

## BriaCell Therapeutics Corp.

(BCTX - NASDAQ)

### Game, Set and Match: HLAs Score Success

Based on our DCF model and a 15% discount rate, BriaCell is valued at approximately \$15.00 per share. With regard to regulatory approval and commercialization, our model applies a success probability of 20% for BRIA-IMT and 8% for Bria-OTS in advanced breast cancer. The model includes contributions from the United States and rest of world.

Current Price (1/4/2022)

\$8.67

Valuation

\$15.00

### INITIATION

BriaCell Therapeutics is a clinical stage oncology-focused biotechnology company using cell-based immunotherapies to target breast and other cancers. The approach stimulates a cancer fighting immune response to destroy tumor cells. The company's lead candidate, Bria-IMT™, is being advanced in combination with other therapies including checkpoint inhibitors to combat breast cancer. Secondary candidate Bria-OTS™ addresses variation between patients with breast cancer and is based on a patient's human leukocyte antigen (HLA) type. If successful, this product could address almost all third-line patients.

In addition to Bria-IMT and Bria-OTS, the company offers a portfolio of other preclinical assets addressing prostate, non-small cell lung, melanoma and other cancers. In clinical work to date, BriaCell has shown a strong correlation between the efficacy of Bria-IMT and patients that have a close HLA match with the therapeutic cells.

BriaCell is conducting a Phase I/IIa combination study and has released interim data demonstrating effective immune response and disease control in heavily pre-treated patients. We anticipate start of a pivotal trial in 2023 and BLA submission to regulatory authorities in 2025.

### SUMMARY DATA

52-Week High	12.47
52-Week Low	2.81
One-Year Return (%)	108
Beta	1.45
Average Daily Volume (sh)	1,545,285

Shares Outstanding (mil)	15.9
Market Capitalization (\$mil)	138
Short Interest Ratio (days)	0.76
Institutional Ownership (%)	22.0
Insider Ownership (%)	22.8

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 2022 Estimate	N/A
P/E using 2023 Estimate	N/A

Zacks Rank	N/A
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Risk Level	Above Average
Type of Stock	Small-Growth
Industry	Med-Biomed/Gene

### ZACKS ESTIMATES

#### Revenue

(In millions of USD)

	Q1	Q2	Q3	Q4	Year
	(Oct)	(Jan)	(Apr)	(Jul)	(Jul)
2021	\$0.0 A	\$0.0 A	\$0.0 A	\$0.0 A	\$0.0 A
2022	\$0.0 A	\$0.0 E	\$0.0 E	\$0.0 E	\$0.0 E
2023					\$0.0 E
2024					\$0.0 E

#### Earnings per Share

	Q1	Q2	Q3	Q4	Year
2021	-\$0.54 A				-\$0.09 A
2022	-\$0.16 A	-\$0.18 E	-\$0.21 E	-\$0.25 E	-\$0.80 E
2023					-\$1.09 E
2024					-\$1.36 E

\*FY:21 EPS not included in totality due to change in reporting currency.

## INITIATION

We are initiating coverage of BriaCell Therapeutics Corp. (NASDAQ: BCTX) with a target price of \$15.00 per share. This value is based on our estimates for a successful development and commercialization of Bria-IMT for advanced breast cancer. The candidate is expected to be submitted to the FDA in 2024 and receive approval in 2025. We forecast pivotal studies and commercialization to be initiated with a partner in the United States and around the world. BriaCell has demonstrated efficacy in its Bria-IMT treatment for advanced breast cancer. The agent has shown a meaningful benefit especially in human leukocyte antigen (HLA)-matched patients with disease control in 75% of patients with two or greater HLA matches.

BriaCell has completed one Phase I/II study investigating Bria-IMT and has launched a second that is now underway. The active study is evaluating Bria-IMT in combination with a checkpoint inhibitor. So far 11 patients have been enrolled with an average of five prior lines of treatment. Trial data shows that there is a strong correlation between HLA type, lower grade cancer and response. Over the next months, additional subjects will be added in order to generate sufficient data to justify an End of Phase II (EOPh2) meeting with the FDA. The outcome of the meeting will guide the design of the pivotal trial. BriaCell expects either a smaller 100 patient single arm study with a synthetic control arm or a larger 300 patient randomized controlled trial that will use Bria-IMT in conjunction with checkpoint inhibitors.

Breast cancer is the most common type of cancer with an estimated 282,000 cases per year in the United States and 2.3 million annually around the globe. While survival rates for this type of cancer are around 90% and higher if caught early, with such a large population, there remain many patients that fail treatment and require second and later lines of therapy. Bria-IMT is now being considered for third line therapy as there is no approved treatment for this group. Bria-IMT has shown success in many patients that have specific HLA genotypes, and/or with Grade I/II disease, which may eventually justify moving up to earlier rounds of treatment.

BriaCell's immunotherapy has broader applications than the narrow HLA-matched subset of breast cancer. The company is now working on another product designated Bria-OTS (Off-the-Shelf). This approach will expand the number of HLA genotypes that are expected to respond to the immunotherapy to capture nearly 99% of all third line patients. Prostate, non-small cell lung and other cancers are also being considered for the cell-based targeted immunotherapy.

Based on the strong data generated to date and favorable capital markets, BriaCell was able to raise a net \$65 million in funding to support further advancement of its pipeline. As of October 31, 2021, the company held \$55.5 million in cash on its balance sheet and has indicated that another \$5 million in proceeds were added after the end of the quarter from warrant exercises. With multiple years of cash available, BriaCell is able to fund the continuation of its Phase I/IIa and launch a pivotal trial, which is expected in 2023. Depending on the outcome of the EOPh2 meeting with the FDA, we anticipate that either the smaller 100 patient or larger 300 patient study could cost anywhere from \$10 to \$50 million depending upon the trial design.

The EOPh2 meeting is targeted for 2H:22 and should lead into a 2023 pivotal study for Bria-IMT. Following the start of the pivotal trial, we estimate that it will take 30 months to enroll, complete treatment and generate the data package necessary for regulatory submission. These assumptions support a late 2025 approval and first sales in 2026. We anticipate BriaCell will start working with a partner on the pivotal trial that will assume global commercialization responsibilities. If successful, Bria-IMT will enter an addressable market of near 70,000 in the United States and almost 500,000 around the globe.

Key reasons to own BriaCell shares:

- **Phase II asset to treat third line metastatic breast cancer**
- **Pivotal trial to be conducted next year, possibly with a partner**
  - **Combination with a checkpoint inhibitor**
- **Bria-IMT offers favorable treatment effect in specific patient groups**
  - **HLA match between patient and Bria-IMT cell line**
  - **Grade I/II Breast cancer**
- **Bria-OTS may be able to HLA match >99% of the overall advanced breast cancer population**
  - **15 unique HLA types**
  - **Will express GM-CSF and other immune stimulators**
  - **Will provide a personalized match of off the shelf (OTS) alleles**
- **Similar safety profile to other approved cancer drugs in early clinical development**
- **Global rights to intellectual property**

In the following sections we describe immunotherapy and immuno-oncology (IO) and the many sub-therapies that it encompasses. We then take a look at breast cancer and discuss the prevalence and incidence of the disease and the many types of breast cancer that exist. We end this section with an assessment of the diversity of drugs and classes of drugs that are used for different types of breast cancer. After a discussion of BriaCell's lead candidates, our initiation explores relevant preclinical and clinical data, trial design and development history for Bria-IMT in breast cancer. An examination of peers and competitors in the oncology space ensues along with a listing of the most relevant companies and their stock market value. The next section reviews recent financial and operational history for the company followed by an introduction to the management team and a summary of risks. Our valuation discussion enumerates the assumptions used to determine our target price. We expect first sales in 2026 for Bria-IMT after a favorable trial outcome conducted with a partner and successful submission of a BLA. Bria-OTS is expected to follow three years later serving an expanded third line breast cancer market. Our work generates a target price of \$15.00 per share for BriaCell Therapeutics.

## Immunotherapy and Breast Cancer

### Immuno-oncology

Immuno-oncology (IO), or cancer immunotherapy, is an approach to fighting cancer that leverages the body's own immune system to attack the disease. Normally, the body's immune system can eliminate cancer cells, but in some cases, these cells can adapt to hide by expressing proteins on their surface among other mechanisms. When IO drugs or biologics are administered, they allow the immune system to recognize harmful cells and destroy them, in many cases with fewer and short-lived side effects compared to surgery, chemotherapy and radiotherapy. Immunotherapy is preferred because it is frequently associated with fewer adverse events, maintains its potency, works well in conjunction with other therapies and is also able to better target the disease. Several classes of immunotherapy exist including therapeutic vaccines, checkpoint inhibitors, immune modulators, adoptive cell therapy (CAR-T), oncolytic viruses and antibody drug conjugates to name the most prominent examples. IO can be either active or passive. Active approaches direct the immune system to kill cancer cells by targeting tumor antigens. Passive approaches augment existing tumor responses by the use of a variety of proteins, lymphocytes and cytokines to enhance their activity.

### Cell-Based Targeted Immunotherapies/Therapeutic Vaccines

Cell-based targeted immunotherapies, which may be classified as therapeutic vaccines, are biological agents that stimulate the body's adaptive immune system to identify a particular disease, destroy it and recognize and eliminate similar threats in the future. Vaccines can be prophylactic similar to the flu shot or they can be therapeutic and attempt to remediate an existing health problem. Cancer vaccines have a similar profile and are used to either prevent a cancer from developing, such as Gardasil for human papillomavirus, or to treat existing cancer, such as Sipuleucel-T for prostate cancer. Cancer vaccines can also be classified as cell-based targeted immunotherapies as the cells used present features specific to cancer that engage the body's immune system to eliminate it. Vaccines help boost and stimulate the immune system to protect the body against infectious agents and viruses. The body's adaptive immune system is able to recognize the antigens that are present in the infectious agent and remember them in case of future attacks on the body. This ability to recognize the signature of the threat on subsequent exposure is the durable benefit the vaccine provides as it contains the unique identifiers, or antigens, that are present in invading bacteria, viruses or abnormal cells.

### Breast Cancer

Cancer can occur as a result of genetic mutations. These mutations can occur spontaneously, through natural errors in cellular management of genetic material, be inherited, or be driven by exposure to carcinogens. When these mutations occur in key genes, such as those responsible for regulating cell growth or angiogenesis, tumors can form and grow in an uncontrolled manner. While these mutations sometimes occur, most often the body is effective in destroying them. Only those cells with a key combination of mutations that program for growth and evasion of immune response are able to develop in the body. Tumors may either be benign or malignant. As malignant tumors progress to late stage, they colonize surrounding tissues and can even metastasize if they invade lymph nodes or blood vessels.

Breast cancer is a malignant tumor specifically of cells and tissues of the breast. Breast cancer typically originates in the cells of the lobules (milk-producing glands) or in the ducts, the passages that allow milk to travel from the lobules to the nipple. Less commonly, breast cancer can develop from the fatty and fibrous connective tissues of the breast. Like other cancers, breast cancer cells can invade nearby breast tissue. They can also grow in adjacent lymph nodes, such as those near the underarm, through which the cancer cells can spread (metastasize) to other parts of the body. The most common breast cancer metastasis sites are the bones, lungs, brain and the liver.<sup>1</sup> The stages of cancer refer to the degree the tumor has invaded neighboring tissues and spread to remote sites.

### Epidemiology

According to the American Cancer Society, 284,200 cases of breast cancer were diagnosed in the United States in 2021 and there were 44,130 deaths. Almost all were diagnosed in women with just under 1% of cases occurring in men and just over 1% of deaths occurring in men.<sup>2</sup> The World Health Organization has estimated that 2.3 million women were diagnosed with breast cancer and 685,000 deaths occurred globally in 2020. At the end of 2020, 7.8 million women were alive who had been previously diagnosed.<sup>3</sup> The breast is the single largest site of cancers in

<sup>1</sup> [Metastatic Breast Cancer Symptoms and Diagnosis](#)

<sup>2</sup> American Cancer Society. Cancer Facts and Figures 2021.

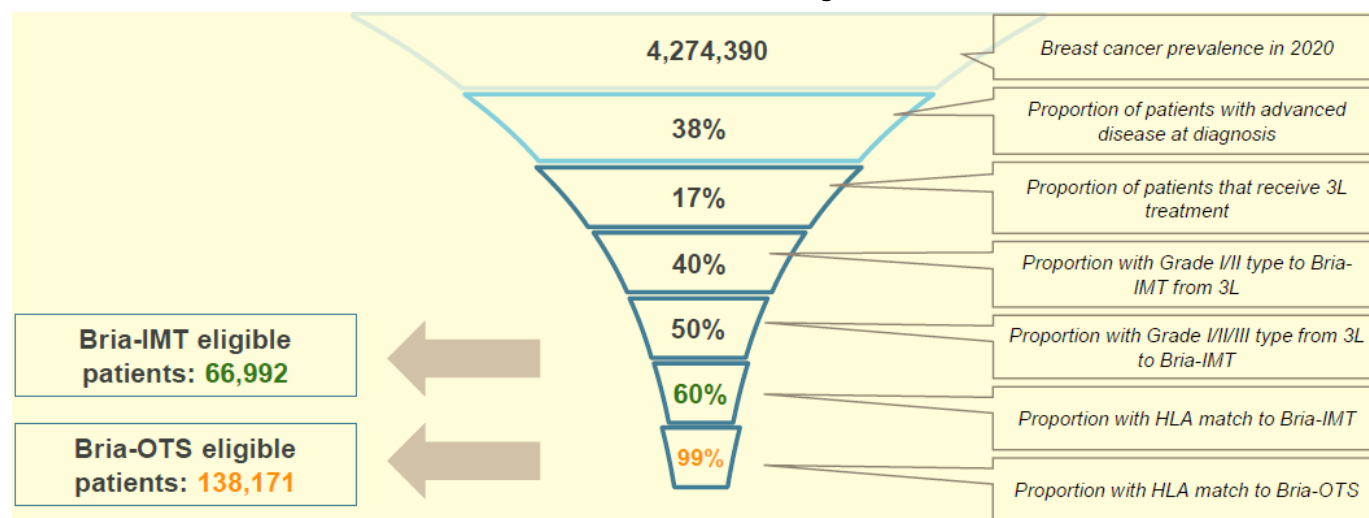
<sup>3</sup> World Health Organization. [Breast cancer](#). Accessed December 2021.

the US for women and overall. Breast cancer is most frequently diagnosed in women between the age of 55 and 64 with a median age of 62. Survival for breast cancer is relatively high with a 90.3% survival rate at 5 years.<sup>4</sup>

Breast cancer has many characteristics that vary based on the hormone receptors (HR) involved. Three receptors that appear are estrogen, progesterone and human epidermal growth factor receptor 2 (HER2). HR+/HER2- is the most common subtype, comprising 68% of the total. HR+/HER2+ make up just over 13% of the total. If the cancer lacks these three receptors, it is known as triple negative (NNN) breast cancer which makes up 13% of all invasive breast cancers.

Analysis performed by IQVIA identifies a prevalence of breast cancer of 4.3 million in the United States.<sup>5</sup> Of this group, about 280,000 advanced cases progress to third line treatment, where there is no standard therapy. Bria-Cell's technology has demonstrated success in high HLA-match grade 1 and 2 patients, which is approximately 205,000 eligible patients according to analysis conducted by IQVIA.

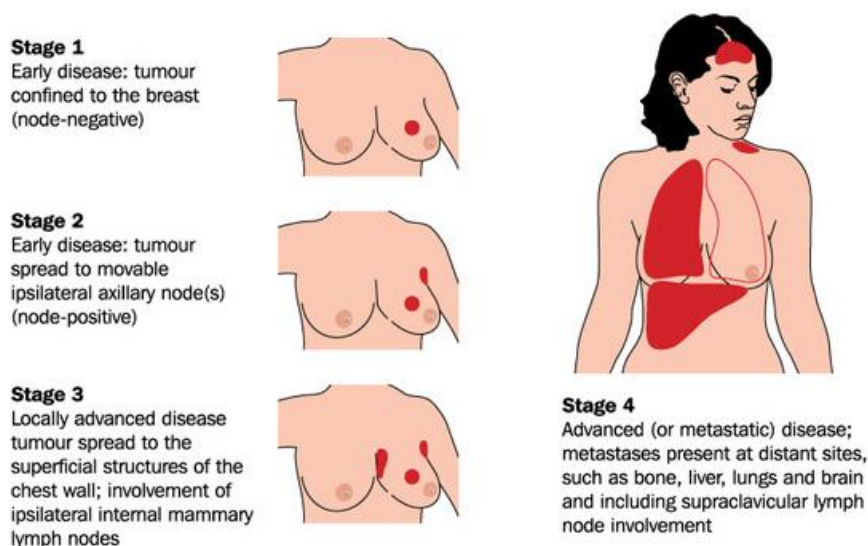
**Exhibit I – Bria-IMT and Bria-OTS Eligible Patients<sup>6</sup>**



### Stages

In general, cancer is defined by five stages: 0 through IV. Stage 0, not depicted in the image below, is non-invasive and can be termed *in situ*. Local therapies or limited surgery is sufficient to treat this stage of disease. Later stages, from Stage 1 to Stage 4 are increasingly advanced and indicate cancer that has spread from the original site.

**Exhibit II - Stages of Breast Cancer<sup>7</sup>**



<sup>4</sup> Cancer Stat Facts: [Female Breast Cancer](#). National Cancer Institute. Based on data from the 2011 to 2018 period.

<sup>5</sup> IQVIA Strategy Portfolio Analysis BriaCell Evaluation and Presentation

<sup>6</sup> IQVIA Strategy Portfolio Analysis BriaCell Evaluation and Presentation

<sup>7</sup> Shutterstock.com. [Image 105721043](#) Red areas denote breast cancer metastases.

### Grades

Breast cancers are graded 1, 2 or 3 corresponding to low, medium and fast growth rates, respectively. Grade also correlates with the structure of cell formation. Grade 1 cells resemble non-cancerous mother cells and are well differentiated. Pathological grade 3 cells look very different from normal cells and are classified as undifferentiated or poorly differentiated. They have the least resemblance to the progenitor cell of cancer and thus can act more aggressively and unpredictably. Images of stage 0 – IV and grade 1 – 3 cancers are found [here](#). Tumors that have invaded deeply into nearby tissues and spread to distant parts of the body are the most advanced.

### Types

Breast cancer is classified by the cell type from which it originates and is also stratified using other criteria such as sensitivity to estrogen and progesterone, expression of certain proteins, namely HER2, and the genetic profile of the tumor. These help to define the breast cancer type and guide treatment.

Common types of breast cancer:<sup>8</sup>

- Ductal carcinoma (DC)
- Invasive ductal carcinoma (IDC)
- Lobular carcinoma (LC)
- Invasive lobular carcinoma (ILC)

Approximately 80% of invasive breast cancers are IDC. Approximately 10% are ILC. There are several less common invasive breast carcinomas including adenoid cystic, low-grade adenosquamous, medullary, mucinous/colloid, papillary and tubular.<sup>9</sup>

### Symptoms

Breast cancer can produce a variety of symptoms, especially if metastasized to various parts of the body, affecting local function. In early stages of the cancer, the most common sign of breast cancer risk is a lump in the breast or underarm. Thickening of the skin overlying the cancer tissue, distortion in the breast shape or irritation in the breast may be other signs. Below we summarize several of the most common symptoms.

**Exhibit III – Breast Cancer Symptoms<sup>10</sup>**

constant nausea, vomiting or weight loss	shortness of breath	severe headaches	chest pain
abdominal bloating, pain or tenderness	difficulty breathing	vision problems	confusion
constant back, bone or joint pain	difficulty urinating	loss of appetite	jaundice
numbness or weakness	constant dry cough	loss of balance	seizures

### Diagnosis

Women over 40 are advised to begin breast cancer screening; women between 45 and 55 are advised to undergo a mammogram every year. If a lump or abnormal area in the breast is suspicious, physicians may also use a variety of imaging techniques to locate and size the tumor and its metastases. These can include ultrasound, MRI, X-ray, CT and PET scans. Other methods used to detect and characterize the cancer include blood tests, biopsy and sampling fluid from around the body to detect for presence of cancer cells.

<sup>8</sup> Common Breast Cancer Types: Ductal, Invasive & More | CTCA ([cancercenter.com](#))

<sup>9</sup> Invasive Breast Cancer (IDC/ILC) | Types of Invasive Breast Carcinoma

<sup>10</sup> Metastatic Breast Cancer Symptoms and Diagnosis compiled by Zacks' analysts

### *Treatment*

A wide variety of breast cancer treatments exist that depend on the stage, mutational profile and whether the cancer cells have hormone or other receptors. Recommended treatments based on tumor type and location are provided in the National Comprehensive Cancer Network ([NCCN](#)) [guidelines](#) and other sources. Surgery, radiation and chemotherapy are frequently applied. However, if the cancer is hormone receptor (HR) (either progesterone or estrogen) positive, hormone therapy may be the first line of therapy. Potential drugs for this subtype of the disease include tamoxifen and aromatase inhibitors.

If breast cancer is HER2 receptor positive, a subtype that comprises about 20% of cases, there are certain chemotherapy and other drugs that are appropriate. Some of the most common HER2-targeted therapies include trastuzumab, margetuximab and pertuzumab. Combinations of these drugs and chemotherapy are also used to treat HER2+ breast cancer.

Drugs centering on HER2+ belong to the targeted therapy category. Targeted therapy is also appropriate for cancers that present gene mutations such as BRCA1 or BRCA2. For HR+ and HER2- breast cancer, oral drugs such as palbociclib, ribociclib and abemaciclib are used as first line treatment in specific populations. Some of the most common targeted therapies include inhibitors of cyclin-dependent kinase (CDK) 4/6, mechanistic target of rapamycin (mTOR), poly ADP ribose polymerase (PARP) and phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha (PIK3CA). Other approaches are used such as targeted antibody-drug conjugates including sacituzumab govitecan (Trodelvy), ado-trastuzumab emtansine (Kadcyla) and (fam-trastuzumab deruxtecan-nxk (Enhertu).

Immunotherapy is used for breast cancer when common targets such as when HR or HER2 is absent. Checkpoint inhibitors such as pembrolizumab (Keytruda) or dostarlimab (Jemperli) may be used in triple negative, DNA mismatch repair deficiency and also in later stage, recurring and metastatic breast cancer. Compared with other cancer types, breast cancer has not responded as well to immunotherapies as there are fewer immune cells in the tissue that can be activated to eradicate the disease.

Combination therapy is another approach to breast cancer that may yield improved effects. There have been numerous studies that examine the safety and efficacy of combinations of the abovementioned drugs. Surgery is commonly combined with chemotherapy and radiotherapy. Different types of chemotherapy are also applied simultaneously or sequentially to enhance their effect. Checkpoint inhibitors may be particularly beneficial when combined with other agents that heat up the tumor and activate an immune response in metastatic breast cancer.



## Technology & Candidates

Immunotherapy has emerged from obscurity into the mainstream of cancer and other disease treatment in the last several decades. While early records of immunotherapy date back centuries, it has only been in the last 20 years or so when dramatic strides have been made in cancer using the approach. The approval of Sipuleucel-T in 2010 for prostate cancer, several checkpoint inhibitors a few years later and chimeric antigen receptor (CAR) T cell therapy in 2017 brought the class to the forefront in oncology.

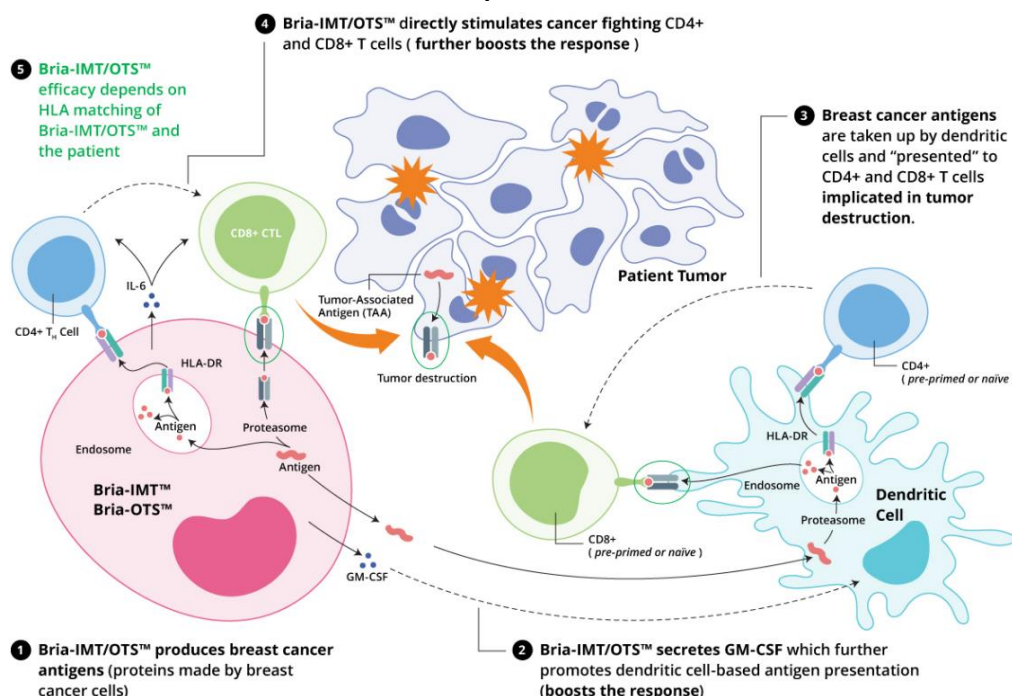
While checkpoint inhibitors and other immunotherapies have improved the survival and side effect profile of cancer treatment and provided a complement and even an alternative to surgery, radiation and chemotherapy, there is still a long way to go. This unmet need has encouraged new candidates to emerge that seek to more precisely stimulate the immune system and work in conjunction with other immunotherapies. One of the emerging areas for cancer treatment is therapeutic vaccines, a subclass of targeted immunotherapies which includes cell-based targeted immunotherapies. In contrast to a prophylactic vaccine which is administered before a disease is contracted, a therapeutic vaccine is given afterwards. While only a few therapeutic vaccines have been approved, there are several in development.<sup>11</sup>

### Bria-IMT™

In the early 2000s, BriaCell's founder, Dr. Charles Wiseman conducted two early stage trials, administering Bria-IMT and its precursor in a total of 18 patients. The studies produced successes in median survival, prompting further investigation and study. One of the patients that participated in this early work developed a complete remission of a lung lesion and near complete regression of multiple breast lesions. The patient had two HLA matches with Bria-IMT.

Bria-IMT is BriaCell's lead candidate, a targeted immunotherapy derived from a human breast cancer cell line. The source of the cell line was a grade II, estrogen receptor (ER) and progesterone receptor (PR) negative tumor over-expressing the HER2/neu protein. The product is genetically engineered to activate the immune system to destroy breast cancer tumors by producing cancer antigens and granulocyte macrophage-colony stimulating factor (GM-CSF), which acts as a cytokine and boosts the presentation of antigens to T cells. While the mechanism of action has not yet been fully characterized, Bria-IMT is thought to leverage the patient's antigen presentation system via the stimulation of dendritic cells which in turn stimulate T cells to attack the cancer.

#### Exhibit IV – Bria-IMT Proposed Mechanism of Action<sup>12</sup>



<sup>11</sup> Source: Evaluate Pharma, Ltd. Accessed October 2021.

<sup>12</sup> MOA - BriaCell



GM-CSF is a hematopoietic growth factor and immune modulator, produced by a variety of cell types. It stimulates stem cells to produce granulocytes and activates dendritic cells, all activities of the innate immune system. Activated dendritic cells trigger CD4+ and CD8+ T cells to recognize tumor cells and eliminate them. Cancer-specific antigens are presented to T cells, which are then activated to seek out and destroy the cancer via direct or indirect means. The indirect approach functions by inducing a humoral immune response while the direct mechanism involves the T cells directly attacking the malignancy. Bria-IMT has also been shown to directly stimulate the cancer-fighting T cells. This direct stimulation depends on HLA matching between the patient and the Bria-IMT cells and is thought to markedly boost the immune response. Bria-IMT's efficacy is enhanced by combining it with other immune system activators, low doses of cyclophosphamide, and interferon- $\alpha$  which are expected to improve the success of the therapy.

Bria-IMT has proven particularly effective in patients whose human leukocyte antigens (HLA) match closely to that of the therapy. HLA markers are proteins and are used by the immune system to determine whether a cell is self or non-self. They also are the molecules in the immune system that initiate immune responses. Antigens, which are proteins recognized by the immune system, bind to HLA molecules and this complex of antigen-HLA is recognized by T cells and activates them. Individuals have many HLA markers which are inherited from our parents. Brothers and sisters are frequently a close match for one of their siblings. Some HLA types are more common than others supporting an allogeneic approach that could address a high proportion of the breast cancer population. BriaCell is developing an off-the-shelf candidate, designated Bria-OTS, which is based on multiple cell lines that can be configured to HLA-match over 99% of all third-line breast cancer patients.

Encouraging results from BriaCell's 23-patient monotherapy study showed improved progression free survival (PFS) in the group matching two or more HLA molecules. The superior performance in this group is attributed to improved communication between the patient's immune system and the HLA-matching cell line where the antigen-HLA complex presented by Bria-IMT can directly stimulate the cancer-fighting T cells. In patients whose HLA profile does not match that of Bria-IMT, the immune system may not recognize it as a legitimate source of disease-associated antigens. Disease control was also more evident in those with a greater number of HLA matches, especially those with Grade I/II disease. Patients with Delayed Type Hypersensitivity (DTH) also produced a high proportion of responders in lower grade cancers.

**Exhibit V – Disease Control by HLA Matching and DTH Responders (Monotherapy)<sup>13</sup>**

	Grade I/II (n=9)	Grade III (n=20)	All (n=31)
Monotherapy (n=23)	6	17	23
Disease Control (SD, PR or CR)	6/9 (67%)	2/20 (10%)	8/31 (26%)
Disease Control in DTH Responders	6/8 (75%)	2/14 (14%)	8/22 (36%)
Disease Control: No HLA Matches	2/2 (100%)	0/6 (0%)	2/8 (25%)
Disease Control: 1+ HLA Match	4/6 (67%)	2/13 (15%)	8/26 (31%)
Disease Control: 2+ HLA Matches	4/5 (80%)	1/6 (17%)	5/11 (45%)

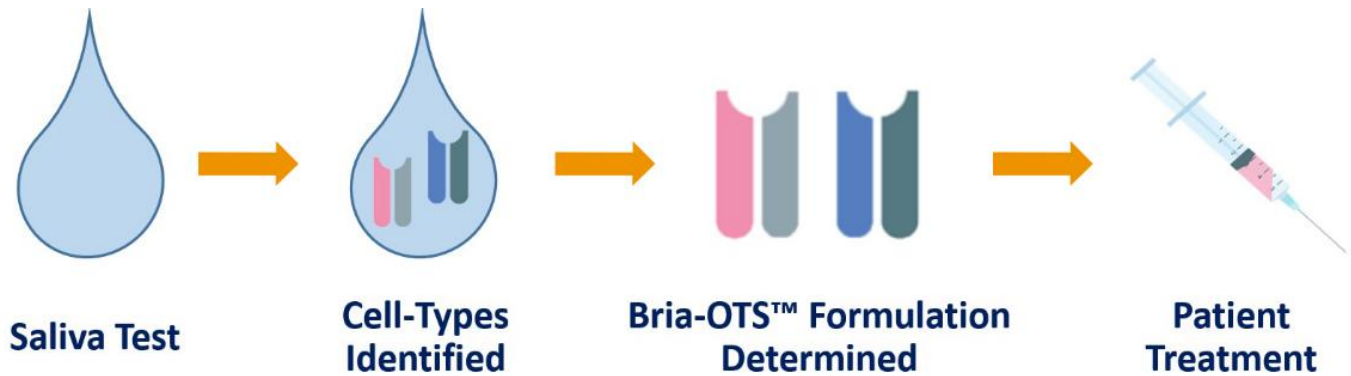
Bria-IMT is administered intradermally in multiple sites on the thighs and upper back every 21 days in combination with other agents. The treatment regimen includes cyclophosphamide to reduce immunosuppression and interferon- $\alpha$  to direct the immune response towards a Th1 response. The candidate is also being investigated in combination with the IDO inhibitor epacadostat and PD-1 inhibitor retifanlimab.

### **Bria-OTS™**

Bria-OTS, or Bria-Off-the-Shelf, is a cellular immunotherapy that builds off of Bria-IMT's successes. It is an off-the-shelf, personalizable immunotherapy that is able to match almost any patient's HLA type. 15 different HLA combinations will be engineered into Bria-IMT, which is expected to provide a match with over 99% of all patients with advanced breast cancer. Bria-OTS is in preclinical development and we expect that it will enter the clinic in the first half of 2022. Bria-OTS will be a stepping off point for further extensions of the "Bria" product line and several other immunotherapy cell lines for prostate cancer, lung cancer and melanoma are being developed. The candidate will allow for personalized treatment without relying on more expensive and time-consuming autologous approaches. Work in conjunction with the National Cancer Institute is also being conducted to investigate the relative importance of HLA matching and what type of match is optimal in a preclinical model. The work will also research Bria-OTS' mechanism of action. Patient HLA type can be determined with a simple saliva test.

<sup>13</sup> BriaCell AACR 2021 Poster Presentation. [Predictors of response to a modified whole tumor cell immunotherapy in patients with advanced breast cancer from two phase I/IIa trials](#). Data compiled by Zacks' analysts.

Exhibit VI – Bria-OTS™<sup>14</sup>



### Full Pipeline

In addition to Bria-IMT, BriaCell is developing other oncology programs using variations of the lead candidate. Bria-OTS, an off the shelf approach, is the subject of an upcoming investigational new drug (IND) application which, if cleared, will allow for the start of studies to support a second breast cancer indication. The pipeline offers other programs harnessing the same technology targeting prostate, non-small cell lung (NSCLC), melanoma and other cancers which are expected to be the subject of INDs submitted over the next two years.

Exhibit VII - BriaCell Pipeline<sup>15</sup>

Therapeutic	Indication	Preclinical	Phase I	Phase II	Phase III	Anticipated Milestones
Bria-IMT™ combined with Incyte Compounds	Advanced Breast Cancer (3rd+ line)	Phase I/II				Further safety and efficacy data through 2022
Bria-OTS™	Breast Cancer					IND Filing 1H2022
Bria-Pros™	Prostate Cancer					IND Filing 2H2022
Bria-Lung™	Non-Small Cell Lung Cancer					IND Filing 2H2022
Bria-Mel™	Melanoma					IND Filing 2H2022
Bria-TILsRx™	Prostate Cancer					IND Filing 2023
Bria-TILsRx™	Epithelial and Glandular					IND Filing 2023
PKCδi*	RAS Transformed Cancers					Candidate Selection 2022

### Bria-IMT™ Clinical Trials

#### Phase I Study

BriaCell has initiated several early-stage studies to investigate Bria-IMT. A small 4-patient [Phase I study](#) was conducted at St. Vincent Medical center in Los Angeles from 2004 to 2006. It showed efficacy in advanced disease with one patient experiencing widespread regression at multiple sites of metastatic breast cancer.

<sup>14</sup> Source: BriaCell [Website](#) accessed December 2021

<sup>15</sup> Source: BriaCell [Website](#) accessed December 2021.

# Exhibit VIII – Patient A002 (Double HLA Match) Response to Bria-IMT<sup>16</sup>



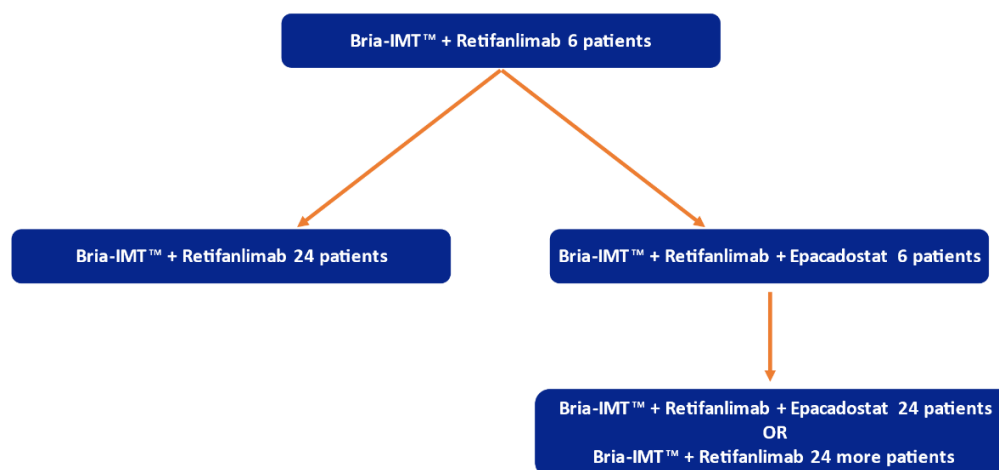
## Phase I/IIa (Completed)

The Phase I success prompted further work in a [Phase I/II study](#) of Bria-IMT for breast cancer patients who were refractory to standard therapies. In this trial, 23 individuals with advanced metastatic breast cancer were dosed over the 2017 – 2018 period. It was designed to administer a pre-treatment of a low dose of the chemotherapeutic agent cyclophosphamide (to reduce immune suppression) then Bria-IMT followed by interferon-α at the inoculation sites to boost the response. Treatment was given every two weeks for the first month, then monthly afterward. Tumor regression was noted in three patients and a clinical benefit of 63% (5/8) was achieved for patients with grade I and II disease. 71% (5/7) of those were able to develop an immune response.

## Phase I/IIa Combination (Ongoing)

A separate and ongoing [Phase I/IIa study](#) is investigating Bria-IMT along with an anti-PD-1 antibody<sup>17</sup> and IDO1<sup>18</sup> inhibitor epacadostat<sup>19</sup> in a combination approach in breast cancer patients that have failed two or more prior lines of therapy. The regimen includes a pre-dose of the chemotherapy cyclophosphamide and post-dose antiviral interferon-α2b. 12 patients have been evaluated so far and three of four patients with grade I/II tumors attained disease control. As [highlighted](#) in the recent poster presentation, disease control was 33% in the combination study. Complete tumor reduction of selected tumors was observed in several patients, including those with two or more HLA matches with Bria-IMT and Grade I/II tumors. For the evaluable Grade I/II patients, disease control was seen in three of four patients in the combination study.

## Exhibit IX - Bria-IMT™ Phase I/IIa Ongoing Combination Therapy Trial Design<sup>20</sup>



<sup>16</sup> Source: BriaCell Scientific Presentation, Fall 2021

<sup>17</sup> The trial has used Incyte/Macrogenics' retifanlimab and Merck's Keytruda in the role of PD-1 inhibitor.

<sup>18</sup> IDO: indoleamine 2,3-dioxygenase

<sup>19</sup> Epacadostat targets and binds to IDO1, an enzyme responsible for the oxidation of tryptophan into kynurenine. By inhibiting IDO1 and decreasing kynurenine in tumor cells, epacadostat increases and restores the proliferation and activation of various immune cells, including dendritic cells (DCs), NK cells, and T-lymphocytes, as well as interferon (IFN) production, and a reduction in tumor-associated regulatory T cells (Tregs). (Source: NIH Drug Dictionary)

<sup>20</sup> BriaCell Investor Presentation Fall 2021

Briacell provided an update of the trial progress in spring 2021 at the American Association for Cancer Research (AACR) Annual Meeting. A [poster](#) was presented with several important highlights related to consolidated performance of Bria-IMT in the multiple Phase I and II trials that have been completed or remain active.

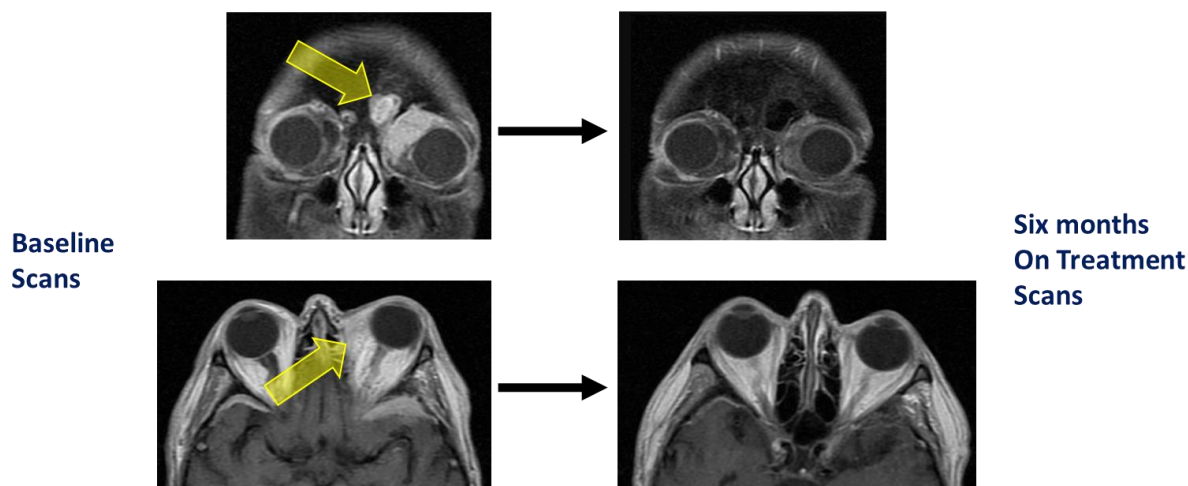
#### *Extraordinary Patients*

A Bria-IMT patient (A002) with recurrent metastases exhibited a remarkable response following treatment with Bria-IMT in the Phase I study (see Exhibit VIII). The patient had stage IV breast cancer and had failed other available therapies. Lesions in the lungs regressed completely and there was a strong response in other lesions. After the treatment regimen was complete, injections were stopped. Three months after the end of treatment, the cancer relapsed into local and distant areas including the brain. Treatment with Bria-IMT resumed after relapse was diagnosed and within two months after the follow-on treatment, there was significant regression in all observed tumor areas. During analysis, the patient was found to allele-match with Bria-IMT in two HLA genes.<sup>21</sup> Further observation has found that more effective immune responses appear to be associated with patients who matched Bria-IMT at certain HLA alleles.

A Bria-IMT patient (06-005) with recurrent metastases exhibited a remarkable response following treatment with Bria-IMT in the Phase I/II combination therapy study with PD-1 inhibitors (See Exhibit X). The patient had stage IV breast cancer and had failed other available therapies. Lesions included a large tumor behind the left eye, causing proptosis (bulging eye), tumors on the outside lining of the brain (the dura mater) and in the adrenal gland. After six months treatment, the tumor behind the left eye completely resolved and there were improvements elsewhere. Further observation has found that better immune responses are associated with patients who matched Bria-IMT at certain HLA alleles.<sup>22</sup>

#### **Exhibit X – Patient A002 (Double HLA Match) Response to Bria-IMT<sup>23</sup>**

##### **Tumor behind the left eye causing proptosis completely resolves**



#### *Consolidated Trial Findings:*

- Bria-IMT induced an effective immune response and disease control in heavily pre-treated patients;
- Patients with grade I and II tumors were more likely to respond to therapy;
- A stronger immune response evidenced by delayed type hypersensitivity (DTH) correlated with disease control and longer progression free survival;
- In the Bria-IMT monotherapy group, there was a correlation between HLA matching and disease control;
- No patients with elevated circulating tumor cells achieved disease control.

While trial enrollment has slowed due to the pandemic, additional patient enrollment and updated analyses are expected to be provided at [AACR](#) and [American Society of Clinical Oncology \(ASCO\)](#) in the spring of 2022.

<sup>21</sup> The two matching genes are [HLA-DRB1](#) and [HLA-DRB3](#)

<sup>22</sup> The two matching genes are HLA-C and HLA-DRB3

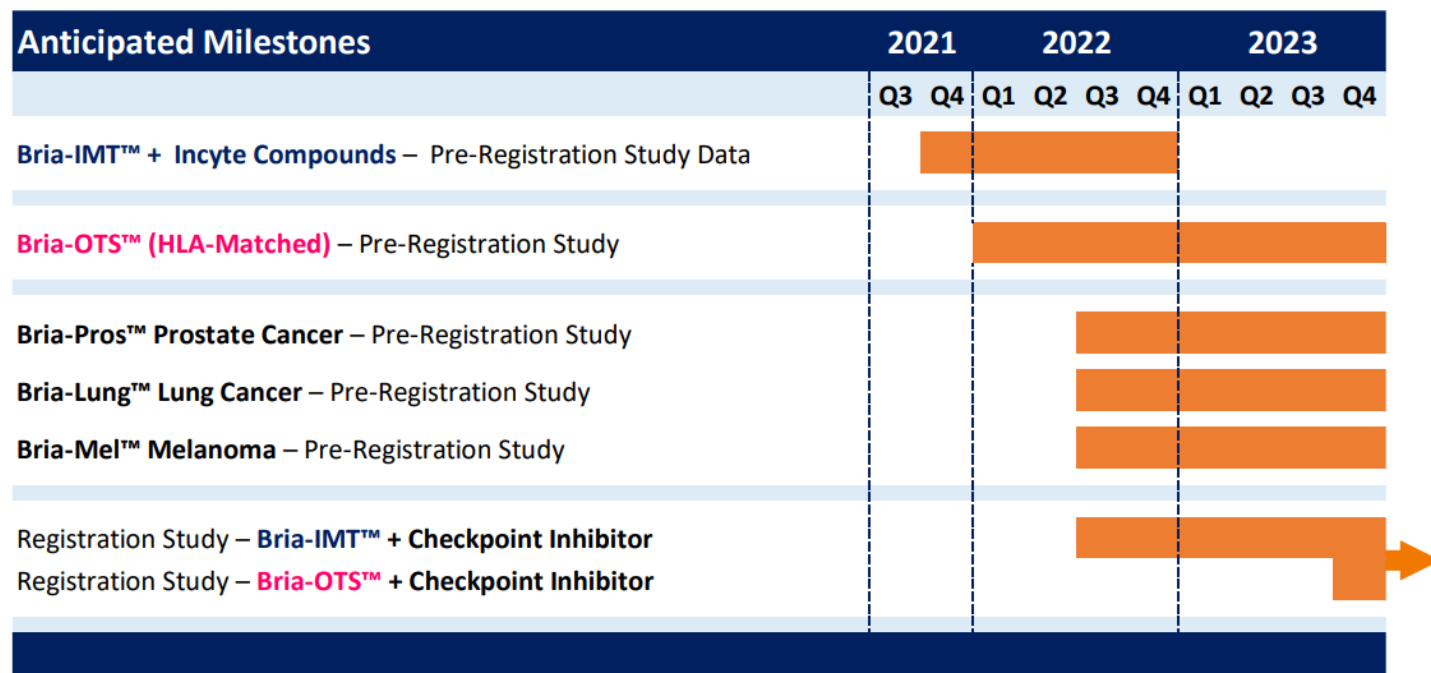
<sup>23</sup> Source: Briacell Scientific Presentation, Fall 2021

### Planned Pivotal Trial

BriaCell expects to meet with the FDA after generating sufficient data with the ongoing Phase I/IIa combination trial. Assuming favorable data, BriaCell will propose a multi-center, open-label study that will either be single-arm with an anticipated 100 enrollees or randomized vs. best alternative treatment with an anticipated 300 patients. The trial will target advanced breast cancer patients that have undergone and failed at least two prior treatments.

As BriaCell is already using Incyte's retifanlimab as the PD-1 inhibitor in the ongoing trial, we see Incyte as a prime candidate for collaborating in the pivotal trial. Estimated cost of the trial is from \$10 to \$15 million for the 100 patient study and from \$30 to \$50 million for the 300 patient study.

Exhibit XI – Development Timeline and Catalysts<sup>24</sup>



<sup>24</sup> Source: BriaCell Winter 2021 Investor Presentation



## Peers and Competitors

There are a number of classes of breast cancer drugs dominating the market including chemotherapy, hormone therapy, aromatase inhibitors and targeted therapy. Leading breast cancer products on the market include Ibrance, Perjeta, Herceptin and Kadcyla, which together generated about \$15 billion in 2020 revenues. Immunotherapy has emerged as an area of significant interest in recent years. Monoclonal antibodies are another subgroup that feature combination approaches and antibody drug conjugates. Large and small companies alike have initiated IO programs in various stages of development. Based on data provided by Evaluate Pharma there are 19 Phase II and 10 Phase III programs in development. One additional product is awaiting FDA approval for breast cancer.

Behemoths such as Roche and AbbVie offer a broad portfolio of oncology drugs including IO, targeted therapies, hormone therapies and others along with an abundant development pipeline. There are many other large players in oncology as well that are targeting a broad array of receptors in cancers. Some names that have breast cancer specific programs include Atossa Therapeutics with a protein kinase C inhibitor, AstraZeneca with the recently approved Enhertu, Oncolytics Biotech with Pelareorep and MacroGenics' Margenza which recently failed to produce a statistically significant advantage.

**Exhibit XII – Peers and Competitors<sup>25</sup>**

Ticker	Company	Price	MktCap (MM)	EV (MM)	Therapeutic Area
ABBV	AbbVie	\$135.16	\$238,851	\$300,651	PARPi for Breast Cancer + broad portfolio of oncology drugs
AGEN	Agenus	\$3.20	\$822	\$573	Cancer vaccines & oncology portfolio
ALLO	Allogene Tx	\$14.49	\$2,065	\$1,582	Broad oncology portfolio for liquid & solid tumors
ALXO	ALX Oncology	\$20.82	\$843	\$458	Block CF47 pathway for SCCHN & breast+hematological cancer
AMGN	Amgen	\$227.84	\$128,335	\$148,705	Wide range of modalities, cancers & molecules in oncology
ATOS	Atossa Tx	\$1.72	\$218	\$78	Breast cancer protein kinase C inhibitor endoxifen
AZN	AstraZeneca	\$57.27	\$177,436	\$198,433	Broad portfolio of products including Enhertu
BCAB	BioAtla	\$18.23	\$672	\$402	Broad portfolio of targets & indications from discovery to Ph2
BCYC	Bicycle Tx	\$55.00	\$1,617	\$1,387	Bicyclic peptide tech/Lead BT1718 in Ph1/2
BEAM	Beam Tx	\$78.31	\$5,336	\$4,402	Gene editing & precision medicines, cancer, rare disease
BMJ	Bristol-Myers Squibb	\$62.13	\$137,907	\$161,921	IO-CAR T, checkpoint inhibit, kinase inhibit + others
CGEM	Cullinan Oncology	\$16.75	\$732	\$411	Targeted IO therapies in NSCLC w/ EGFR exon 20 mutations
CLLS	Collectis	\$8.28	\$377	\$188	Allogeneic CAR T cells for blood cancers
FATE	Fate Therapeutics	\$55.94	\$5,342	\$4,663	Off-the-shelf cellular immunotherapies: cancer, immune disorders
GILD	Gilead Sciences	\$72.21	\$90,579	\$110,978	Trodelvy for BC, CAR T, kinase inhibit + dev portfolio
GRCL	Gracell Biotech	\$5.20	\$351	\$56	Allogeneic CAR T cell for blood cancers
GRTS	Gritstone Oncology	\$7.02	\$477	\$267	IO using neoantigen prediction via AI
GSK	GlaxoSmithKline	\$43.54	\$117,236	\$140,715	IO, cell therapy, epigenetics, synthetic lethality; large dev portfolio
IGMS	IGM Biosciences	\$27.21	\$883	\$624	IgM antibodies for cancer & COVID
INCY	Incyte Corp	\$71.81	\$15,862	\$13,609	clusig for leukemia, retifanlimab & many others in dev for cancer
IPHA	Innate Pharma	\$4.67	\$370	\$265	Antibodies for IO, NK: lacutamab, monalizumab, avdoralimab etc.
KRON	Kronos Bio	\$13.69	\$771	\$373	Targeting oncogenic TRNs, TKI for leukemia
LLY	Eli Lilly	\$266.81	\$255,228	\$266,926	Verzenio for BC + portfolio of other oncology medicines
MGNX	MacroGenics	\$16.16	\$990	\$691	Margenza for BC, + other IO candidates
MRK	Merck & Co.	\$77.01	\$194,523	\$207,414	Keytruda + broad portfolio of other oncology
MRKR	Marker Tx	\$0.98	\$81	\$33	IO for liquid & solid tumors, Ph2 TPIV100/110/200 for BC & ovarian
NVS	Novartis	\$87.47	\$195,648	\$210,587	Oncology assets + Kisqali, Piqray for BC
ONCY	Oncolytics Biotech	\$1.39	\$77	\$38	Oncolytic virus for BC in combo with IO & targeted therapies
PDSB	PDS Biotech	\$7.71	\$219	\$149	Versamune platform for HPV cancers, PDS0102 in dev for BC
PFE	Pfizer	\$54.53	\$306,070	\$312,624	Ibrance + others in development for BC & oncology portfolio
PSTX	Poseida Tx	\$6.86	\$429	\$260	CAR T cell & gene therapies
REPL	Replimune Group	\$29.75	\$1,395	\$984	Oncolytic immunotherapies; lead: RP1 in Ph2 for CSCC
RGBPP	Regen BioPharma	\$0.05	\$2	\$2	NR2F6 inhibition leading to immune cell activation for oncology
RHHBY	Roche	\$50.72	\$346,418	\$362,080	Broad oncology portfolio for liquid & solid tumors
RUBY	Rubius Tx	\$10.17	\$914	\$726	Red blood cell tx for cancer & other disease treatment
SANA	Sana Biotechnology	\$15.40	\$2,908	\$2,304	Cell engineering for cancer & other diseases
ZIOP	Ziopharm Oncology	\$1.09	\$236	\$156	IO based on non-viral genetic engineering of immune cells
BCTX	BriaCell Tx	\$8.67	\$138.26	\$82.77	Breast cancer IO: Bria-IMT & Bria-OTS

<sup>25</sup> Compiled by Zacks' analysts as of January 4, 2022



## Financial & Operational Results

### Year-to-date 2021 Events

- Clinical data [presented](#) at 2021 Keystone Symposium - January 2021
- NASDAQ [listing](#) (BCTX, BCTXW) - February 2021
- [Pricing](#) and [closing](#) of US\$25 million public offer - February 2021
- [Presentation](#) at AACR<sup>26</sup> Annual Meeting 2021 - April 2021
- [Closing](#) of over-allotment option for gross proceeds \$28.7 million - April 2021
- [Enlisting](#) IR and PR groups - April 2021
- CEO [interview](#) with SmallCapVoice.com - April 2021
- Miguel A. Lopez-Lago, PhD [appointed](#) Senior Director, R&D - May 2021
- [Update](#) on Overall Survival, top responder - June 2021
- [Announcement](#) and [closing](#) of \$27.2 million private placement - June 2021
- Clinical update conference [call](#) - June 2021
- \$12.9 million [proceeds](#) from warrant exercise - June 2021
- [Expansion](#) of Bria-OTS in additional indications - June 2021
- Bria-IMT Phase I/IIa [open](#) for enrollment - July 2021
- [Collaboration](#) with ImaginAb - August 2021
- Marc Lustig [appointed](#) to Board - September 2021
- Share and warrant buyback [announced](#) - September 2021
- TSXV [accepts](#) normal course issuer bid - September 2021
- [Interview](#) with SmallCapVoice.com - September 2021
- Jane Gross, PhD [appointed](#) to Board - November 2021
- Suzanne Ostrand-Rosenberg, PhD [appointed](#) to Scientific Advisory Board - November 2021
- Poster [presentation](#) at San Antonio Breast Cancer Symposium - December 2021
- Shares [uplist and trade](#) on the TSE from TSX Venture Exchange under BCT - December 2021

### Fiscal Year 2021 and 1Q:22 Financial Results

BriaCell reported FY21 results filing with [SEDAR](#). Loss for the fiscal year totaled (US\$428,000)<sup>27</sup> or (\$0.09) per share.

For the fiscal year ending July 31, 2021 and versus the prior fiscal year operational expenses rose as Nasdaq listing expenses, personnel expenses and share based compensation rose substantially more than the decline in research in development stemming from slower trial enrollment due to SARS-CoV-2 and lack of funds:

- Research and development expenses totaled \$1.3 million, down 46% from \$2.4 million;
- General & Administrative expenses were \$3.7 million, up 144% from \$1.5 million;
- Share based compensation was \$2.0 million, up materially from \$1,686;
- Change in fair value of warrant liability was \$9.0 million versus nil;
- Net loss was (\$428,000) vs. (\$4.1) million or (\$0.09) and (\$5.64) per share, respectively.

As of July 31, 2021, cash totaled \$57.3 million. This amount compares to the \$21,000 balance in cash held at the end of FY20. Long-term liabilities for BriaCell include warrant liability of \$199,458 and government loans of \$25,986. Cash used in operations was (\$7.7) million versus (\$1.3) million for FY21 and FY20, respectively. BriaCell generated cashflow from financing of \$65.0 million versus \$1.2 million.

<sup>26</sup> American Association for Cancer Research

<sup>27</sup> All dollar amounts are in US Dollars

First quarter fiscal year 2022 generated an operating loss of (\$2.3) million and a net loss of (\$2.4) million or (\$0.16) per share. For 1Q:22 ending October 31, 2021 and compared with the prior year 1Q:21 ending October 31, 2020 operational expenses were up across the board with increases in trial and drug costs, wages and salaries on the addition of new personnel, and greater professional, consulting and insurance costs all contributing to the sixfold increase:

- Research and development expenses totaled \$876,000, up almost 500% from \$149,000;
- General & administrative expenses were \$891,000 up 285% from \$231,000;
- Share based compensation was \$518,000, up from \$0;
- Other items were (\$101,000) vs. (\$41,000);
- Net loss was (\$2.4) million vs. (\$421,000) or (\$0.16) and (\$0.54) per share, respectively.

Operating burn was (\$1.8) million over the three month period producing a cash balance of \$55.5 million as of October 31, 2021. Following the end of the quarter management indicated that there had been warrant exercises that generated near \$5 million in proceeds.

## **Financial & Operational Highlights**

### *Fundraising & Capital*

On February 23, 2021, BriaCell [announced](#) pricing for 5.9 million units with each unit consisting of one share of common stock and one warrant at a price of \$4.25 per unit. The warrants have an exercise price of \$5.3125 with expiry five years from date of issuance and are exercisable immediately. The underwriter was also granted a 45-day option to purchase up to 882,000 additional units. The offer closed on February 26, 2021. ThinkEquity acted as sole book-running manager for the offer. Gross proceeds, including over-allotment option totaled \$28.7 million as [announced](#) on April 12. Concurrent with the February release was the announcement that BriaCell's common shares and warrants were approved to list on the Nasdaq Capital Market under the symbols BCTX and BCTXW.

On June 3, 2021, BriaCell [announced](#) a \$27.2 million private placement. BriaCell entered into purchase agreements with accredited investors expected to gross \$27.2 million, issuing 5.2 million units with each unit comprising one share of common stock and one warrant. Each unit was priced at \$5.26. The warrants have a five and one-half year term and an exercise price of \$6.19. The private placement [closed](#) June 7, 2021, grossing \$27.2 million. ThinkEquity acted as sole placement agent.

On June 10<sup>th</sup>, BriaCell [announced](#) proceeds of \$12.9 million from warrant exercises. Share price doubled after June 2<sup>nd</sup> positive clinical [results](#), moving February 26 warrants into the money. Investors exercised 2.4 million warrants with an exercise price of \$5.3125 per common share. Proceeds from the warrants will be used to advance clinical and R&D and support general corporate purposes.

On September 9, 2021, BriaCell [announced](#) its intent for a board-approved buyback up to 10% of common shares and up to 10% of listed warrants. The company may purchase through the TSX Venture Exchange or NASDAQ up to 1.3 million common shares and up to 412,000 warrants over the next 12 months. On September 22, BriaCell informed investors that the TSXV had [accepted](#) BriaCell's intention to implement a normal course issuer bid (share repurchase) for the 12-month period starting September 28, 2021 and ending September 27, 2022.

### *Collaborations & Partnerships*

In April 2019, BriaCell [announced](#) a non-exclusive clinical trial collaboration with [Incyte Corporation](#) (NASDAQ: INCY) where it will provide compounds from its portfolio for use in combination studies with Bria-IMT. The two compounds initially identified are retifanlimab, an anti-PD-1 monoclonal antibody and epacadostat, an IDO1 inhibitor. Retifanlimab replaced pembrolizumab in the combination study. BriaCell's CEO, Dr. Bill Williams was previously VP of Exploratory Development at Incyte Corporation, and he has deep knowledge of their operations and research team. Incyte may also collaborate with BriaCell and its pivotal trial for Bria-IMT. It also has commercialization assets which may also make it a contender for selling and marketing BriaCell's approved products.

BriaCell and the [National Cancer Institute \(NCI\)](#) will work together to conduct preclinical studies on Bria-OTS as discussed in a November 2020 [press release](#). The collaboration will examine the immunologic trigger for an immune response against cancer with particular emphasis on the role of HLA types on immunogenicity. Research will be conducted by the Vaccine Branch and headed up by the Chief of the department, Dr. Jay Berzofsky.

On August 19, 2021, BriaCell [announced](#) that it had entered into a multi-year, non-exclusive license agreement with ImaginAB where ImaginAb will supply clinical doses of its CD8 ImmunoPET technology (89Zr-Df-Crefmirlimab) to BriaCell for use in its ongoing Phase I/II study with Incyte in recurrent breast cancer patients. ImaginAb will receive license fees and payments for providing ongoing technical, clinical, and regulatory support to enable the successful implementation of its CD8 ImmunoPET technology.

#### *Appointments*

On May 11, 2021, BriaCell [announced](#) that it had appointed Miguel A. Lopez-Lago, PhD as Senior Director, Research and Development. Since 2000, Dr. Lopez-Lago has worked as a cancer scientist at Memorial Sloan-Kettering Cancer Center in New York, investigating various aspects of tumor biology, including the development of targeted therapies for mesothelioma and the underlying mechanisms of cancer metastasis. More recently, he has been interested in the tumor immune-microenvironment and the development of immunotherapies for thoracic cancers using CAR T cells. Dr. Lopez-Lago received his Bachelor of Science in Bio-Sciences and his doctorate in Molecular Biology from Santiago of Compostela University, Spain.

There have also been several board appointments including the fall announcements that [Marc Lustig](#) and [Jane Gross, Ph.D.](#) had been appointed to the Board of Directors. Suzanne Ostrand-Rosenberg, Ph.D. was [appointed](#) to Scientific Advisory Board in November 2021.

#### *Posters*

In December 2021, R&D head Dr. Lopez-Lago presented a [poster](#) on Bria-IMT at the San Antonio Breast Cancer Symposium which was held from December 7<sup>th</sup> to 10<sup>th</sup>. The poster summarized the results for 35 patients that had received the targeted immunotherapy, 27 of which received monotherapy, 12 that received Bria-IMT with a checkpoint inhibitor and four that crossed over from monotherapy. The disease control rate for monotherapy was 30% which improved to 33% with the addition of a PD-1 inhibitor. Several patients exhibited objective complete regression of selected metastases. Median progression free survival (PFS) was 2.8 months for monotherapy and 4.2 months for combination. Median overall survival (OS) was 7.0 months for the Bria-IMT alone (9 patients) and 12.0 months for the checkpoint inhibitor combination (7 patients). These heavily pre-treated patients, with an average of five or more prior regimens demonstrated better PFS and OS in patients with an HLA match and who presented Grade I/II tumors. The data generated to date will help guide the focus of future studies on those with HLA matches and lower grade tumors.

BriaCell has presented a number of other posters reviewing the results of its clinical trials with two others in 2021 for the AACR Annual meeting in April and May 2021 and the Keystone Symposium in January 2021. A summary of BriaCell's [scientific publications can be found here](#).

## Management and Board of Director Profiles

### **Jamieson Bondarenko, CFA, CMT - Chairman of the Board**

Jamieson began serving as Board Chair for BriaCell in March of 2019. He is an active investor and provides strategic capital markets & corporate development advice to early-stage life sciences companies through his merchant capital company, JGRNT Capital Corp. Jamieson was most recently Principal, Managing Director, Equity Capital Markets at Eight Capital. In addition to his role on BriaCell's Board, he is Capital Markets Advisor to MustGrow Biologics Corp (MGRO). His previous roles include Equity Capital Markets and Investment Banking positions at Dundee Capital Markets, Wellington West Capital Markets, and HSBC Securities.

Jamieson is a CFA Charterholder and a Chartered Market Technician. He holds a Bachelor of Business Administration from Wilfrid Laurier University.

### **William V. Williams, MD, FRCP - President & Chief Executive Officer**

Dr. Williams is a seasoned biopharmaceutical executive with over 35 years of industry and academic expertise, including significant clinical management in multinational pharmaceutical companies. Dr. Williams has served as BriaCell's President & CEO since November 2016. Previously, Dr. Williams was appointed as VP of Exploratory Development at Incyte Corporation during 2005 - 2016. He facilitated entry of over 20 compounds into the clinic, including approvals for ruxolitinib (Jakafi) and baricitinib (Olumiant). As VP of Clinical Pharmacology and Experimental Medicine at GlaxoSmithKline, Dr. Williams evaluated numerous molecules in clinical studies in various therapeutic areas. He was involved in new or supplemental drug authorizations for a number of oncology drugs including Bexxar (lymphoma), Hycamtin (ovarian cancer), and Navelbine (non-small cell lung cancer) as well as ibandronate (Boniva) for osteoporosis. As Head of Rheumatology Research at the University of Pennsylvania, he ran a major research program in receptor biology, collaborated with David B. Weiner, PhD to develop DNA vaccines and was able to bring novel DNA vaccines into the clinic for the treatment of cutaneous T cell lymphoma. He has worked in the molecular immunology laboratory of Mark I. Greene, MD, PhD, FRCP, at the University of Pennsylvania, developed novel methods of bioactive peptide design, and collaborated in the study of the activation of the p185/Human epidermal growth factor receptor 2 (HER2) receptor. Dr. Williams is the named author of over 130 peer reviewed publications, over 15 patents and numerous Investigational New Drugs (INDs) and NDAs.

Dr. Williams earned his BSc. in Chemistry and Biotechnology from MIT and Medical Doctorate from Tufts University School of Medicine.

### **Gadi Levin, CA, MBA - Chief Financial Officer & Corporate Secretary**

Mr. Levin was appointed Chief Financial Officer in February 2016. Most recently, he acted as CFO of Labstyle Innovations Ltd, a biotechnology company focused on diabetes. Levin served as the Vice President of Finance and CFO for two Israeli investment houses in the fields of private equity, hedge funds and real estate (2008 to 2009 and 2010, respectively). Prior to that, Mr. Levin acted as Financial Consultant to various firms. Mr. Levin began his career at the accounting firm, Arthur Andersen, where he worked in the Cape Town, London and Tel Aviv offices for nine years.

He has a Bachelor of Commerce degree in Accounting and Information Systems from the University of Cape Town, South Africa, and a post graduate diploma in Accounting from the University of South Africa. He received his Chartered Accountant designation in South Africa and has an MBA from Bar Ilan University in Israel.

### **Miguel A. Lopez-Lago, Ph.D. – Senior Director, Research and Development**

Since 2000, Dr. Lopez-Lago has been working as a cancer scientist at Memorial Sloan-Kettering Cancer Center, New York (MSKCC). Specifically, he has investigated various aspects of tumor biology, including the development of targeted therapies for Mesothelioma and the characterization of the biological mechanisms underlying cancer metastasis. More recently, Dr. Lopez-Lago has been interested in the study of the tumor immune-microenvironment and in the development of immunotherapies for thoracic cancers using chimeric antigen receptor (CAR) T cell technologies. Since 2013, Dr. Lopez-Lago has been working as Senior Research Scientist at MSKCC.

Dr. Lopez-Lago received his Bachelor of Science in Bio-Sciences and his doctorate in Molecular Biology from Santiago de Compostela University, Spain.

## RISKS

All investments contain an element of risk which reflects the uncertainty of a business and what it will ultimately achieve. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

The biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical powerhouses that have multiple products currently generating revenues, to small operations with a handful of employees conducting pre-clinical studies. Many of the risks faced by the large pharmaceutical companies and smaller biotechnology-focused firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products.

For smaller early-stage companies, investing in drug development is a lengthy process. The timeframe for conducting pre-clinical research to eventually commercializing a drug can take from 12 to 15 years or even longer given market and company-specific conditions. And with, on average, only one in one thousand compounds eventually making it to the market from the preclinical stage, the risks are substantial.

Even if a company has a strong, experienced team that is developing a therapy with a high likelihood of success and a large addressable market, securing funding may be difficult. Access to financing comes and goes in cycles. During periods of improving confidence, capital may be easy to obtain; however, during a liquidity crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they are dependent on the financial markets to fund their work. If capital is needed to sustain operations and it is not readily available, the company may be forced to suspend research and development, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising therapies without a viable route to progress or force a company to accept onerous terms.

All drugs must navigate the regulatory approval process in the US, EU, Japan and other countries before commercialization. Success is uncertain and may take years depending upon the needs and desires of the determining authority. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Isolating companies that have a long history of research success in drug development, with opinion leaders and experts in the field are important factors that can help mitigate this risk. Companies that have had previous success with the FDA or other regulatory agencies also are more attractive than those who may be new to the process. Some accelerated pathways to approval have been put forth such as those outlined in the Orphan Drug Act and the Breakthrough Therapy designation; however, changes in sentiment or perceived safety for pharmaceuticals drugs could change the regulatory environment to demand a more thorough process and these pathways may be extended or additional requirements may be put in place.

**Exhibit XIII – Success of Phased Trials and Regulatory Approval<sup>28</sup>**

Phase	I - II	II - III	III - NDA/BLA	NDA/BLA - Approval	I - Approval
Probability	52.0%	28.9%	57.8%	90.6%	7.9%

BriaCell has developed a platform based on its highly immunogenic cell lines. The primary indication that it is pursuing is in breast cancer, but the pipeline also includes other related oncology targets. In many cases, due to the unmet need, expedited treatment is available to drugs in this category, which may allow for smaller and simpler trials to obtain approval as well as accelerated review. There are many firms competing in the oncology space and products must compete against established treatments that are entrenched in the health care system. In oncology, for example, there are hundreds of approved agents available. For immuno-oncology in particular, according to Evaluate Pharma, there are 85 marketed and 23 approved drugs. On the development side, there are 23 IO agents filed, 148 in Phase III and 697 in Phase II. For breast cancer, there is one filed, 10 Phase III and 19 Phase II assets in development.

In recent years, contract research organizations (CROs) have taken on a larger role in the development of drug candidates as the complexity and cost of trials has increased. Finding appropriate populations to participate in clinical trials has become increasingly difficult due to the shift to personalized medicine and orphan indications that address only a small group of patients. This shift has increased the dependence on specialized CROs for project

<sup>28</sup> Summarized from [Clinical Development Success Rates 2011-2020](#). Compiled by Zacks Analysts.

management and clinical monitoring services that add additional risks related to third parties. For BriaCell in particular, while the clinical trials are targeting the largest indication in oncology of breast cancer, the population thins markedly when adjusting for third line patients with a specific HLA type and grade of tumor. Despite this limitation, next generation BriaCell products such as Bria-OTS will materially increase the size of the population that is appropriate for clinical trial enrollment.

Disruptions due to the coronavirus have been severe throughout the globe and there have been reports of many clinical trials being halted and delayed. Travel restrictions and reallocation of resources may also affect the manufacture and distribution of drug product. Hospitals where clinical trials are conducted are at risk of high demand for services related to the pandemic drawing away resources. The high prevalence of coronavirus infections may dissuade patients from keeping appointments for on-site visits, negatively affecting enrollment and increasing the withdrawal rate. BriaCell has suffered from this disruption in the enrollment of its active Phase I/IIa trial which has only reported on 12 patients, despite launching prior to the start of the pandemic.

Drug price inflation has gained attention as it and other health care costs have risen at a materially faster pace than inflation. As new therapies have been approved, drug prices have increased to reflect higher development costs and improved pricing power of pharmaceutical and biotech companies. On the demand side, deductibles have been steadily increasing over the last decades, and in some cases, individuals and families must cover several thousand dollars in costs before the benefits of insurance begin. Cost sharing or co-insurance is another component of insurance plans that directly increases the burden on patients. This has resulted in greater elasticity in demand for drugs than was previously the case. Individuals with high deductibles or no insurance may be very sensitive to price and avoid treatments with high cost.

While we have discussed a broad variety of risks above, we believe that our forecast parameters, discount rates, success probabilities and valuation metrics address these potential outcomes and our target price reflects an assumption of these risks faced by biotechnology companies.



## VALUATION

BriaCell's lead candidate, Bria-IMT, is a vaccine or targeted immunotherapy for advanced breast cancer. While Bria-IMT is most effective in patients with low grade cancers and matching HLA types, the secondary candidate in the pipeline, Bria-OTS, is expected to address near 99% of all third line patients. As there are no fixed guidelines for this advanced group, the hurdles are lower for a new entrant to obtain approval and BriaCell has naturally sought this path. Despite the start with heavily pretreated patients, Bria-IMT may have the opportunity to work its way up towards earlier lines of therapy.

Bria-IMT is now in a Phase I/IIa combination trial with a checkpoint inhibitor and has reported on 12 patients. During 1H:22, we expect sufficient additional patients will be added to the data readout to support a meeting with the FDA in 2H:22 to inform the design of a pivotal trial. The ensuing trial is anticipated to be launched in late 2022 or early 2023 along with a partner. While it is possible a smaller 100 person effort may receive a nod by the FDA, we forecast a larger, 300 patient, randomized controlled trial that will run from 2023 to 2024. 2025 will encompass the regulatory submission and commercialization is forecasted to start in 2026.

We rely on the analysis performed by IQVIA that finds an addressable market of 68,000 women in the United States for Bria-IMT and validate this figure with our own analysis based on the prevalence of third line patients with the appropriate HLA and cancer grade characteristics. We assume a similar proportion of breast cancer patients in the global sphere will comprise the addressable market in this segment. Out of a total of 2 million new cases (ex-US), this generates an addressable market of 487,000.

There are many treatment options for breast cancer. The competitive environment offers established drugs for early disease and over 35 breast cancer-specific agents recommended for first line treatment. In the development domain, hundreds of new candidates are being researched and are in various stages of advancement. Given the impressive treatment effect in certain patients, we believe that Bria-IMT can carve a niche for itself upon approval. We forecast an initial 100 basis point penetration rate into the US market in year one rising to 400 basis points of penetration by year four where it will hold until the expiry of the biologic's 12 years of exclusivity. International markets are forecast to achieve 75 basis points of penetration in year one rising to 200 basis points by year four where it will also hold until 2037. Pricing is expected to be in line with other allogeneic immunotherapies which we see at around \$175,000 per course of treatment growing at 3% per annum. In the rest of the world, we observe a 50% reduction in pricing which yields an \$87,500 cost per course of treatment. We project a 20% probability of success given the stage of development and strength of the data.

While at an earlier stage than Bria-IMT, Bria-OTS can potentially more than double the addressable market for the targeted immunotherapy in breast cancer. Based on the analysis performed by IQVIA, there are approximately 140,000 in the addressable market for Bria-OTS in the United States, which is expected to HLA-match near 99% of patients. For the global (ex-US) market, we anticipate a similar proportion of patients in this segment as we do in the United States which yields an addressable population of approximately one million.

Bria-OTS is now in preclinical development for this broader, third line therapy cohort and we expect the product to enter clinical trials in 2023. Phase II and/or pivotal work will follow and biologic license data may be available for regulatory submission by 2028. Commercialization will ensue the following year with an anticipated 75 basis points of penetration in the US. This is expected to grow to 400 basis points of penetration by year four, where it will remain for the 12 years of expected exclusivity. In ex-US markets, we see an initial 50 basis points of penetration in year one (2029) rising to 200 basis points by year four (2032) where it will remain until intellectual property protections run out. Pricing for Bria-OTS will match that of Bria-IMT where a course of treatment will run \$175,000 in the United States and \$87,500 outside of the United States. Given the early stage of development, we apply an 8% probability of ultimate approval and commercialization for Bria-OTS.

Management has voiced its desire to work with a larger partner to help fund the pivotal trial, preferably one that has commercialization assets in place. Based on the stage of development at which the partner is expected to be added and the strength of the data for Bria-IMT, we model a 28% royalty to be paid to BriaCell for both Bria-IMT and Bria-OTS. The royalty amount includes all economic value from the arrangement including upfronts, milestones and royalties paid on revenues.

Estimates for operational costs call for about \$10 million in cash expense for 2022, \$17 million in 2023 and \$23 million in 2024 after which costs are estimated to grow at a 3% per annum rate. After consuming net operating losses, we forecast a 25% cash tax rate on earnings. After tax cash flows to the company are discounted at a 15% rate

with a terminal growth rate of -10%. After weighting our individual probabilities for the two programs we apply an overall 15% probability of success.

Option and warrants are assumed to be exercised if below our target price with proceeds added to cash and exercised shares added to shares outstanding. Despite the conservative stance of our assumptions, penetration into addressable markets can potentially be higher for Bria-IMT and Bria-OTS if study results demonstrate strong efficacy and safety. We note that the determinant for many of the variables in our model will be the ultimate performance of BriaCell's candidates in the clinic and in pivotal studies. We will update our model accordingly as data is made available.

Based on the assumptions identified in our discounted cash flow model, we generate a valuation of \$15.00 per share.

## CONCLUSION

BriaCell has developed a novel cell-based targeted immunotherapy that has shown beneficial effects on overall survival in heavily pretreated advanced breast cancer patients. Bria-IMT has produced a particularly favorable response in patients with closely matching HLA types and who present lower grade cancers. The company is currently conducting its second Phase I/II study and expects to generate sufficient data by 2H:22 to obtain a meeting with the FDA to discuss pivotal trial design.

Breast cancer is the most common cancer type with 284,000 cases in the United States and 2.3 million diagnoses around the globe. While most patients can expect survival for many years, some progress to successive lines of therapy and treatment can fail. For patients that have failed on several previous lines of therapy, new approaches such as BriaCell's targeted immunotherapy may be appropriate. Based on our review of available research, there are approximately 70,000 patients that can benefit from each year in the US and near seven times that number overseas. Follow-on candidate, Bria-OTS, may be able to address twice the population as Bria-IMT and is expected to submit an IND in 2022.

A Phase I/IIa trial for Bria-IMT is now underway in combination with a checkpoint inhibitor and has continued to show benefit to patients that have failed previous therapies. Results from clinical trials have shown favorable overall survival and progression free survival in both monotherapy and combination therapy groups. The agent has also shown particular success in HLA-matching and lower grade cancers and is observed to be safe and well tolerated.

BriaCell is continuing to enroll patients in this trial in an effort to generate sufficient data to support pivotal efforts that could begin in 2023. If successful, we see sufficient data available to support a BLA submission in 2025 leading to commercialization in 2026. With the validation of Bria-IMT, Bria-OTS will be close behind and we predict a similar pathway to registrational approval. Bria-OTS should be ready for commercialization by 2029.

Management has voiced its intent to partner for the next stage of trials and in commercialization of their lead assets. The most likely candidate for this collaboration is Incyte, whose checkpoint inhibitor, retifanlimab, is now being used in the combination approach along with Bria-IMT. However, other prospects may also be considered.

In the last year, BriaCell has benefited from the market's recognition of Bria-IMT's performance, especially in several extraordinary patients. It was able to raise \$65 million in FY:21 and is expected to add another \$5 million to its coffers from warrant exercises this quarter. The company has sufficient cash to fund the Bria-IMT and Bria-OTS programs, especially if done in conjunction with a partner.

Key reasons to own BriaCell shares:

- **Phase II asset to treat third line metastatic breast cancer**
- **Pivotal trial to be conducted next year, possibly with a partner**
  - **Combination with a checkpoint inhibitor**
- **Bria-IMT offers favorable treatment effect in specific patient groups**
  - **HLA match between patient and Bria-IMT cell line**
  - **Grade I/II Breast cancer**
- **Bria-OTS may be able to HLA match >99% of the overall advanced breast cancer population**
  - **15 unique HLA types**
  - **Will express GM-CSF and other immune stimulators**
  - **Will provide a personalized match of off the shelf (OTS) alleles**
- **Similar safety profile to other approved cancer drugs in early clinical development**
- **Global rights to intellectual property**

Based on our analysis of Bria-IMT and Bria-OTS and the clinical trial data generated to date, we see a pathway forward to commercialize this cell-based targeted immunotherapy. Our valuation work takes into account commercialization of both of these assets around the globe, assuming a 15% combined probability of success. As other assets in the clinic move closer to the clinic, we anticipate adding these to the valuation model as well. As we initiate on BriaCell Therapeutics Corp., our analysis and forecasts generate a target price of \$15.00 per share.

## PROJECTED FINANCIALS

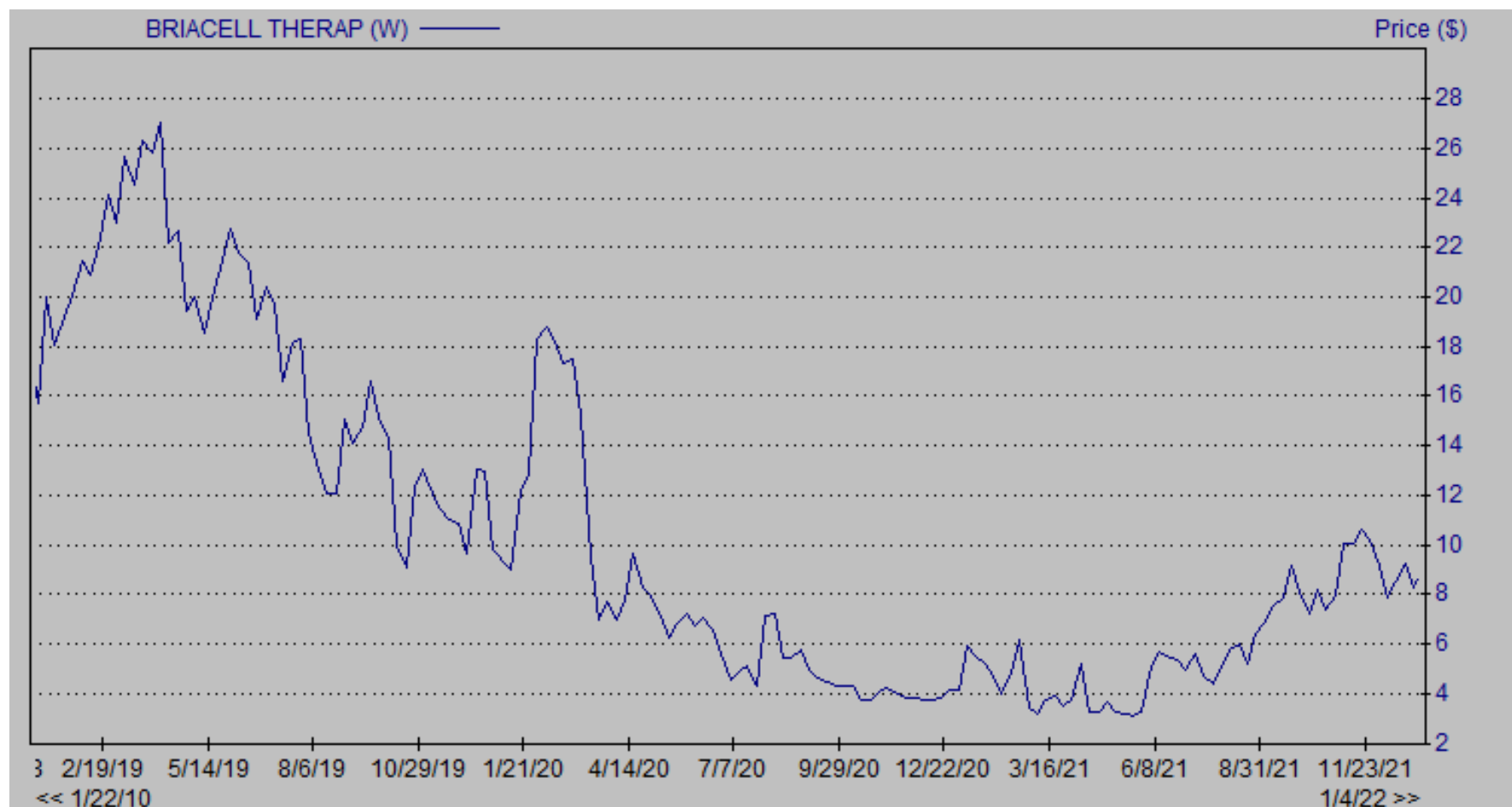
### BriaCell Therapeutics Corp. - Income Statement

BriaCell Therapeutics Corp	2021 A	Q1 A	Q2 E	Q3 E	Q4 E	2022 E	2023 E	2024 E
<b>Total Revenues (\$USD)</b>	<b>\$0</b>	<b>\$0</b>	<b>\$0</b>	<b>\$0</b>	<b>\$0</b>	<b>\$0</b>	<b>\$0</b>	<b>\$0</b>
Research & Development	\$1,315	\$876	\$1,400	\$1,835	\$2,520	\$6,631	\$12,852	\$18,945
General & Administrative	\$3,690	\$891	\$950	\$1,020	\$1,005	\$3,866	\$4,100	\$4,500
Share Based Compensation	\$1,968	\$518	\$450	\$450	\$400	\$1,818	\$1,200	\$1,200
<b>Income from operations</b>	<b>(\$6,973)</b>	<b>(\$2,285)</b>	<b>(\$2,800)</b>	<b>(\$3,305)</b>	<b>(\$3,925)</b>	<b>(\$12,315)</b>	<b>(\$18,152)</b>	<b>(\$24,645)</b>
Other Items	\$6,545	(\$101)	\$0	\$0	\$0	(\$101)	\$0	\$0
<b>Pre-Tax Income</b>	<b>(\$428)</b>	<b>(\$2,386)</b>	<b>(\$2,800)</b>	<b>(\$3,305)</b>	<b>(\$3,925)</b>	<b>(\$12,416)</b>	<b>(\$18,152)</b>	<b>(\$24,645)</b>
Provision for Income Tax	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>Tax Rate</i>	<i>0.0%</i>	<i>0.0%</i>	<i>0.0%</i>	<i>0.0%</i>	<i>0.0%</i>	<i>0.0%</i>	<i>0.0%</i>	<i>0.0%</i>
<b>Net Income</b>	<b>(\$428)</b>	<b>(\$2,386)</b>	<b>(\$2,800)</b>	<b>(\$3,305)</b>	<b>(\$3,925)</b>	<b>(\$12,416)</b>	<b>(\$18,152)</b>	<b>(\$24,645)</b>
<b>Reported EPS</b>	<b>(\$0.09)</b>	<b>(\$0.16)</b>	<b>(\$0.18)</b>	<b>(\$0.21)</b>	<b>(\$0.25)</b>	<b>(\$0.80)</b>	<b>(\$1.09)</b>	<b>(\$1.36)</b>
Basic Shares Outstanding	4,520	15,239	15,400	15,650	15,900	15,547	16,623	18,100

Source: Company Filing // Zacks Investment R

## HISTORICAL STOCK PRICE

BriaCell Therapeutics Corp. – Share Price Chart<sup>29</sup>



<sup>29</sup> Source: Zacks Research System

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