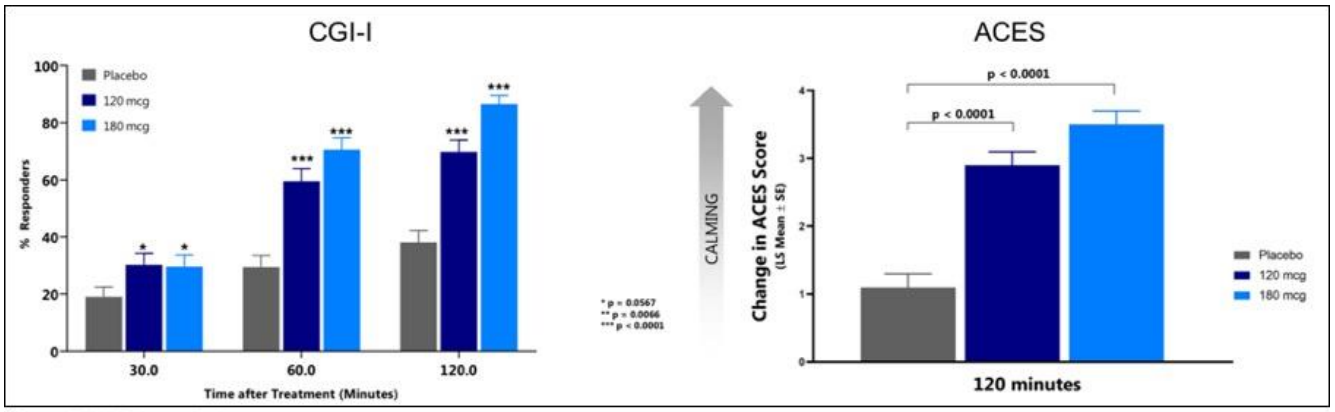
SERENITY II

Very similar results were seen in SERENITY II, with patients administered BXCL501 experiencing a robust and highly statistically significant decrease in PEC compared to placebo. Similar to SERENITY I, the difference from placebo became statistically significant at the 20-minute mark.



Source: BioXcel Therapeutics, Inc.

Just as in SERENITY I, results from SERENITY II showed clinically meaningful responses in the CGI-I and the ACES, as shown in the following figures.



Source: BioXcel Therapeutics, Inc.

Importantly, there were no serious adverse events reported and the tolerability was comparable in both of the SERENITY trials. In addition, all patients were able to self-administer the treatments.

		180 mcg BXCL501 (N=252)	120 mcg BXCL501 (N=255)	Placebo (N=252)
Somnolence	Mild	40 (15.9)	43 (16.9)	15 (6.0)
	Moderate	16 (6.3)	11 (4.3)	1 (0.4)
Dizziness	Mild	13 (5.2)	7 (2.7)	2 (0.8)
	Moderate	2 (0.8)	3 (1.2)	0
Hypotension	Mild	10 (4.0)	10 (3.9)	0
	Moderate	3 (1.2)	4 (1.6)	0
Orthostatic hypotension	Mild	9 (3.6)	7 (2.7)	1 (0.4)
	Moderate	4 (1.6)	0	0
Hypoaesthesia oral		12 (4.8)	7 (2.7)	1 (0.4)
Dry mouth		11 (4.4)	19 (7.5)	3 (1.2)
Nausea		7 (2.8)	6 (2.4)	4 (1.6)
Headache		6 (2.4)	12 (4.7)	12 (4.8)
Paraesthesia oral		6 (2.4)	7 (2.7)	1 (0.4)

Source: BioXcel Therapeutics, Inc.

BXCL501 Compares Favorably with Adasuve®

Adasuve® (loxapine) inhalation powder was approved in 2012 for the treatment of agitation associated with schizophrenia or bipolar disorder. It is administered using a handheld, single-use inhaler. It was approved based on the results of two Phase 3 trials in schizophrenia and bipolar patients with agitation (Lesem *et al*., 2011; Kwentus *et al*., 2012; Faden *et al*., 2019).

The following table gives a comparison between the 10 mg dose of inhaled loxapine and the two doses of BXCL501. The 180 μg dose of BXCL501 is superior to Adasuve® in both change in PEC score as well as the percentage of PEC responders (defined as a ≥40% improvement in PEC score) while the 120 μg dose of BXCL501 is highly comparable.

Schizophrenia

	Placebo	Adasuve	Placebo	120 μg BXCL501	180 μg BXCL501
Change in PEC Score	-5.8	-8.7	-4.8	-8.5	-10.3
% PEC Responders (≥40% improvement in PEC Score)	38%	70%	34%	67%	87%

Bipolar

	Placebo	Adasuve	Placebo	120 μg BXCL501	180 μg BXCL501
Change in PEC Score	-4.7	-9.2	-5.0	-9.1	-10.4
% PEC Responders (≥40% improvement in PEC Score)	28%	73%	37%	69%	85%

Sources: Lesem et al., 2011; Kwentus et al., 2012; Faden et al., 2019; BioXcel Therapeutics, Inc.

While clinically successful, Adasuve® has yet to be commercially successful based on the fact that it has a black box warning and Risk Evaluation and Mitigation Strategy (REMS) associated with its potential to cause bronchospasm. In addition, there is a black box warning for an increased risk of death in elderly patients with dementia-related psychosis treated with antipsychotic drugs.

In discussing the potential for inhaled loxapine to treat acute agitation associated with schizophrenia or bipolar disorder, Faden *et al*. state that:

> *"An ideal medication for the treatment of agitation would be efficacious, tolerable, non-painful, and have a rapid onset of action"* (Faden *et al*., 2019).

Based on the SERENITY data we believe this perfectly describes BXCL501 and clinicians would welcome the opportunity to treat agitated patients with the drug.

TRANQUILITY Readout Possible in 4Q20

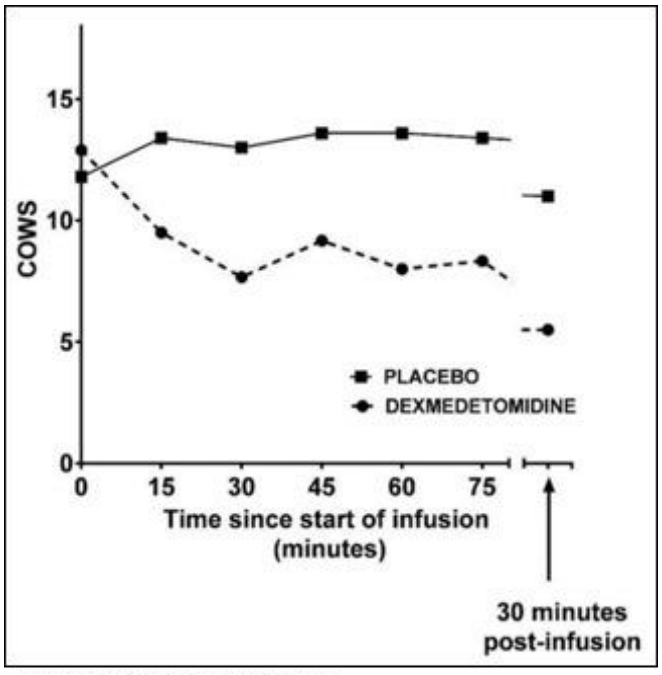
BioXcel is currently conducting the Phase 1b/2 TRANQUILITY clinical trial of BXCL501 for the acute treatment of agitation in patients with dementia, including Alzheimer's disease (AD). The multicenter, randomized, double blind, placebo controlled, ascending dose trial is designed to evaluate the safety, 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.

Thus far, the company has completed dosing two cohorts (30 μg and 60 μg) in a total of 30 patients and is now dosing a third cohort at 90 μg. The company may report topline results for the TRANQUILITY trial in the fourth quarter of 2020 unless the trial proceeds to an additional dosing cohort, which will depend on the safety and tolerability of BXCL501 in the 90 μg dosing cohort.

Phase 1b/2 trial of BXCL501 in Opioid Withdrawal Results in 1Q21

BioXcel is currently conducting the Phase 1b/2 RELEASE trial, which is a multicenter, randomized, double blind, placebo controlled study of BXCL501 in patients with opioid use disorder who are physically dependent on opioids and experiencing symptoms of opioid withdrawal. Multiple dose cohorts of BXCL501 or placebo are being administered twice daily for seven days and patients are assessed using both the Clinical Opiate Withdrawal Scale (COWS), an 11-item scale that measures a range of withdrawal symptoms experienced after quitting opioids (Wesson *et al*., 2003), and Short Opiate Withdrawal Scale (Gossop, 1990). We anticipate results from the study being released in the first quarter of 2021.

The company had previously tested intravenous (IV) dexmedetomidine in patients suffering from opioid withdrawal symptoms and announced results in February 2019. A total of 15 patients (10 treated with dexmedetomidine and five administered placebo) with opioid dependence were enrolled and opioid withdrawal symptoms evaluated using the COWS. All 10 patients treated with dexmedetomidine responded to treatment, with the following graph showing the average decrease for treated patients, while no patients treated with placebo responded.



Source: BioXcel Therapeutics, Inc.

Phase 2 Trial in Delirium to Initiate Soon

BioXcel will be initiating a Phase 2 clinical trial of BXCL501 in patients with delirium in the next few months. The trial is planning to include patients who experience agitation in the intensive care unit (ICU) associated with and without COVID-19. In July 2020, the company announced the initiation of a compassionate use program for BXCL501 to investigate its use in treating delirium in patients suffering from COVID-19 in the ICU. There have been numerous reports in the media about COVID-19 patients suffering from delirium and agitation after having been admitted to the ICU, particularly in patients that were put on ventilators (see here and here). Treating delirium represents another large potential market opportunity and we look forward to updates for this program later this year.

Clinical Results for BXCL701 Presented at SITC

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 other solid tumors.

BXCL701 in Advanced Prostate Cancer

BioXcel is currently conducting a Phase 1b/2 clinical trial of BXCL701 in combination with Keytruda® (anti-PD-1 mAb) in patients with tNEPC and castration resistant prostate cancer (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®.

The company recently presented data from the Phase 1b portion of the trial at the Society for Immunotherapy of Cancer (SITC) 35th Annual Meeting. The poster presentation can be accessed here. Data was reported for patients from three dosing cohorts; 0.4 mg BXCL701 once daily (n=3), 0.6 mg BXCL701 once daily (n=3), and 0.6 mg BXCL701 daily split dose (n=7). Each dosing cohort also received pembrolizumab. The data showed that one patient experienced an 84% decrease in prostate specific antigen (PSA) and that four patients had stable disease according to RECIST 1.1.

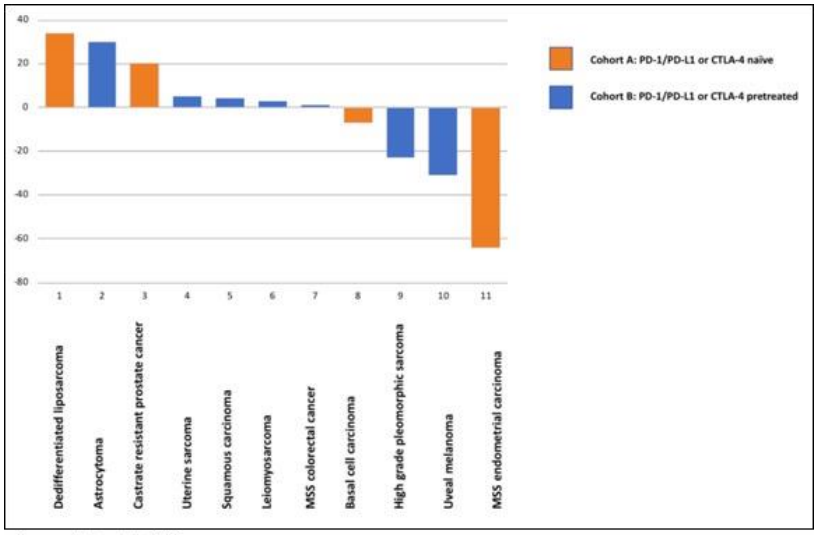
On-target adverse events (e.g., hypotension, peripheral edema) were seen that are consistent with cytokine activation at the highest dose tested. However, splitting the dose resulted in improved tolerability as shown by no dose-limiting toxicities and lower rates of adverse events.

The trial has advanced to the Phase 2 portion and we anticipate an additional efficacy update in the coming months.

BXCL701 in Solid Tumors

In Dec. 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.

Results from the ongoing trial were recently presented at SITC. A copy of the poster presentation can be accessed here. The following graph shows the best change in sum of target lesions per RECIST 1.1 in 11 patients, with those who were checkpoint inhibitor naïve (Cohort A, n=4) indicated by orange and those who had previously had checkpoint inhibitor therapy in blue (Cohort B, n=7). One patient in Cohort A who had microsatellite stable (MSS) endometrial carcinoma exhibited a partial response (PR, -64%) with another patient in Cohort A that had basal cell carcinoma exhibiting stable disease. In Cohort B, one patient with uveal melanoma exhibited a PR (-31%) and three others exhibited stable disease.



Source: Janku *et al.*, 2020

These results are encouraging, particularly the PR's in both MSS endometrial carcinoma and uveal melanoma. The trial is continuing to enroll patients and we look forward to updates in 2021.

BXCL701 in Pancreatic Cancer

BioXcel had planned to conduct a clinical trial of BXCL701 in combination with NKTR-214 and avelumab (anti-PD-L1 mAb) following a Phase 1b dose-escalation trial of NKTR-214 and avelumab. However, that trial was delayed and now all parties have agreed to discontinue activities on the triple combination study with the clinical trial collaboration agreement terminated in Nov. 2020.

Financial Update

On November 12, 2020, BioXcel announced financial results for the third quarter of 2020. As expected, the company did not report any revenues. Net loss for the third quarter of 2020 was $24.8 million, compared to a net loss of $9.0 million for the third quarter of 2019. R&D expenses for the third quarter of 2020 were $16.3 million, compared to $7.1 million for the third quarter of 2019. The increase was primarily due to an increase in clinical trial expenses, personnel costs, and non-cash stock-based compensation. G&A expenses in the third quarter of 2020 were $8.5 million, compared to $2.0 million for the third quarter of 2019. The increase was primarily due to increased professional fees, salaries, and non-cash compensation costs.

As of September 30, 2020, BioXcel had cash and cash equivalents of approximately $233.4 million. In July 2020, the company raised net proceeds of $187.5 million from the sale of 4 million shares of common stock at $50 per share. We estimate that the company has sufficient capital to fund operations well into 2022. As of November 11, 2020, the company had approximately 24.4 million shares outstanding and, when factoring in stock options, a fully diluted share count of approximately 28.2 million shares.

Valuation

BioXcel has taken the next step toward becoming a commercial-stage entity with the initiation of the rolling NDA for BXCL501 for treating acute agitation in schizophrenia and bipolar patients. We anticipate the NDA filing being finalized in the first quarter of 2021, with a decision from the FDA on whether to accept the NDA filing occurring 60 days later. At that time, we will learn whether the application will be reviewed under a standard review (10 months) or a priority review (6 months), which will ultimately dictate when the PDUFA is scheduled (either late 2021 or first half of 2022). In addition, the company continues to advance BXCL501 in multiple other indications and the early data for BXCL701 is encouraging. With no changes to our model, our valuation remains at $118.

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*

HISTORICAL STOCK PRICE

Source: Zacks SCR

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