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BioXcel Therapeutics, Inc. (BTAI-NASDAQ)

BTAI: Initiating Coverage of BioXcel Therapeutics, Inc.; AI Driven Drug Development…

Based on our probability adjusted DCF model that takes into account potential future revenues of the cellular oncology and stem cell therapies, BTAI is valued at $21.00/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 (10/30/19)	$4.40
Valuation	**$21.00**

OUTLOOK

We are initiating coverage of BioXcel Therapeutics, Inc. (BTAI) with a $21.00 valuation. BioXcel Therapeutics is a biopharmaceutical company utilizing an artificial-intelligence (AI) based approach to drug development. The company uses proprietary machine learning algorithms together with large datasets to identify new treatment approaches for approved medications or clinically validated drug candidates. BioXcel Therapeutics' two most advanced candidates are BXCL501, a sublingual formulation of the α2a adrenergic receptor agonist dexmedetomidine for the treatment of neurological and psychiatric disorders, and BXCL701, an immuno-oncology agent for the treatment of prostate and pancreatic cancer. The company will be initiating two Phase 3 clinical trials of BXCL501 for the treatment of agitation in schizophrenia and bipolar disorder in the fourth quarter of 2019 and we anticipate Phase 1 data readouts for BXCL701 in prostate and pancreatic cancer over the next six months.

SUMMARY DATA

52-Week High	**$11.79**
52-Week Low	**$2.41**
One-Year Return (%)	**-18.52**
Beta	**2.96**
Average Daily Volume (sh)	**74,875**
Shares Outstanding (mil)	**16**
Market Capitalization ($mil)	**$69**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**20**
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	**-2.9**
P/E using 2020 Estimate	**-2.1**

Risk Level	**High**
Type of Stock	**Small-Blend**
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 E	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 E	-$0.56 E	-$0.50 E	-$2.10 E
2020					-$1.68 E
2021					-$1.68 E

WHAT'S NEW

Initiating Coverage

We are initiating coverage of BioXcel Therapeutics, Inc. (BTAI) with a valuation of $21.00. BioXcel Therapeutics is a biopharmaceutical company utilizing an artificial-intelligence (AI) based approach to drug development. In combination with large datasets, the company uses a proprietary machine learning algorithm to identify new treatment paradigms for clinically validated and/or approved drugs. The company has 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.

Novel Drug Re-Innovation Approach
BioXcel uses an artificial intelligence (AI)-based drug discovery engine, EvolverAI, to identify drugs for re-innovation. The system is designed to utilize vast data sources to discover novel connections between pharmaceutical compounds and disease targets. The use of AI allows BioXcel to screen thousands of compounds in a systematic fashion in order to select those most likely to benefit patients with a shortened development timeline. While EvolverAI is novel, the re-innovation of drugs is a validated approach to drug development as shown through the success of such drugs as Tecfidera®, Thalomid®, and Viagra®.

Targeting Large and Growing Agitation Market
BXCL501, a sublingual formulation of dexmedetomidine, was identified as a potential treatment for agitation in neurological and psychiatric disorders. Currently, agitated patients are treated with antipsychotics and/or benzodiazepines, both of which are associated with a number of adverse side effects. BXCL501 targets the underlying mechanism of agitation and allows for the treatment of patients in a non-invasive fashion without sedation, thus allowing physicians to better understand the origin of the agitation.

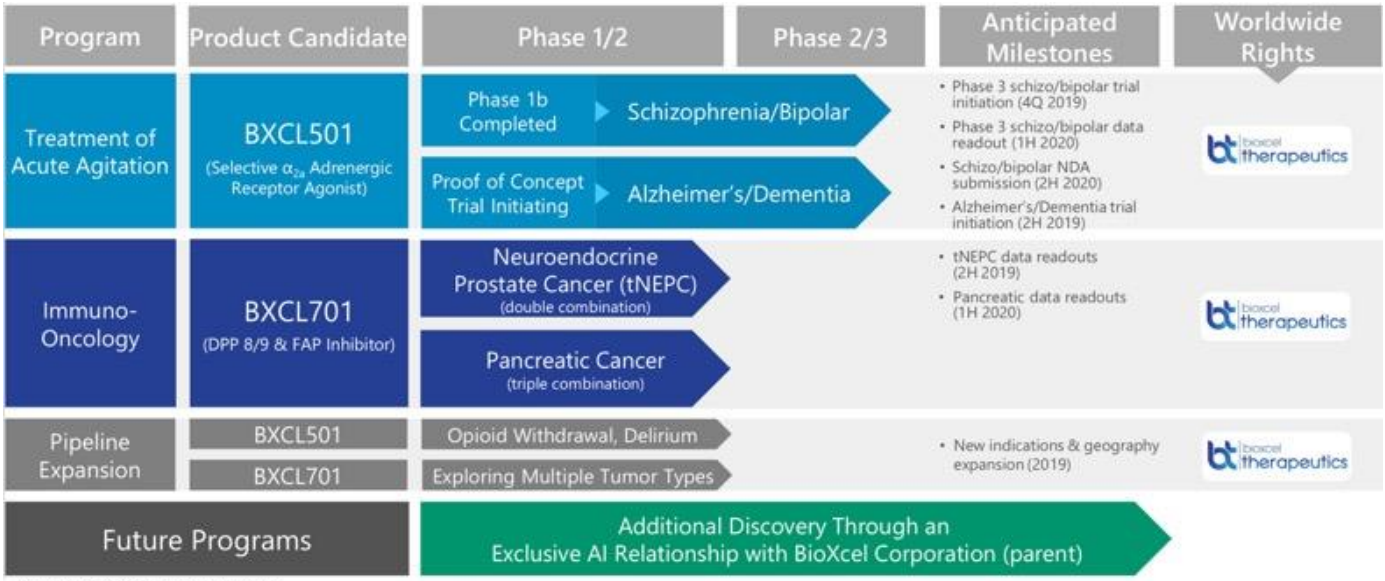
Oral Immuno-Oncology Agent Targeting Rare Prostate Cancer and Pancreatic Cancer
BXCL701 is an oral immuno-oncology agent designed to activate the innate immune system through inhibition of dipeptidyl peptidase (DPP) 8/9 and fibroblast activation protein (FAP). The drug has previously been tested in >700 patients in various clinical trials where it was unsuccessful in combination with chemotherapy in NSCLC. However, EvolverAI predicts that the drug's activity could be increased when used as a combination therapy with checkpoint inhibitors (e.g., anti-PD-1 antibodies) and other immune stimulators in indications where DPP8/9 and FAP are overexpressed or upregulated. The company has initiated two clinical proof-of-concept trials: in treatment-emergent neuroendocrine prostate cancer (tNEPC) in combination with Keytruda® (pembrolizumab) and in pancreatic cancer in combination with NKTR-214 (bempegaldesleukin) and avelumab (anti-PD-L1 mAb).

Near-Term Milestones Include Phase 3 Data in 2020
We anticipate BioXcel initiating two Phase 3 clinical trials of BXCL501 for the treatment of agitation in schizophrenia and bipolar disorder in the fourth quarter of 2019 and topline data being reported in the first half of 2020. If successful, this could lead to a new drug application (NDA) for BXCL501 in the second half of 2020. In addition, we anticipate data readouts from the two clinical trials for BXCL701 over the next six months.

INVESTMENT THESIS

BioXcel Therapeutics, Inc. (BTAI) is a biopharmaceutical company developing novel therapeutics using EvolverAI, the company's proprietary research and development engine designed to utilize artificial intelligence (AI) and machine learning to evaluate millions of data points to identify new therapeutic indices for clinically validated and/or approved drugs. By using an AI-driven approach, the company targets areas of high unmet medical need with limited competition and is able to design more efficient clinical trials to speed up development timelines.

Drug re-innovation is a proven business model, as shown by a number of successes such as Tecfidera®, Thalomid®, and Viagra®. EvolverAI was developed to sift through the vast amounts of data that are currently available for the thousands of active pharmaceutical agents in an unbiased fashion to discover never before appreciated connections between drug compounds, mechanisms of action, and disease attributes. Compounds identified by EvolverAI (of which there are > 20) are then tested in preclinical models to determine the optimal agents to move forward in clinical trials. The combination of AI-driven identification coupled with human expertise should lead to a reduction in product development timelines and reduced risk compared with traditional drug development pathways. BioXcel Therapeutics' two lead assets were discovered by EvolverAI.



Source: BioXcel Therapeutics, Inc.

BXCL501

BXCL501 is a sublingual formulation of dexmedetomidine (Dex) that is currently being tested as a treatment for agitation in neurodegenerative and psychiatric disorders. Dex was initially approved in 1999 as an injectable for sedation in the intensive care setting and sold under the name Precedex®. It has been prescribed to millions of patients and has an excellent safety record. The sublingual formulation of Dex is designed to be administered in a non-invasive way and have a rapid onset of action. The company has completed a Phase 1b trial of BXCL501 in schizophrenia patients for which positive results were announced in July 2019. BioXcel will be initiating two Phase 3 trials in patients with schizophrenia and bipolar disorder before the end of 2019.

Agitation Overview

Agitation is a common condition for those suffering from neurological or psychiatric conditions and is characterized by excessive verbal and motor behavior that may also be accompanied by hostility, poor

impulse control, uncooperativeness, and occasionally violence and anger. Approximately 1.7 million emergency department visits and approximately 20% of psychiatric emergency services visits each year are the result of agitation (Zeller *et al.*, 2010). Psychoses, including schizophrenia and bipolar disorder, are common causes of emergency department visits for agitation, and its estimated that approximately 20% of the 2.4 million adults suffering from schizophrenia in the U.S. will suffer episodes of agitation in their lifetime.

A number of rating scales have been developed in order to quantify agitation, with the five-item Positive and Negative Syndrome Scale-Excited Component (PEC) used extensively in clinical trials of agents for the treatment of agitation (Montoya *et al*., 2011).

In 2010, the American Association for Emergency Psychiatry initiated Project BETA (Best practices in Evaluation and Treatment of Agitation) to develop detailed guidance on treating agitated patients including medical evaluation and triage, psychiatric assessment, verbal de-escalation, and the avoidance of seclusion and restraint (Holloman *et al*., 2012). De-escalation was recommended as a means to get the patient's cooperation so the root cause of the agitation can be determined in an expedited fashion.

Agitation Treatments

Traditionally, agitated patients in an emergency setting have been treated with intramuscular (IM) haloperidol (5 mg) and lorazepam (2 mg) (the combination is sometimes referred to as the "B-52" shot). Other antipsychotic agents used for the treatment of agitation include ziprasidone, olanzapine, and aripiprazole, either alone or in combination with a benzodiazepine. However, benzodiazepines have a number of potential adverse effects, including respiratory and cardiac depression, hypotension, dependence, and (paradoxically) increased agitation (Nasraway *et al*., 2002). In addition, the length of sedation when using benzodiazepines can differ from patient to patient, with some requiring an overnight stay in the hospital due to somnolence, further adding to the cost of treatment.

In elderly dementia patients who experience agitation, the use of benzodiazepines is also complicated by altered pharmacodynamics and pharmacokinetics that occur with advanced age. Additionally, the long half-lives of those agents can cause accumulation in the body. The use of antipsychotics in elderly dementia patients is contraindicated due to an increased risk of mortality, and all antipsychotics carry a 'black-box' warning.

A 2011 systematic review found that oral, IM, and intravenous (IV) treatment of agitation with the aforementioned agents are all acceptable routes of administration, however IM is preferred (Zeller *et al*., 2010). A survey of 59 patients who used psychiatric emergency services indicated that pills or capsules were preferred, followed by liquid medication, and then an injection (Allen *et al*., 2003). In summary, IM treatments are fast acting but are highly invasive, while oral treatments are preferred but slow acting. In addition, safety is an important consideration as all currently available agitation treatments have adverse effects. Thus, an ideal treatment for agitation appears to be one that would be non-invasive and easily administered with a rapid onset of activity, long duration of action, and a benign side effect profile.

Dexmedetomidine for the Treatment of Agitation

Dex is a specific and selective α2-adrenergic receptor agonist (Gertler *et al*., 2001). It is currently marketed as Precedex™ for IV administration to sedate patients prior to or during surgical procedures and to sedate intubated and mechanically ventilated patients. The sedative effect of dex is the result of the dense postsynaptic α2 receptors found in the locus coeruleus region of the brain, which is considered the hypnotic or wakefulness modulator area (Atzori *et al*., 2016). One of the unique features of dex is that even with a calming effect the patient is still easily arousable, which is unique among sedative agents.

In addition to the studies supporting the use of dex in sedation, we identified a few case studies in which dex was used in the emergency department in agitated patients, including:

- Tobias, 2010: Three case reports of teenagers admitted to the emergency department for severe agitation brought about by the abuse of dextromethorphan. In each case, dex was given as a loading dose of 1

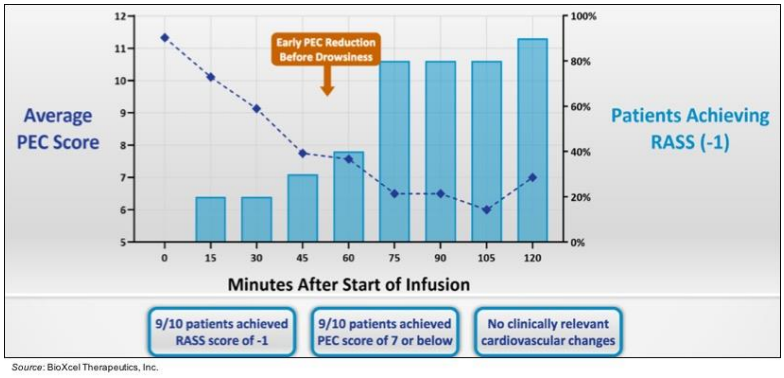
μg/kg IV over 10 minutes followed by an infusion of 1 μg/kg/hr. After administration of dex, each patient became quiet with no further episodes of agitation.

- Lam *et al*., 2017: Two case reports of a 42 and 38-year-old man with unstable emotion after smoking methamphetamine. In each case, neither patient responded to large, cumulative doses of benzodiazepines, however each individual's agitation was controlled with dex.

IV Dex Studies

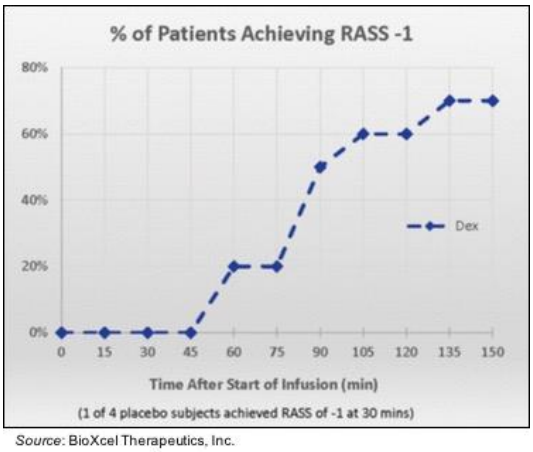
Healthy Volunteers: BioXcel initially studied IV dex in multiple, proof-of-concept Phase 1 studies. The initial study occurred in 16 healthy volunteers aged 55-75, with the primary outcome being mild sedation, which served as a surrogate endpoint for treating agitation, using the Richmond Agitation-Sedation Scale (RASS) Score (Sessler *et al*., 2002). Results showed a mild sedation caused by dex (RASS score of -1) in 11/12 subjects without any clinically meaningful changes in blood pressure or heart rate. In contrast, only 1/4 individuals treated with placebo experienced a mild sedating effect.

Schizophrenia Patients: In November 2018, BioXcel announced results from a proof-of-concept efficacy study of IV dex for the treatment of acute agitation in schizophrenia patients. A total of 14 patients were enrolled in the trial, with 10 patients treated with an escalating dose of dex ranging from 0.2 to 0.6 μg/kg/hr over a period of 30 minutes while four patients received placebo. The results showed that 9/10 patients achieved a RASS score of -1 while no patients in the placebo arm experienced meaningful sedation. A secondary endpoint in the trial was reduction in agitation as determined by a PEC score of 7 or below, which was achieved by 9/10 treated patients and 0/4 placebo patients. The results are shown below.



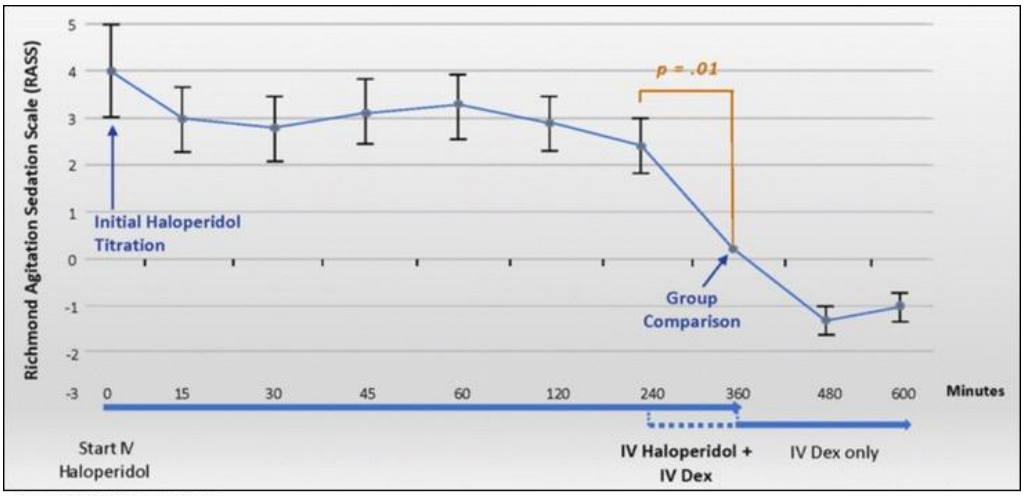
Source: BioXcel Therapeutics, Inc.

SDAT Patients: In January 2019, BioXcel announced results from a proof-of-concept Phase 1 study of IV dex for the treatment of acute agitation in patients with Senile Dementia of the Alzheimer's Type (SDAT). A total of 14 patients were enrolled in the trial, with 10 patients treated with an escalating dose of dex ranging from 0.1 to 0.5 μg/kg/hr over a period of 30 minutes while four patients received placebo. The following figure shows that 7/10 patients achieved a RASS score of -1, with only 1/4 patients in the placebo arm experiencing meaningful sedation.



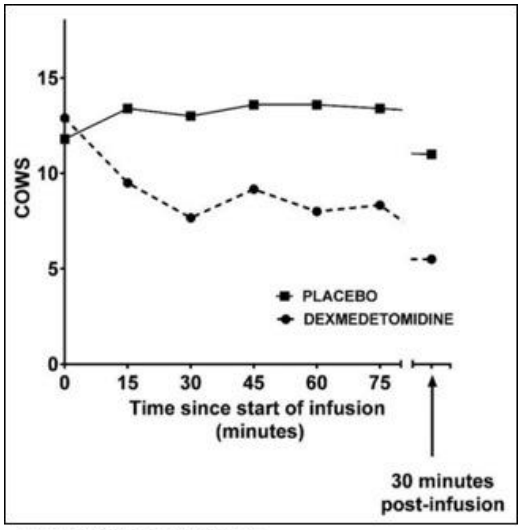
Source: BioXcel Therapeutics, Inc.

Delirium Patients: A 2016 study examined the effect of IV dex in treating agitated delirium in intensive care unit (ICU) patients refractory to haloperidol (Carrasco *et al*., 2016). A total of 132 patients were enrolled in the trial, with 46 of them considered non-responders to haloperidol. The following figure shows that all 46 haloperidol-refractory patients (RASS score of +1 to +3) responded to dex, as measured by the attainment of a RASS score of 0. In addition, while 10/86 haloperidol-treated patients experienced over-sedation, 0/46 patients treated with dex were over-sedated.



Source: BioXcel Therapeutics, Inc.

Opioid Withdrawal: In February 2019, BioXcel announced the results of a Phase 1b study of IV dex in patients suffering from opioid withdrawal symptoms. A total of 15 patients (10 treated with dex and five administered placebo) with opioid dependence were enrolled. Opioid withdrawal was evaluated using the Clinical Opioid Withdrawal Scale (COWS), an 11-item scale that measures a range of withdrawal symptoms experienced after quitting opioids (Wesson *et al*., 2003). All 10 patients treated with dex responded to treatment, with the following graph showing the average decrease for treated patients, while no patients treated with placebo responded.

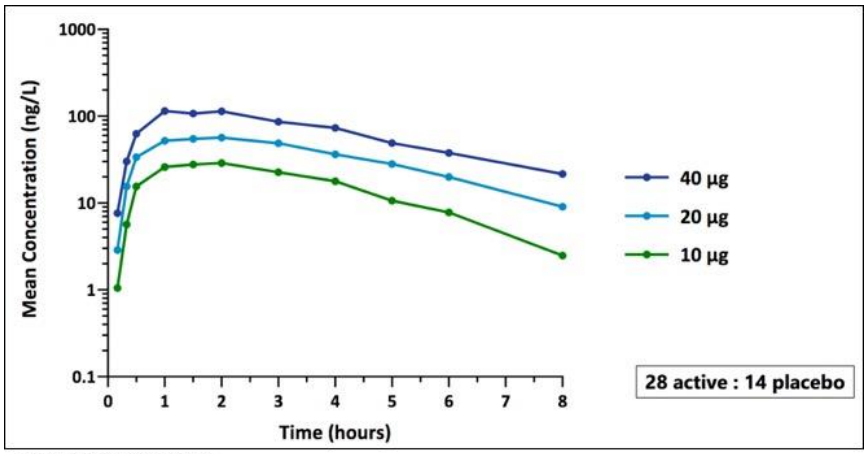


Source: BioXcel Therapeutics, Inc.

BXCL501 Studies

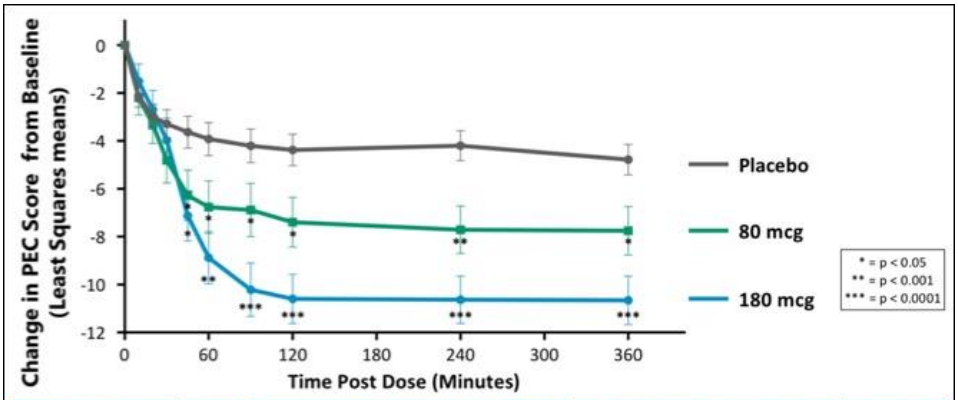
BXCL501 is a sublingual thin film formulation of dex designed for rapid absorption and ease of administration. It has been granted Fast Track designation by the FDA, which allows for more frequent meetings with the agency, the potential for a rolling submission of a New Drug Application (NDA), and the potential for priority review.

Pharmacokinetic Study: In May 2019, BioXcel announced positive top line data from a Phase 1 pharmacokinetic study of BXCL501, which was a double blind, placebo controlled, single dose, dose escalation trial in 42 healthy adult volunteers. Results showed that BXCL501 produced a predictable, dose-dependent pharmacokinetic response.



Source: BioXcel Therapeutics, Inc.

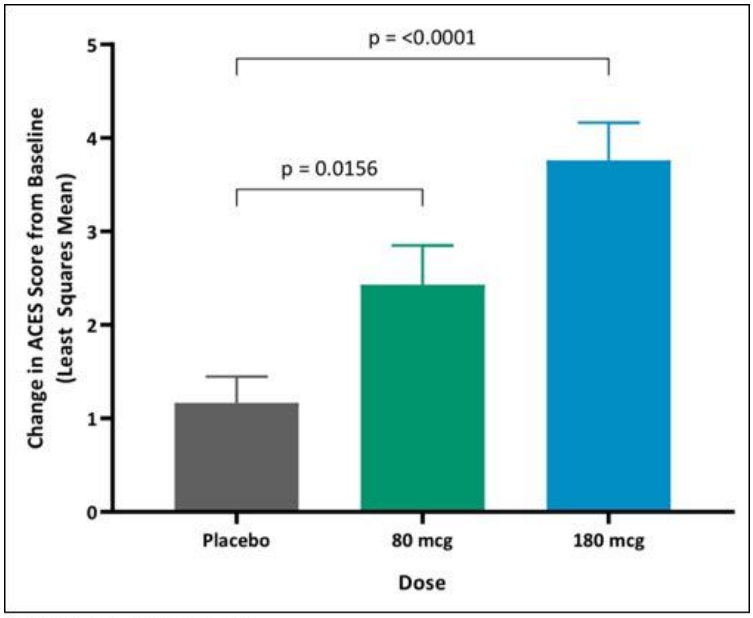
Schizophrenia Patients: In July 2019, BioXcel announced positive top line results from a Phase 1b, randomized, double blind, placebo controlled, multi-center U.S. trial evaluating multiple doses of BXCL501 for the treatment of agitation in 135 schizophrenia patients (NCT04010305). The primary endpoint was the reduction in PEC score. Results showed rapid calming without excessive sedation at two hours, with the 80 µg, 120 µg, and 180 µg doses showing reductions in PEC scores of -7.1, -9.2, and -10.8, respectively, compared to -4.5 for placebo. These results were all statistically significant. The following slide shows a rapid and durable response with statistically significant separation from placebo <60 minutes following dosing. The reduction in PEC scores attained by BXCL501 was comparable to levels achieved by IM antipsychotics in other trials (Breier *et al*., 2002).



Drug/Dose	#	% Responders (Reduction in PEC of ≥ 40%)	Mean Change in PEC Score	P-Value
Placebo	N=36	28%	-4.5	
BXCL501 (180 mcg)	N=18	89%	-10.8	< 0.0001
BXCL501 (120 mcg)	N=18	67%	-9.2	0.0003
BXCL501 (80 mcg)	N=18	56%	-7.1	0.0152
BXCL501 (60 mcg)	N=18	39%	-6.0	0.1227

Source: BioXcel Therapeutics, Inc.

A secondary endpoint in the trial included assessment using the Agitation-Calmness Evaluation Scale (ACES), which is a single item that rates the overall agitation and sedation at the time of evaluation, ranging from 1-marked agitation, 2-moderate agitation, 3-mild agitation, 4-normal behavior, 5-mild calmness, 6-moderate calmness, 7-marked calmness, 8-deep sleep, and 9-unarousable. The following graph shows a statistically significant change in ACES from baseline at both 180 µg and 80 µg BXCL501 compared to placebo, consistent with what was seen in the primary endpoint.



Source: BioXcel Therapeutics, Inc.

BXCL501 was well tolerated with no serious adverse events reported across the entire dose range tested. The most common treatment emergent adverse event was mild somnolence and dry mouth. In addition, all study subjects were able to self-administer the film and complete the study.

BXCL501 Development Plan

BioXcel is planning to conduct two pivotal Phase 3 trials for BXCL501 in the treatment of schizophrenia and bipolar disorder. We anticipate a total of approximately 500 patients total (250 each for schizophrenia and bipolar disorder patients) randomized 1:1:1 to one of two doses of BXCL501 or placebo. The primary endpoint will be the change in PEC score at two hours with a 24-hour evaluation period. We anticipate the trials initiating in the fourth quarter of 2019 with top line data available in the first half of 2020.

In addition to schizophrenia and bipolar disorder, we anticipate BioXcel initiating a Phase 1b trial in agitated Alzheimer's/dementia patients in the fourth quarter of 2019. The company is also continuing to plan for clinical trials examining BXCL501 as a treatment for agitation in opioid withdrawal and delirium.

BXCL501 Market Opportunity

Agitation represents a sizeable market opportunity. 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. 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 price of $130 per treatment, the total market opportunity is over $1 billion.

Precedent for the successful use of a sublingual formulation comes from Cynapsus Therapeutics, Inc., which developed a sublingual formulation of apomorphine for use by Parkinson's Disease patients. Cynapsus was acquired by Sunovion Pharmaceuticals, Inc. for $624 million in 2016. In addition, Indivior Plc sells Suboxone®, a sublingual formulation of buprenorphine and naloxone that is used for the treatment of opioid dependence, which generated revenues of close to $1 billion in 2018.

BXCL701

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.

tNEPC Overview

Prostate cancer is the most common non-cutaneous cancer diagnosed in men. It is typically a slow growing cancer, although it still accounts for approximately 10% of all cancer related deaths in men. The 2020 estimated incidence of prostate cancer in the U.S. is approximately 550,000 with a prevalence of approximately 3 million (Scher *et al*., 2015). In addition, the disease will be responsible for approximately 30,000 deaths. Prostate cancer is quite rare in men less than 40 years of age, and is still uncommon in men younger than 50. Sixty percent of cases are in men aged 65 or older and the average age of diagnosis is 66.

For patients whose cancer advances despite initial treatment for localized disease, or for those who present initially with more advanced disease, treatment typically begins with androgen deprivation therapy (ADT). Prostate cells (and subsequently prostate cancer cells) are dependent on androgens (e.g., testosterone and dihydrotestosterone) for growth, as removal of androgens through castration results in apoptosis of prostate epithelial cells. However, almost all patients will invariably develop resistance to ADT, which is referred to as castration-resistant prostate cancer (CRPC). When this occurs, patients are typically treated with second-generation anti-androgen drugs such as Zytiga® or Xtandi®. While initially effective, virtually all patients will progress and require additional treatment. Following ADT, approximately one-quarter of patients will develop very aggressive, androgen receptor (AR)-independent tumors (tNEPC), for which there currently exists no effective treatment (Aggarwal *et al*., 2018). We estimate approximately 30,000 individuals develop tNEPC each year.

Pancreatic Cancer Overview

Pancreatic cancer is responsible for 7% of all cancer deaths in both men and women, making it the fourth leading cause of cancer death in the U.S. (American Cancer Society). The disease is notoriously difficult to diagnose in early stages due to initial symptoms (anorexia, malaise, nausea, fatigue, and back pain) quite often being nonspecific and subtle in nature.

Surgical resection is the only potential curative therapy for pancreatic cancer. Due to differences in locations of the tumors and their proximity to nearby blood vessels, only 20% of cases are eligible for surgery. Of the tumors that are surgically resected, 80% of those patients will still develop metastatic disease within two to three years following surgery (Daniel *et al*., 2008). For those with pancreatic cancer that cannot be surgically removed, the median overall survival is 10 to 14 months. For those with Stage IV disease (meaning the cancer has metastasized), the 5-year survival rate is 9% (American Cancer Society).

Gemcitabine is the standard of care chemotherapy agent for metastatic pancreatic cancer. The FDA has approved its use in combination with two other chemotherapeutic agents: erlotinib (Tarceva®) and nab-paclitaxel (Abraxane®). FOLFIRINOX (leucovorin + 5-fluorouracil + oxaliplatin + irinotecan) is a combination regimen that significantly improved overall survival compared to treatment with gemcitabine, however it is accompanied by serious adverse events and for that reason is only recommended for the healthiest patients. Onivyde® (irinotecan liposome injection) was approved by the FDA in 2015 in combination with fluorouracil and leucovorin to treat patients with metastatic pancreatic cancer who failed treatment with gemcitabine-based chemotherapy.

BXCL701 in tNEPC

Existing data shows that inhibiting DPP8/9 and FAP can affect tNEPC through multiple mechanisms, including:

- Neuropeptide Y (NPY), a substrate for DPP8/9, is upregulated in tNEPC and associated with an increased risk of mortality (Iglesias-Gato *et al*., 2016), thus inhibiting DPP8/9 can augment the activity of NPY.

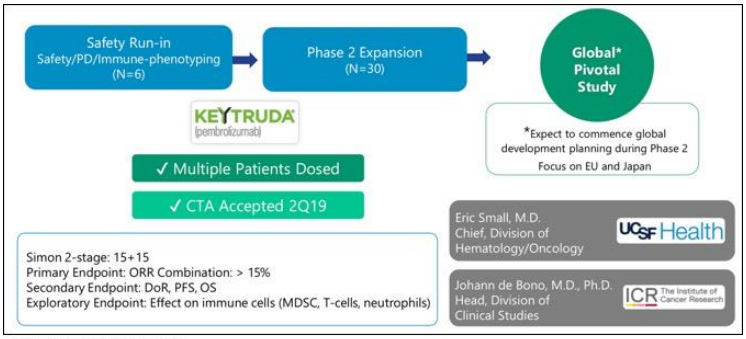
- Cancer associated fibroblasts (CAF) express FAP and are activated by ADT, thus by inhibiting FAP it may be possible to delay or prevent the development of CPRC (Fiori *et al*., 2019).

- Depleting FAP+ cells from the tumor microenvironment reduces immunosuppressive cells and improves the function of CD8+ T cells within tumors, thus making them more amenable to checkpoint inhibition therapy, such as with an anti-PD-1 antibody (Zhang *et al*., 2016).

- BXCL701 stimulates the priming, migration, and cytotoxicity of T cells (Walsh *et al*., 2013).

- tNEPC is associated with osteoclastic metastasis. BXCL701 was shown to reduce osteoclast activity, bone resorption, and tumor formation in a mouse model of tNEPC (Pennisi *et al*., 2009).

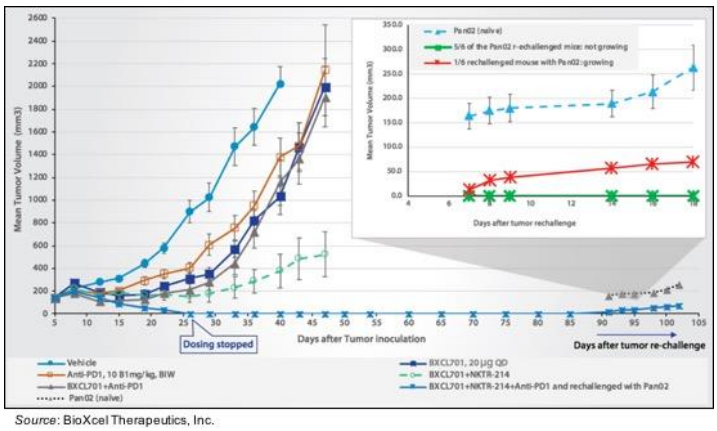
Based on the aforementioned data, BioXcel initiated a Phase 1/2 clinical trial of BXCL701 in combination with Keytruda® (anti-PD-1 mAb) in patients with tNEPC (NCT03910660). It is a single arm, open label trial to examine the safety, pharmacokinetics, and anti-tumor activity of the combination of BXCL701 and Keytruda®. An overview of the trial is shown below and we anticipate a data readout before the end of 2019.



Source: BioXcel Therapeutics, Inc.

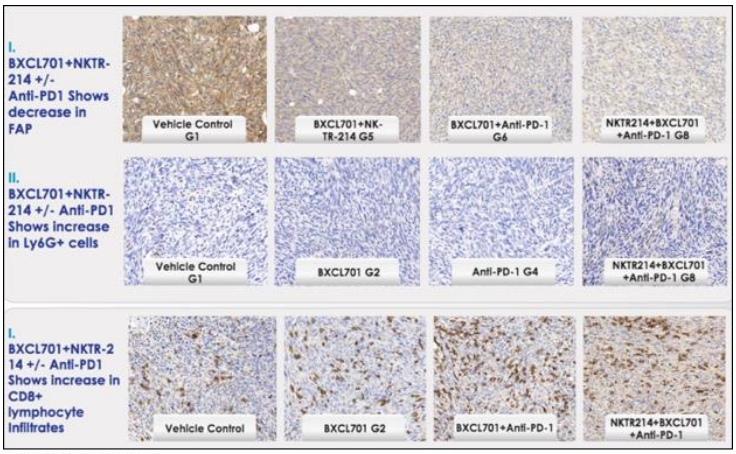
BXCL701 in Pancreatic Cancer

Given the mechanism of action of BXCL701, which stimulates the host immune system, it is likely that combination therapy with other immuno-oncology agents will be required to optimize its anti-cancer effect. In support of this, the company has performed preclinical studies with BXCL701 in combination with various immune stimulating agents. The following graph shows complete tumor regression in a mouse model of pancreatic cancer when BXCL701 is used in combination with an anti-PD-1 antibody and NKTR-214, which is a modified IL-2 that preferentially binds preferentially to CD122 to stimulate T cells and natural killer (NK) cells. In addition, when mice with complete regressions were re-challenged with tumor cells, only 1/6 exhibited tumor growth, indicating that immunological memory to the tumor occurred.



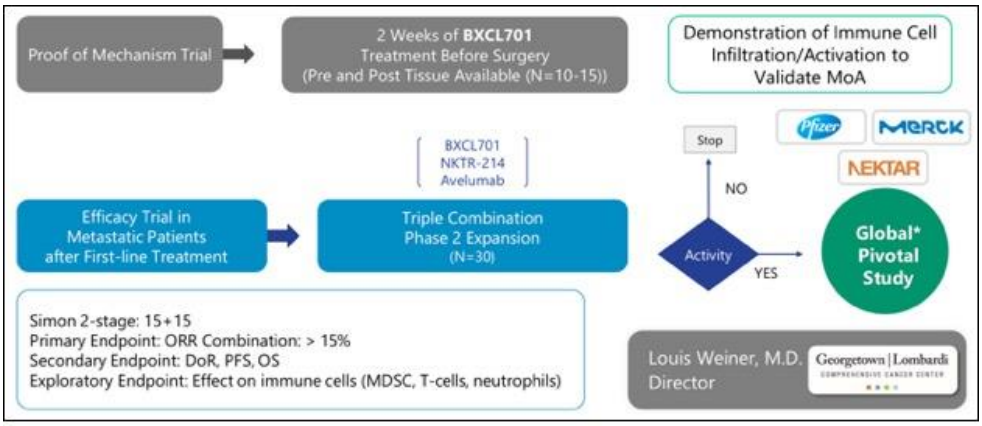
Source: BioXcel Therapeutics, Inc.

The study also demonstrated involvement of both the innate and adaptive immune responses through increases in Ly6G+ neutrophils, CD8+ T cells in the tumor, and increases in immune stimulatory cytokines while simultaneously decreasing FAP, as shown in the following figures.



Source: Rastelli *et al.*, 2018

BioXcel has received FDA clearance to initiate 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. The first part of the trial is a proof of mechanism trial that will involve two weeks of treatment with BXCL701 prior to surgery, with the primary output being a demonstration of immune cell infiltration and activation. This will be followed by a proof of concept trial in metastatic pancreatic cancer patients following first-line treatment with a primary endpoint of overall response rate. We anticipate a data readout in the second half of 2020. An outline of the trial is shown below.



Source: BioXcel Therapeutics, Inc.

Financials and Capital Structure

On August 6, 2019, BioXcel Therapeutics announced financial results for the second quarter of 2019. The company reported a net loss of $8.5 million compared to a net loss of $3.0 million for the second quarter of 2018. R&D expenses were $6.5 million for the second quarter of 2019 compared to $1.8 million for the second quarter of 2018. The increase in expenses was due to increased personnel costs, clinical trial expenses, manufacturing costs, and professional fees. G&A expenses for the second quarter of 2019 were $2.1 million compared to $1.5 million for the second quarter of 2018. The increase was primarily due to increased payroll expenses and professional fees.

As of June 30, 2019, BioXcel had cash and cash equivalents of $30 million. On September 26, 2019, the company announced the pricing of a public stock offering of approximately 2.3 million shares of common stock

at an offering price of $8.25 per share for gross proceeds of approximately $19 million. We estimate that following the stock offering the company has sufficient capital to fund operations through the end of 2020.

We estimate that the company currently has approximately 18 million shares of common stock outstanding, and when factoring in employee and non-employee stock options a fully diluted share count of approximately 21.1 million.

Risks to Consider

Clinical Risks: BioXcel is currently dependent upon the clinical success of BXCL501 and BXCL701. While the results from the Phase 1b clinical trial of BXCL501 in treating agitation in schizophrenia were encouraging, there is no guarantee that results in the Phase 3 trial will show the same efficacy and safety profile. BXCL701 has been unsuccessful in a number of prior clinical trials, thus there is no guarantee that the compound will be successful in treating tNEPC or pancreatic cancer.

Development Risk: The use of EvolverAI for the discovery of compounds for clinical development is novel and unproven, thus it may not lead to the discovery of a therapeutically or commercially successful drug. The biopharmaceutical industry is highly competitive and there are a large number of compounds under development for the treatment of pancreatic cancer, thus even if successful in clinical testing there is no guarantee the BXCL701 would be accepted by physicians, patients, or payers. In addition, competitors may develop more effective therapies that could render BioXcel's products obsolete.

Financing Risk: BioXcel just recently completed a financing, which we estimate will fund the company through the end of 2020, however the company will need to obtain additional financing to continue the development of BXCL701 and the commercialization of BXCL501, if approved.

Stock Risk: As of June 30, 2019, the directors, executive officers, and principal stockholders own approximately 62% of outstanding shares of BioXcel Therapeutics, Inc., thus if those stockholders acted together they would have the ability to control all matters submitted to stockholders for approval.

MANAGEMENT PROFILES

Vimal Mehta, PhD – Chief Executive Officer

Dr. Mehta brings over two decades of experience in the pharma and biotech industry, during which he has successfully designed and implemented innovative solutions, established global commercial operations, and led cross-functional teams. During his career, he has garnered a deep understanding of the biopharma and healthcare ecosystem and has been actively involved in generating a range of value creation initiatives in corporate strategy and planning, global business development and corporate fundraising. He is a Co-founder, Chairman of the Board, and Chief Executive Officer of BioXcel Corporation. Dr. Mehta has held various senior scientific and business development positions, including Senior Vice President of Business Development at Inpharmatica Ltd. and Jubilant Life Sciences. Previously, Dr. Mehta served as Business Development Manager at CuraGen Corporation. Dr. Mehta holds a Ph.D. in chemistry from the University of Delhi, India and completed a Post-Doctoral Fellowship in chemistry at the University of Montpellier, France.

Frank D. Yocca, PhD – Chief Scientific Officer

Dr. Yocca is an accomplished R&D executive and scientist with extensive experience leading global biopharmaceutical companies. He has wide-ranging expertise in leading high performance, world-class teams in drug discovery and development whose efforts have resulted in a number of prominent neuroscience products including Buspar®, Serzone®, Abilify®, and Hetlioz®. Frank has held executive research leadership roles at AstraZeneca and Bristol Myers Squibb. He is a recognized scientific leader in the neuroscience community and member of the Institute of Medicine of the National Academy of Science, and a Fellow of the American College of Neuropsychopharmacology. He has 45 referred articles, 96 abstracts and 65 invited presentations. Dr. Yocca holds a B.S. in biochemistry from Manhattan College, as well as an M.S. in pharmacology and a Ph.D. in neuropharmacology from St. John's University.

Vincent J. O'Neill, MD – Senior Vice President & Chief Medical Officer

Dr. O'Neill has proven expertise in therapeutic and diagnostic product development and has held senior leadership roles at global pharmaceutical companies, including Sanofi, Genentech, and GlaxoSmithKline. Most recently, he served as Chief Medical Officer at Mirna Therapeutics and Exosome Diagnostics, where he oversaw global product development and medical affairs. At both Genentech and GlaxoSmithKline, he managed the clinical and biomarker development programs of several oncology therapeutic candidates. He was instrumental in the expanded approvals of Genentech's oncology therapeutics, Avastin® and Tarceva®. At GSK, he oversaw the signal transduction discovery unit and led the first IND application and clinical trial of the MEK inhibitor, MEKINIST®. He has authored several peer-reviewed publications and conference presentations. Dr. O'Neill is also a member of the Royal College of Physicians. He received his M.D. and B.Sc. in molecular pathology from the University of Glasgow, Scotland.

Richard I. Steinhart – Vice President & Chief Financial Officer

Mr. Steinhart brings significant financial and strategic experience in the biotechnology and medical device industries. Prior to joining BioXcel Therapeutics, Richard served as Vice President and CFO at Remedy Pharmaceuticals, Inc., until it sold its only asset, CIRARA, to Biogen for $120M plus earn-outs. Prior to joining Remedy Pharmaceuticals, Mr. Steinhart served as an independent consultant to biotechnology and medical device companies. Previously, he was the Senior Vice President, Finance and Chief Financial Officer of MELA Sciences. Prior to joining MELA Sciences, Mr. Steinhart held a variety of senior-level positions at Forest Street Capital/SAE Ventures, a boutique investment banking, venture capital, and management consulting firm focused on healthcare and technology companies, Emisphere Technologies, Inc., and CW Group, Inc., a venture capital firm focused on medical technology. He began his career at PriceWaterhouseCoopers.

Chetan D. Lathia, PhD – Senior VP & Head, Translational Medicine, Clinical Pharmacology & Regulatory Affairs

Dr. Lathia has co-led the IND submissions for a number of new molecular entities and eight new drug applications (NDA) / biologics license application (BLA) in the US, Europe, Japan, China, etc. In addition to presenting clinical pharmacology & clinical strategy at meetings with drug regulators, he has made presentations to the Special Advisory Group (SAG) of the EMA and an advisory meeting held by Taiwanese regulators. Dr. Lathia has delivered invited presentations to the FDA Office of Clinical Pharmacology. Most recently, Dr. Lathia served as the VP and Head of Clinical Pharmacology at Intarcia Therapeutics where he was responsible for leading the pharmacokinetics (PK)/ pharmacodynamics (PD), immunogenicity and bioanalytical strategy. Prior to that, Dr. Lathia served as the Executive Director, Clinical Pharmacology at Alexion Pharmaceuticals where he led the global clinical and nonclinical PK/PD, pharmacometrics, and bioanalytics functions. Previously, Dr. Lathia served as the Global Head, Oncology Biomarkers and Pharmacokinetics and as the Global Clinical Pharmacology Leader for Nexavar at Bayer. Prior to this he was a Senior Research Associate at Parke-Davis Research where he co-led drug metabolism, nonclinical & clinical PK functions for the oncology & cardiovascular portfolio.

VALUATION

We are initiating coverage of BioXcel Therapeutics Inc. (BTAI) with a valuation of $21.00. BioXcel Therapeutics is a biopharmaceutical company utilizing an artificial-intelligence (AI) based approach to drug development. In combination with large datasets, the company uses a proprietary machine learning algorithm to identify new treatment paradigms for clinically validated and/or approved drugs. The company has 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.

BXCL501

BXCL501 is a sublingual formulation of dexmedetomidine (Dex) that is currently being tested as a treatment for agitation in neurodegenerative and psychiatric disorders. Dex was initially approved in 1999 as an injectable for sedation in the intensive care setting and sold under the name Precedex®. It has been prescribed to millions of patients and has an excellent safety record. The sublingual formulation of Dex is designed to be administered in a non-invasive way and have a rapid onset of action. The company has completed a Phase 1b trial of BXCL501 in schizophrenia patients for which positive results were announced in July 2019. BioXcel will be initiating two Phase 3 trials in patients with schizophrenia and bipolar disorder before the end of 2019.

Agitated patients in an emergency setting are typically treated with intramuscular (IM) haloperidol (5 mg) and lorazepam (2 mg) (the combination is sometimes referred to as the “B-52” shot), however the use of benzodiazepines is accompanied by a number of potential adverse side effects, including respiratory and cardiac depression, hypotension, dependence, and (paradoxically) increased agitation. In elderly dementia patients with agitation, the use of antipsychotics is contraindicated due to an increased risk of mortality.

A 2011 systematic review found that IM agitation treatments are fast acting but highly invasive, while oral treatments are preferred but slow acting. We believe BXCL501 could prove to be an ‘ideal treatment’ for agitation that is non-invasive, easily administered, has a rapid onset of action, a long duration of action, and a benign side effect profile.

BXCL701

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), which develops in approximately one-quarter of prostate cancer patients following androgen deprivation therapy, and pancreatic cancer, one of the deadliest cancers with a five-year survival rate of only 9%.

Based on an extensive amount of data showing that BXCL701 can affect tNEPC through multiple mechanisms, including activation of T cells, BioXcel has initiated a Phase 1/2 clinical trial of BXCL701 in combination with Keytruda® (anti-PD-1 mAb) in patients with tNEPC, with a potential data readout before the end of 2019. In pancreatic cancer, preclinical studies of BXCL701 in combination with various immune stimulating agents has shown tumor regressions and the development of immunological memory. Based on these studies, BioXcel has received FDA clearance to initiate a Phase 1/2 clinical trial of BXCL701 in combination with NKTR-214 and avelumab (anti-PD-L1 mAb).

Valuation

We value BioXcel Therapeutics using a probability adjusted discounted cash flow model that takes into account potential future revenues for BXCL501 and BXCL701.

For BXCL501, we model for Phase 3 data in schizophrenia and bipolar disorder to be reported in the first half of 2020, with an NDA filing in the second half of 2020 and approval in the first half of 2020. We estimate that the company will receive approval for treatment of agitation in dementia is 2023 and in opioid withdrawal and delirium in 2024. We model for each treatment to cost $130 and we forecast for peak sales of $200 million in schizophrenia, $350 million in dementia, $200 million in opioid withdrawal, and $220 million in delirium. We estimate for a 75% probability of approval in schizophrenia and a 40% probability of approval in each of the other indications. Using a 15% discount rate leads to a net present value for BXCL501 of $274 million.

For BXCL701, we model for BioXcel to partner and to receive a 15% royalty on net sales. Assuming positive results in the Phase 1/2 clinical trials, we model for pivotal trials in both tNEPC and pancreatic cancer to initiate in 2021 with potential approval in 2024. Given the limited treatment options for each of those indications, we believe $1 billion in peak sales is possible for each indication. We estimate for a 33% probability of approval for each indication and using a 15% discount rate leads to a net present value for BXCL701 in tNEPC of $54 million and in pancreatic cancer of $63 million.

Combining the net present values for each of the company's assets along with the current cash balance and potential money from exercised warrants leads to a net present value for the company of $446 million. Dividing by the fully diluted share count of approximately 21.1 million shares leads to a valuation of $21.00 per share.

PROJECTED FINANCIALS

BioXcel Therapeutics, Inc.	2018 A	Q1 A	Q2 A	Q3 E	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	$6.5	$6.7	$25.4	$27.0	$30.0
General & Administrative	$5.4	$1.7	$2.1	$2.2	$2.3	$8.4	$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)	($8.7)	($9.0)	($33.8)	($37.0)	($42.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.7	($0.2)	($0.2)	($0.1)	($0.1)	($0.6)	$0.0	$0.0
Pre-Tax Income	($19.2)	($7.2)	($8.5)	($8.8)	($9.1)	($34.3)	($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)**	**($8.8)**	**($9.1)**	**($34.3)**	**($37.0)**	**($42.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.32)**	**($0.46)**	**($0.54)**	**($0.56)**	**($0.50)**	**($2.10)**	**($1.68)**	**($1.68)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	14.6	15.7	15.7	15.8	18.3	16.4	22.0	25.0

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

HISTORICAL STOCK PRICE

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