Zacks Small-Cap Research
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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: Encouraging Data for BXCL701 in Heavily Pretreated mCRPC Patients…

Based on our probability adjusted DCF model that takes into account potential future revenues of BXCL501 and BXCL701, BTAI is valued at $110.00/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 (09/17/21)	$30.61
Valuation	**$110.00**

OUTLOOK

On September 15, 2021, BioXcel Therapeutics, Inc. (BTAI) announced data from the ongoing Phase 1b/2 trial of BXCL701 in patients with metastatic castration-resistant prostate cancer (mCRPC) was presented at the 2021 European Society for Medical Oncology (ESMO) Congress. BXCL701 is being evaluated in combination with pembrolizumab in heavily pre-treated mCRPC patients with adenocarcinoma. Results showed that 26% of patients achieved a composite response, (defined as RECIST 1.1 response, circulating tumor cell (CTC) conversion, or >50% prostate-specific antigen (PSA) decline from baseline), with all responders showing a decrease in tumor size. Previous studies with pembrolizumab as a monotherapy in this patient population showed minimal activity, thus a 26% composite response rate is quite encouraging, particularly since the majority of responders did not have strong predictive markers of pembrolizumab response.

SUMMARY DATA

52-Week High	**$64.60**
52-Week Low	**$23.84**
One-Year Return (%)	**-36.61**
Beta	**1.08**
Average Daily Volume (sh)	**232,829**
Shares Outstanding (mil)	**28**
Market Capitalization ($mil)	**$856**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**47**
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	**-6.5**
P/E using 2020 Estimate	**-7.9**

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

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	0 A	0 A	0 A	0 A	0 A
2021	0 A	0 A	0 E	0 E	0 E
2022					126 E
2023					297 E

Earnings per Share

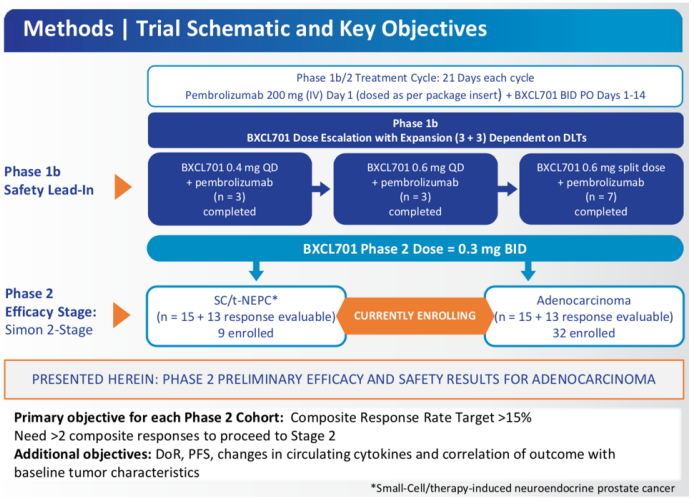
	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	-$0.79 A	-$1.06 A	-$1.07 A	-$0.87 A	-$3.79 A
2021	-$1.07 A	-$1.11 A	-$0.93 E	-$0.95 E	-$4.05 E
2022					-$1.10 E
2023					$2.81 E

Business Update

Encouraging Data for BXCL701 in Heavily Pretreated mCRPC Population

On September 15, 2021, BioXcel Therapeutics, Inc. (BTAI) announced that data from the ongoing Phase 1b/2 clinical trial of BXCL701 in patients with metastatic castration-resistant prostate cancer (mCRPC) was presented at the 2021 European Society for Medical Oncology (ESMO) Congress (the poster can be found here). 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). Its purpose is to initiate inflammation in the tumor microenvironment, thus potentially turning "cold" tumors "hot" and making them more amenable to immunotherapy treatment.

The following image gives an overview of the Phase 1b/2 trial. The Phase 2 portion of the trial consists of two patients cohorts: mCRPC with either therapy-induced neuroendocrine (t-NEPC) or adenocarcinoma phenotype. The current data up date is for the adenocarcinoma cohort.



Source: BioXcel Therapeutics, Inc.

The following table lists the patient characteristics for all those enrolled as of July 8, 2021. As can be seen, this is a very heavily pretreated population with a mean number of 5.3 prior therapies, almost all having had prior androgen signaling inhibitors, and all having received prior taxane chemotherapy.

Baseline Characteristics		Phase 2 Adenocarcinoma Cohort | N (%)
Enrolled		32
Age (years)	Mean (range)	68.2 (51-82)
ECOG Performance Status	0 1 2	12 (38) 19 (59) 1 (3)
Bone Only disease		14 (44)
Prior Cancer Therapies	Mean number of prior regimens (SD)	5.3 (2.35)
Prior Systemic Therapies	2nd Generation ASI *1 ASI* *2 ASI* Taxane Chemotherapy Provenge (sipuleucel-T) Radiation Therapy	31 (97) *12 (37)* *19 (59)* 32 (100) 10 (31) 6 (19)

Source: BioXcel Therapeutics, Inc.

The best responses recorded for each patient are indicated in the following table. A few highlights from the table include:

- 1 confirmed and 2 unconfirmed partial responses (PR) for an **objective response rate (ORR) of 16%**
- A **disease control rate** (PR + stable disease [SD] + non-complete response [CR]/non-progressive disease [PD]) of **63%**
- A **PSA_{50}** (representing a ≥50% reduction in PSA level from baseline) of **17%**

To put these numbers in perspective, when pembrolizumab was evaluated as a monotherapy in a similar patient cohort the DCR was 12%, the ORR was ~5%, and the PSA_{50} was 6% (Antonarakis *et al.*, 2019).

Best Response	Phase 2a Adenocarcinoma Patients n (%)
RECIST 1.1 by Investigator Assessment[a]	
RECIST Evaluable	19
Best RECIST Response	
Confirmed PR	1 (5)
Unconfirmed PR	2 (11)
SD (any duration) including Minor Response	8 (42)
Non-CR / Non-PD	1 (5)
PD	7(37)
Disease Control Rate (PR + SD + Non-CR / Non-PD)	12 (63)
PSA	
PSA Evaluable[b]	29[c]
PSA_{50} Response	5 (17)
CTC[d]	
CTC Evaluable[e]	8
CTC Response[f]	2 (25)
Composite Response n = 23	6 (26)

Composite response rate is 26%:
- RECIST-defined PR is 16%
- Disease control rate (PR + SD + non-CR / non-PD) is 63%
- PSA_{50} is 17% including 3 patients who had a PSA decrease around 90%
- CTC response is 25%

CTC data cut-off MAY-21
RECIST 1.1 / PSA data cut-off 23-AUG-21

[a] Patients who received ≥2 cycles of study therapy and 1 on-treatment tumor assessment [b] Baseline value >4 ng/mL and one on-treatment PSA assessment [c] 23 patients evaluable for composite response [d] Circulating tumor cell [e] Baseline CTC value ≥5/7.5 mL and one measurable on-treatment assessment [f] CTC conversion from ≥5/7.5 mL to <5/7.5 mL

Source: BioXcel Therapeutics, Inc.

The following table gives a summary of the six (23%) composite responders, who had either a PSA_{50}, a circulating tumor cell (CTC) conversion from ≥5/7.5 mL to ≤5/7.5 mL, or RECIST 1.1 response. All of the composite responders had a decrease in tumor size, with three of the patients exhibiting a partial response (1 confirmed, 2 unconfirmed).

Patient	Prior Systemic Therapies	PSA ≥-50%*	CTC ≥5/7.5 ml to <5/7.5 ml*	RECIST 1.1 ≥-30%*	Tumor Biology
106-908	Enzalutamide, sipuleucel-T docetaxel, cabazitaxel	-99%	5 to 0	-60% (confirmed)	TMB = 20.7 MSI-high /unstable PD-L1 low
101-934	Nilutamide, abiraterone enzalutamide, sipuleucel-T docetaxel, cabazitaxel	-52%	Baseline CTC = 0	-19%	TMB = 2 MSI stable PD-L1 low
112-937	Abiraterone, sipuleucel-T docetaxel	-98.5%	-	-24%	TMB = 1 MSI stable
106-939	Abiraterone, enzalutamide docetaxel, cabazitaxel	-57%	26 to 1	-15%	Data pending
101-940	Abiraterone, enzalutamide docetaxel, cabazitaxel	-99.9%	-	-52% (unconfirmed)	MSI stable
101-944	Carboplatin docetaxel, cabazitaxel	0%	3 to 2	-55% (unconfirmed)	TMB = 3 MSI stable PD-L1 low

*change from baseline - Sampling error Response TMB = Tumor Mutation Burden | MSI = Microsatellite Instability

Source: BioXcel Therapeutics, Inc.

Lastly, the following table provides a summary of the adverse events, with all those listed being reported by ≥3% of patients. The majority of the events were low grade and importantly there was no indication that BXCL501 potentiates any adverse events typically seen with immune checkpoint inhibitors. One patient who initiated dosing with 0.3 mg BID experienced Grade 3 hypotension, however step-up dosing was then implemented for all new patients with BCXL701 0.2 mg BID on Day 1 through Day 7 and escalation was permitted to 0.3 mg BID if no treatment emergent AEs greater than Grade 1 or no skipped doses due to hypotension or orthostasis occurred during the first week of treatment.

Treatment Emergent Adverse Events	N = 32 n (%)			
Subjects with any TEAE	**27 (84)**			
AE related to BXCL701 or pembrolizumab	**10 (31)**			
SAE related to BXCL701 or pembrolizumab	**2 (6)**			
AE Preferred Term	**Grade 1**	**Grade 2**	**Grade 3**	**Total**
Fatigue	3	2	-	**5**
Hypotension*	3	1	-	**4**
Pruritus and Rash	4	-	-	**4**
Dizziness	2	-	1	**3**
Arthralgia/Myalgia	-	2		**2**
Oedema peripheral	1	-	-	**1**
Dehydration		1	-	**1**
Vomiting	-	1	-	**1**
Decreased appetite	1	-	-	**1**
Decreased lymphocyte count	-	1	-	**1**
Blood lactic acid increased	1	-	-	**1**
Pyrexia	1	-	-	**1**
Cytokine Release Syndrome	-	1	-	**1**

*Includes orthostatic hypotension

Source: BioXcel Therapeutics, Inc.

Conclusion

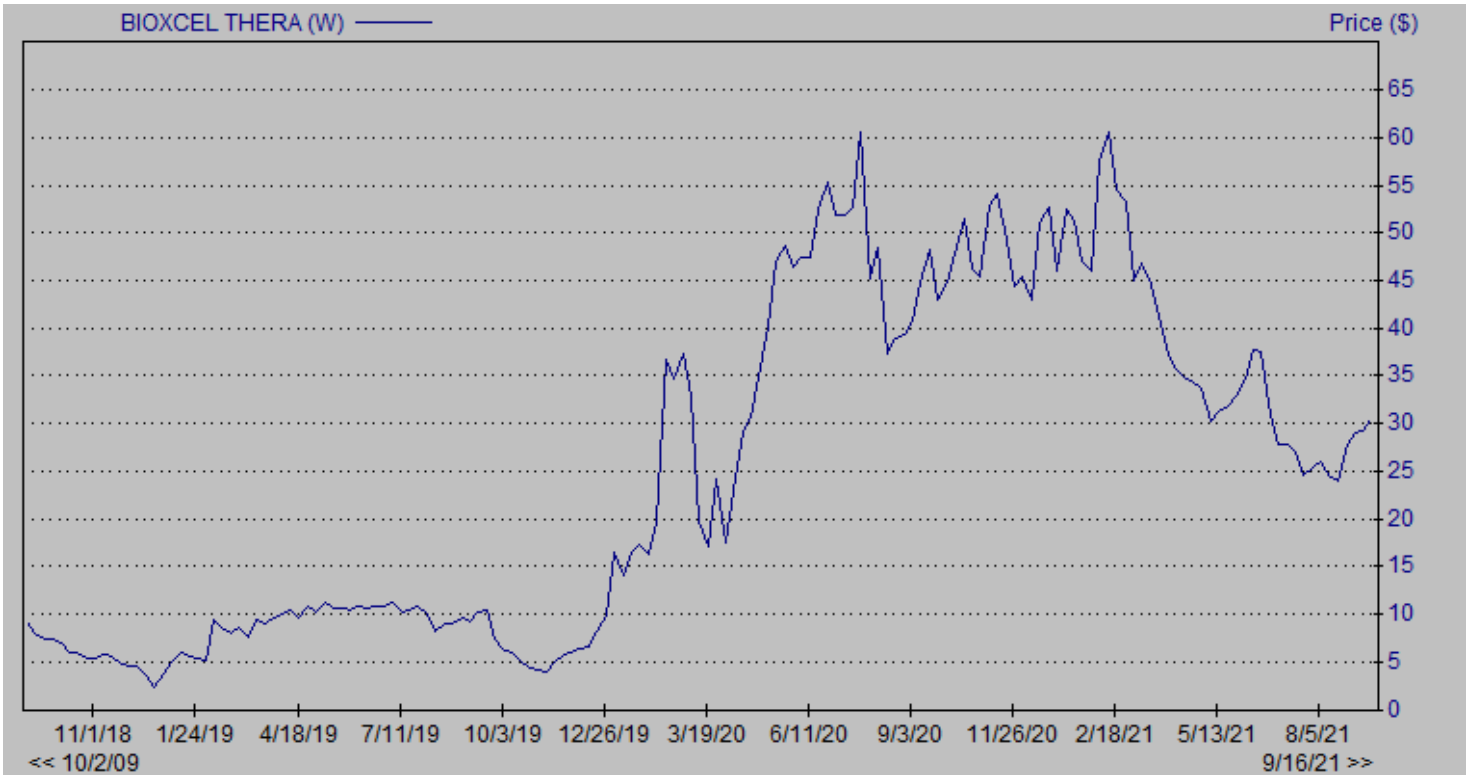
The data presented by BioXcel on BXCL701 in a very heavily pretreated mCRPC population are very encouraging, particularly when viewed in relation to monotherapy pembrolizumab. While difficult to compare data across different clinical trials, pembrolizumab did not show robust activity in a mCRPC population and it appears as though BXCL701 may be potentiating its activity. Since BXCL701 is predicted to turn “cold” tumors “hot”, with prostate cancer known to be immunologically “cold”, and the majority of the responders not having strong predictive markers of pembrolizumab response (e.g., PD-L1 low or MSI stable), these data are indicative of BXCL701 causing inflammation in the tumor microenvironment and increasing the susceptibility to immune checkpoint therapy. We look forward to additional updates from this study. With no changes to our model our valuation remains at $110.

PROJECTED FINANCIALS

BioXcel Therapeutics, Inc.	2020 A	Q1 A	Q2 A	Q3 E	Q4 E	2021 E	2022 E	2023 E
BXCL501	$0	$0	$0	$0	$0	$0	$126	$297
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**	**$126**	**$297**
Cost of Sales	$0	$0	$0	$0	$0	$0	$15	$33
Product Gross Margin	-	-	-	-	-	-	*88%*	*89%*
Research & Development	$58.0	$14.7	$13.5	$14.5	$15.0	$57.8	$65.0	$75.0
General & Administrative	$24.3	$11.6	$14.1	$11.5	$11.8	$49.0	$80.0	$100.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($82.3)	($26.3)	($27.6)	($26.0)	($26.8)	($106.8)	($34.0)	$89.0
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.1	$0.0	($0.0)	$0.0	$0.1	$0.1	$1.0	$1.0
Pre-Tax Income	($82.2)	($26.3)	($27.6)	($26.0)	($26.7)	($106.7)	($33.0)	$90.0
Income Taxes	$0	$0.0	$0.0	$0.0	$0.0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($82.2)**	**($26.3)**	**($27.6)**	**($26.0)**	**($26.7)**	**($106.7)**	**($33.0)**	**$90.0**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($3.79)**	**($1.07)**	**($1.11)**	**($0.93)**	**($0.95)**	**($4.05)**	**($1.10)**	**$2.81**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	21.7	24.5	25.0	28.0	28.0	26.4	30.0	32.0

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

HISTORICAL STOCK PRICE



Source: Zacks SCR

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