BriaCell Therapeutics Corp. (TSXV: BCT) – $0.12 / Share

Last week, BriaCell Therapeutics Corp. (TSVX: BCT) (BCTXF) announced a major expansion of the company's pipeline through the acquisition of privately-held Sapientia Pharmaceuticals, Inc. Through Sapientia, a biotechnology company based in Havertown, PA, BriaCell gains control of a pipeline of novel small molecules with solid intellectual property for the potential treatment of several cancers and fibrotic diseases. The acquisition expands the company's pipeline beyond BriaVax, a therapeutic cancer vaccine currently in a Phase 1/2 clinical trial for patients with advanced breast cancer.

Sapientia's Novel PKCδ Platform

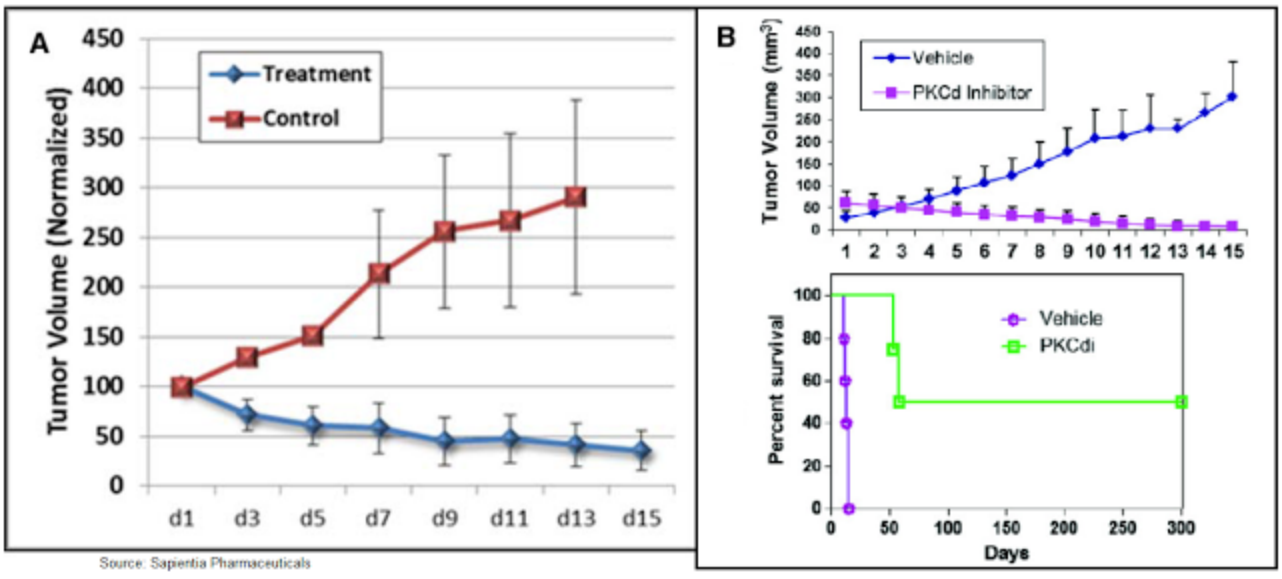
Sapientia Pharmaceuticals is currently developing a platform of novel PKCδ inhibitors for both oncology and fibrotic disease indications. These candidates are potentially first-in-class and offer an innovative approach to both targeted cancer therapies and immunotherapeutic drug candidates.

- Oncology Development Programs -

PKCδ is a serine/threonine kinase of the Protein Kinase C family that functions in proliferation, survival, and apoptosis of cells (1). Recent research shows that PKCδ may play an important role in KRAS-dependent tumors and that PKCδ inhibition may lead to an improvement in overall survival in model systems (2). Specifically, activated PKCδ inhibits RAS degradation, which in turn stimulates tumor growth. Therefore, inhibition of PKCδ and has potential therapeutic utility for cancers where RAS is activated (3). Unlike other members of the PKC family, which are essential for important biological processes, knockout mice have been developed that completely lack PKCδ expression. These mice are viable and able to procreate, indicating that inhibition of PKCδ should not have any serious side effects.

Sapientia is currently developing fourth generation PKCδ inhibitors that greatly improve the potency and selectivity of the molecules, while also optimizing the pharmacokinetic characteristics of the drug candidates versus older generation candidates. This is important because improved selectivity of PKCδ targeting, avoiding interaction with PKCα and PKCβ, should help to reduce or eliminate potential endothelial cell cytotoxicity or cardiotoxicity previously seen with less target-specific molecules (4).

The most logical development path for BriaCell is to focus on tumors with KRAS-transformed mutations. Previous clinical work with older generation PKCδ inhibitors such as Rottlerin, KAM1, and BJE6-106 suggest a potential anti-apoptotic and pro-survival effect of activated PKCδ in KRAS-transformed tumors, including some non-small cell lung, pancreatic, and colon cancers (5). Inhibition of PKCδ reduces tumor burden in a xenograft model of a human lung cancer with mutant-KRAS (A) and in xenograft models of human pancreatic cancer stem cells (B).



Source: Sapientia Pharmaceuticals

For its initial focus, BriaCell will focus on neuroendocrine tumors (NET), melanoma, and pancreatic cancer. Work by Chen *et al*, 2011 shows that blocking PKCδ inhibits cellular proliferation and survival of human neuroendocrine tumors (6). According to Sapientia market research, there are 65,000 individuals in the U.S. with RAS-transformed NET, approximately 20% (~13,000) with metastatic disease. Since there are currently no approved chemotherapy regimens for NETs, a novel PKCδ inhibitor is likely to have significant market interest. At competitive pricing of $12,000 per month, the market opportunity in NET is between $250 and $450 million.

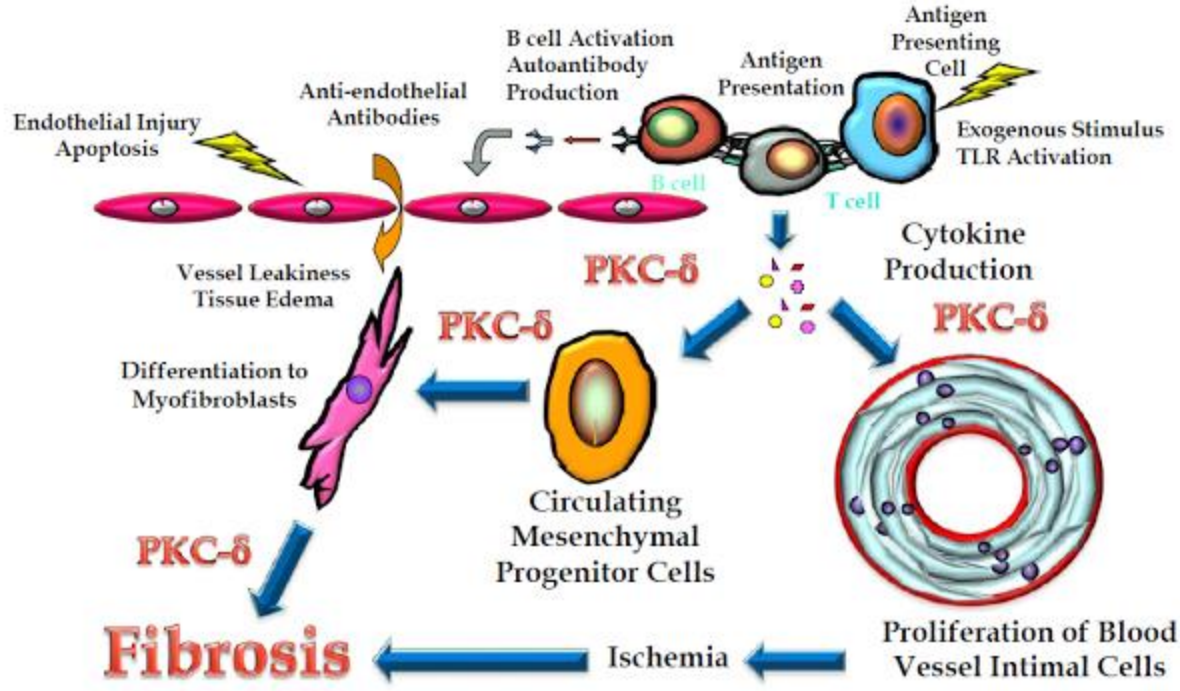
Metastatic melanoma is another significant market opportunity where preclinical work proves PKCδ inhibition suppresses the growth of RAS/RAF/MEK mutated cell lines (7). Targeted immunotherapy (anti PD-1) has become the new standard for first line treatment, but the best median overall survival is still well below five years. A clear opportunity exists to combine a novel PKCδ inhibitor with targeted anti-PD-1 or anti-CTLA4 antibodies. Even in a second-line indication, this is another $200 to $400 million peak opportunity.

One final solid tumor it makes sense for BriaCell to investigate the potential utility of any novel Sapientia candidate is in metastatic pancreatic cancer. This is for a number of reasons, but mainly due to high frequency (~63%) of RAS mutations in pancreatic tumors (8). There is also a lack of effective treatment options and PKCδ inhibition should synergize well with commonly used chemotherapic agents such as paclitaxel and capecitabine, while likely not adding any additional toxicities. Estimated peak sales are an additional $500 million to $1.0 billion depending on the level of response.

RAS mutation is also present in a number of other cancer types, including colon, non-small cell lung, prostate and breast cancer. In addition, the activity of PKCδ in potentiating Transcription Growth Factor beta (TGFβ) signaling leads to immunosuppression. This supports a role for PKCδ inhibitors in immunotherapy approaches. For this reason, PKCδ inhibitors should potentiate the activity of BriaVax™ as well as in combination with other immunotherapies.

- Potential In Fibrotic Disease -

Sapientia also believes that targeted PKCδ inhibition may have utility in the treatment of fibrotic diseases such as systemic sclerosis (SSc). This is because PKCδ potentiates TGFβ signaling, which has been proven to drive myofibroblast differentiation and fibrogenesis, and is implicated in SSc disease progression.



Preclinical work shows that PKCδ inactivation inhibits collagen deposition and myofibroblast differentiation in a mouse model of fibrotic disease, thereby blocking the fibrosis. Work shows that PKCδ inhibitors also block both TGFβ and CTGF activity in dermal fibroblasts, as well as block TGFβ-induced endothelial-mesenchymal cell transition. The hypothesis is that a potent and selective PKCδ inhibitor should act in several stages of SSc pathogenesis to inhibit fibrosis and vascular changes.

Next Steps

BriaCell is currently engaging in preclinical discovery with Sapientia. The company hopes to enter lead optimization and candidate selection during the second half of 2018. This should allow for preclinical toxicology and ADME work in 2019 and the first U.S. IND filing for cancer in 2020. Because the company is targeting specific indications with high unmet medical needs, management believes they can move expeditiously through Phase 1/2 and into registration studies by 2021, and be in the position to file the first U.S. NDA in 2023. In fibrotic diseases, the U.S. IND filing is expected in 2021 with a Phase 3 registration study planned for 2023. The estimated cost of the pre-IND work in both indications is small, likely less than $3.0 million.

CEO Investment Adds Credibility

BriaCell President and CEO, Dr. William Williams, has been investing his own money into the company. In late February 2017, Dr. Williams entered into a non-brokered private placement of approximately 5.42 million shares of BriaCell common stock at C24¢ per share. The company used those proceeds of approximately C$1.5 million to help fund the ongoing Phase 1/2a study with BriaVax as well as develop a companion diagnostic platform known as BriaDx. On August 2, 2017, Dr. Williams entered into a new private placement of 4.06 million shares at C16¢ per share to infuse gross proceeds of C$0.65 million. These funds will be used to continue the Phase 1/2 BriaVax program as well as advance initial work with Sapientia.

I'm a big fan of these transactions. The CEO is stepping up and funding work he believes will add tremendous value in the long-run. I believe this adds credibility and confidence to the story.

Valuation

Last month, I wrote an article for investors providing a brief update on the Phase 1/2 clinical trial with BriaVax for the treatment of advanced breast cancer. I think BriaVax is a very interesting and has the making of a potential ideal immunotherapy - powerful enough to induce both a broad-scale innate and adaptive immune reaction, targeted to reduce systemic side-effects, and personalize based on genetic biomarkers to improve the odds of success.

My work shows that BriaVax has - at a minimum - $300 million peak sales potential. The drug is currently in Phase 1/2 clinical trials, which based on a 15% probability of success, a 20% discount rate, and 5x multiple on peak sales puts the asset worth $44 million. Obviously, the success of the current Phase 1/2 trial will increase this valuation and I believe $300 million in peak sales is a very conservative estimate.

Peak sales from the Sapientia platform are likely $2 billion, which includes oncology indications of neuroendocrine tumors, melanoma, and pancreatic cancer, as well as fibrotic indications, including systemic sclerosis. Using similar metrics, only adjusting the probability of success down to 1% for pre-IND candidates, we still arrive at an NPV of $9 million.

BriaCell Valuation

BriaVax Peak Sales	$300 Million	*PKC-d Inhibitors*	$2000 million
Estimated Year of Peak	2026	*Estimated Year of Peak*	2030
Multiple on Sales	5X	*Multiple on Sales*	5X
Discount Rate	20%	*Discount Rate*	20%
Probability of Success	15%	*Probability of Success*	1%
BioNap, Inc. *Net Present Value*	$43.6 Million	*Net Present Value*	$9.3 Million

This puts the overall valuation of BriaCell at $53 million. BriaCell's current market value is only $17 million. Thus, the shares offer 200% upside from today with additional upside as BriaVax and novel PKCδ candidates advance through clinical and preclinical work.

Conclusion

The concept of targeting cancer therapeutics toward specific mutations or abnormalities in tumor cells, which are not found in normal tissues, has the potential advantages of high selectivity for the tumor and correspondingly low secondary toxicities. The literature suggests that PKCδ may play an important role in RAS-dependent tumors and that PKCδ inhibition may correlate to an improvement in overall survival in a number of solid tumors. In Sapientia, BriaCell was able to acquire a potentially first-in-class platform for developing novel PKCδ inhibitors. The acquisition price is a song compared to the potential upside here, so I'm happy to see management expanding its pipeline and positioning the company to create significant value for shareholders.

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BioNap owns stock options in shares of BCT.V