



*The Future of Cancer Immunotherapy*



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## Clinical Development Update

September 2018

OTCQB: BCTXF

TSX: BCT.V

# Forward-Looking Statements

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Except for historical information, this presentation contains forward-looking statements, which reflect BriaCell's current expectations regarding future events. These forward-looking statements involve known and unknown risks and uncertainties that could cause BriaCell's actual results to differ materially from those statements. Those risks and uncertainties include, but are not limited to, our ability to access capital, the successful and timely completion of clinical trials, the receipt of all regulatory approvals and other risks detailed from time to time in our ongoing quarterly and annual filings. The forward-looking statements in this presentation are also based on a number of assumptions which may prove to be incorrect.

Forward-looking statements contained in this presentation represent views only as of the date of this presentation and are presented for the purpose of assisting potential investors in understanding BriaCell's business, and may not be appropriate for other purposes. BriaCell does not undertake to update forward-looking statements, whether written or oral, that may be made from time to time by or on its behalf, except as required under applicable securities legislation.

Investors are cautioned not to rely on these forward-looking statements and are encouraged to read BriaCell's continuous disclosure documents, including its financial statements which are available on SEDAR at [www.sedar.com](http://www.sedar.com).

- Completed enrollment of MBC patients in the Phase I/IIa “monotherapy” study of Bria-IMT™

## We have confirmed our mechanism of action and achieved proof of concept

- Initial safety data appears superior to that of the other advanced or approved drugs for breast cancer when they were at a similar clinical stage of development
- Initial efficacy data is similar or superior to those of other advanced or approved drugs for breast cancer when they were at a similar clinical stage of development
- Transitioning into **Combination Study of Bria-IMT™ with Keytruda or Yervoy in patients with MBC** expecting better response rates than those in the “monotherapy” study
  - Initial safety data is expected in 4Q2018
  - Initial efficacy data is expected in 1Q2019
- Bria-OTS™, the first off-the-shelf personalized treatment for metastatic breast cancer, is expected to enter the clinic in 2019

**Outstanding Safety Data. Our recent data confirms “HLA matching Hypothesis”, and supports our strategy for the development of Bria-OTS™**

## **Data (4 patients)-Preliminary Ph I/IIa Study (2004-2005)**

- Bria-IMT™ resulted in a near complete tumor regression in a patient (top-respondent) with MBC
  - The top-respondent patient matched Bria-IMT™ at key HLA types (see Slide 19)

## **Interim Data (20 patients)-Ongoing Phase I/IIa Study (2017-2018)**

- **Outstanding safety data.** Comparable or superior to data to approved drugs for breast cancer at a similar stage of development
- **Tumor shrinkage or decreased circulating tumor cells.** Was observed in 33% of patients who matched Bria-IMT™ at one HLA type and 75% of patients who matched Bria-IMT™ at 2 HLA types further confirming “HLA matching hypothesis”

## **Clinical Development Strategy**

- Initiating combination study of Bria-IMT™ with Keytruda or Yervoy
- BriaCell’s off-the-shelf personalized immunotherapy, Bria-OTS™, is expected to enter the clinic in 2019

**Based on the current study, Bria-IMT™ has an excellent safety profile**

- To date, Bria-IMT™ has been dosed in 24 patients (4 in 2004-2005, 20 in 2017-2018)

## **Interim Data (20 patients)-Ongoing Phase I/IIa Study (2017-2018)**

- Bria-IMT™ has been very well tolerated ( $\geq 60$  doses given to date)
- The majority of adverse events (AEs) were limited to expected minor local irritation at the injection sites
- No related grade  $>3$  or unexpected AEs
- No related serious AEs
- No serious, unexpected, related AEs
- Most patients who have dropped out did so due to worsening of their underlying disease

- **Bria-IMT™ appears to be most effective in patients who match with Bria-IMT™ at 2 HLA loci (types) further supporting our “HLA Matching Hypothesis”, and the development of Bria-OTS™ to cover 90% of the patient population**
- **Combination with immune checkpoint inhibitors may induce a more potent anti-cancer response, leading to our strategy of combination studies of Bria-IMT™ with Keytruda or Yervoy**

## **Interim Data - Ongoing Phase I/IIa Study (2017-2018)**

- Definite tumor shrinkage in 3 patients in the current study (4 total)
- Another patient had evidence of reduced circulating cancer-related cells
- First tumor assessment of 5 patients – pending
- 3/15 did not match Bria-IMT™ at any HLA types - none have responded to the treatment
- Of those who matched at least at 1 HLA type, the response rate was 4/15 (27%) for tumor shrinkage & 5/15 (33%) for a biological response
- **Of those who matched at 2 HLA types the tumor shrinkage rate was 2 of 4 (50%) and 3 of 4 (75%) for a biological response**
- Expression of PD-L1 on circulating cancer cells and cancer-associated cells in 100% of patients evaluated to date supporting use with a PD-1 inhibitor such as Keytruda

- Bria-IMT™ appears to be most effective in patients who match with Bria-IMT™ at 2 HLA loci (types) further supporting our “HLA Matching Hypothesis”, and the development of Bria-OTS™ to cover 90% of the patient population
- Combination with immune checkpoint inhibitors may induce a more potent anti-cancer response, leading to our strategy of combination studies of Bria-IMT™ with Keytruda or Yervoy

Interim Data (19 patients)-Ongoing Phase I/IIa Study (2017-2018) & Original Study (2004-2005)

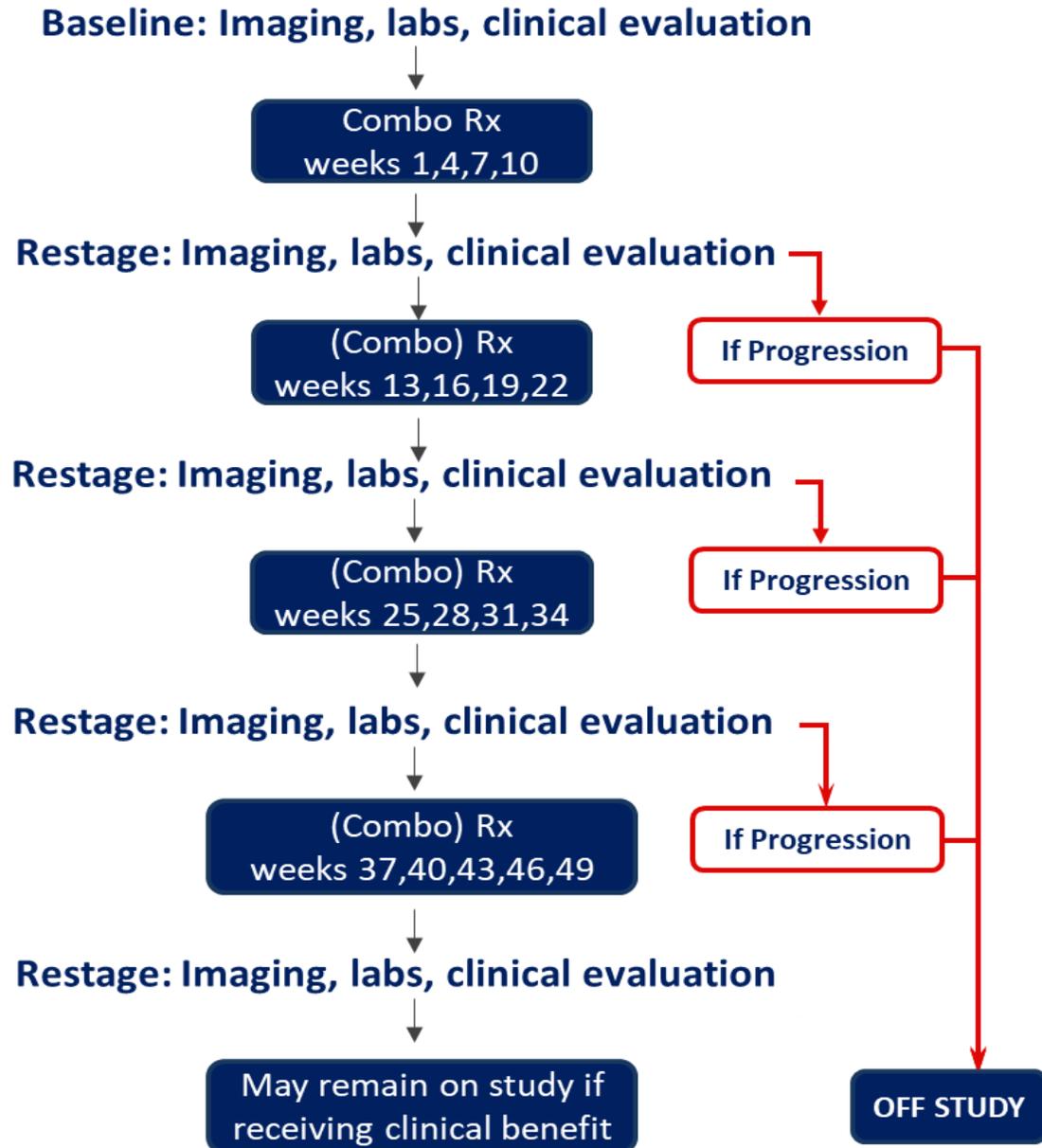
Patients (n)	HLA Match	Tumor Shrinkage	Lower Circulating Cancer Cells
4	≥2	50%	75%
11	≥1	27%	33%
4	0	0%	0%

- PD-L1 expression on circulating cancer cells & cancer-associated cells in 100% of patients (to date) → Strong rationale for combination with checkpoint inhibitors like Keytruda

**The data of the combination study is of great interest by big pharma for potential partnership opportunities with a manufacturer of a PD-1 or a PD-L1 Inhibitor**

- Phase I/II “Monotherapy” Study has enrolled 31 with data available on 20 subjects dosed to date.
- This study will be closed and emphasis switched to the **combination therapy** study with Keytruda or Yervoy.
- The **combination therapy study** has recently been altered so that patients can enter directly into that study
- The FDA approved protocol states that 6 patients can be treated, and the safety data should be evaluated before enrollment of additional patients.
- We expect a rapid enrollment schedule, and initial safety data in 4Q2018
- Efficacy data on these initial patients is expected in 1Q 2019 with additional patient enrollment in the study

# Combination Study of Bria-IMT™ with Keytruda or Yervoy



## Currently Recruiting:

- Treatment in combination with Keytruda® for PD-L1(+) or PD-L2(+) tumors q3wks x up to 24 cycles, then Bria-IMT™ alone q3wks

-OR-

- Treatment in combination with Yervoy® for PD-L1/2(-) tumors q3wks x 4 cycles, then Bria-IMT™ alone q3wks
- Imaging every 6-12 weeks

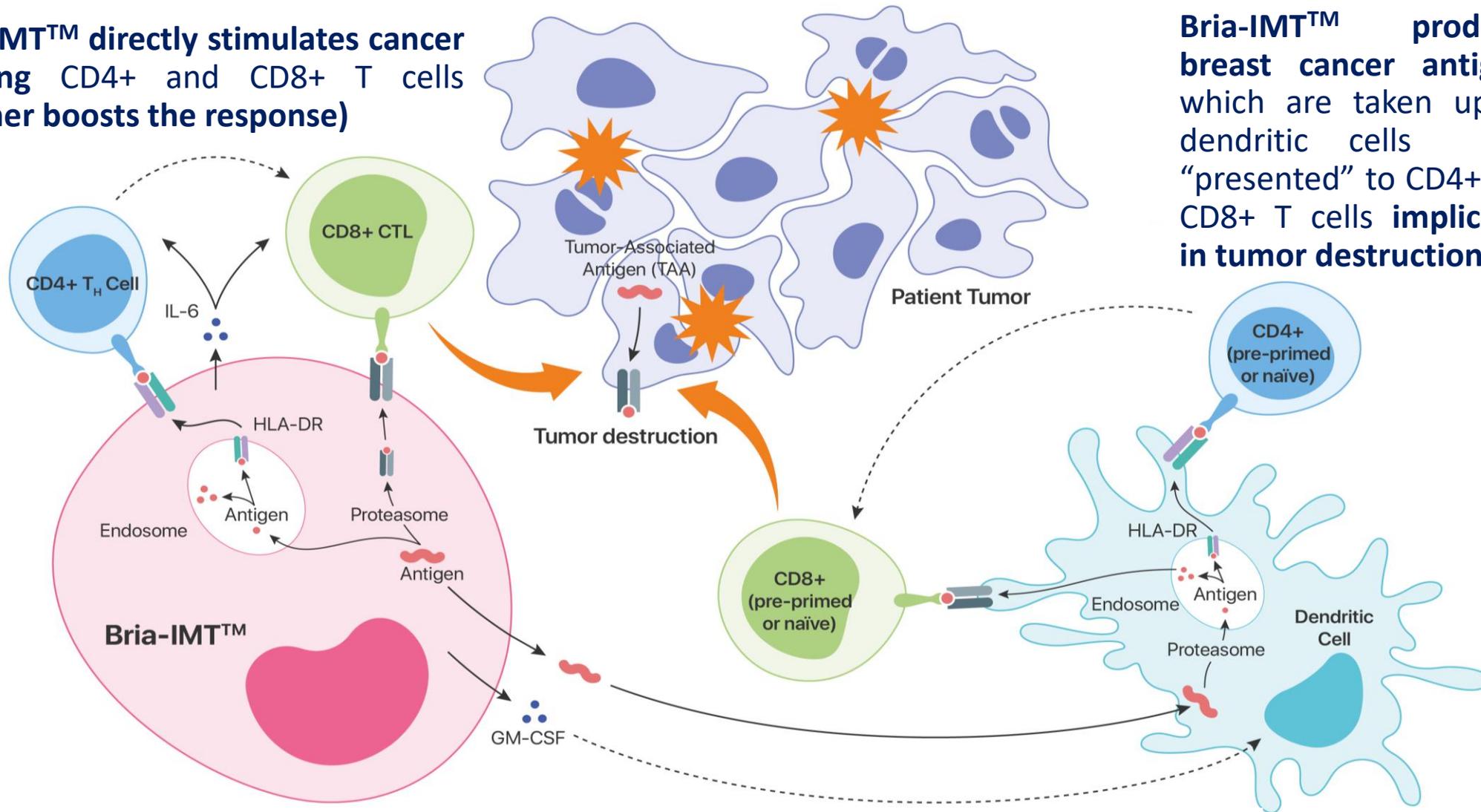
Keytruda® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.

Yervoy® is a registered trademark of Bristol-Myers Squibb Company

# Bria-IMT™ - Potential Mechanisms of Action

**Bria-IMT™ directly stimulates cancer fighting CD4+ and CD8+ T cells (further boosts the response)**

**Bria-IMT™ produces breast cancer antigens which are taken up by dendritic cells and “presented” to CD4+ and CD8+ T cells implicated in tumor destruction.**



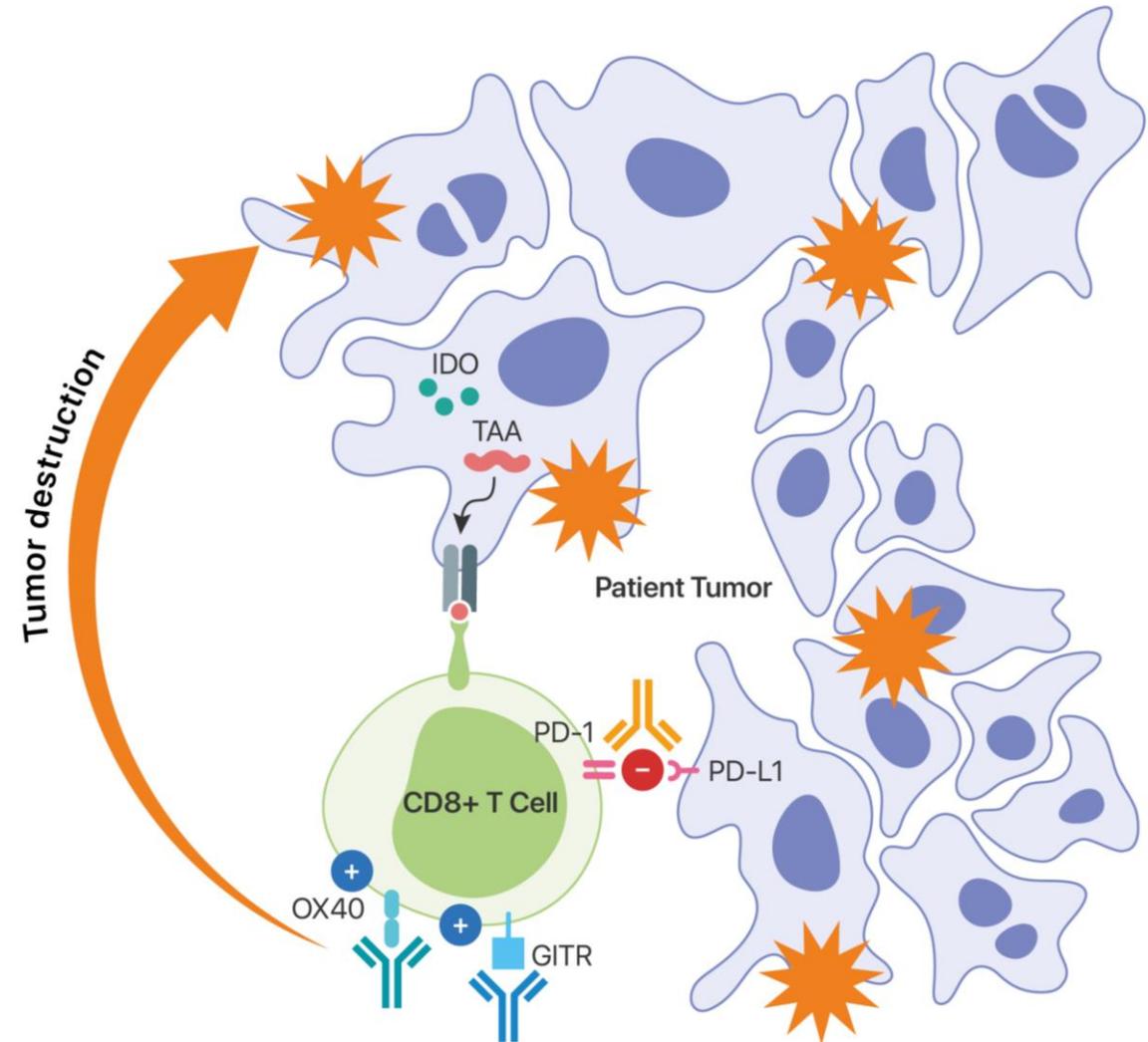
**Bria-IMT™ secretes GM-CSF which further promotes dendritic cell-based antigen presentation (boosts the response)**

# Bria-IMT™ & Bria-OTS™ - Combination Therapy Rationale

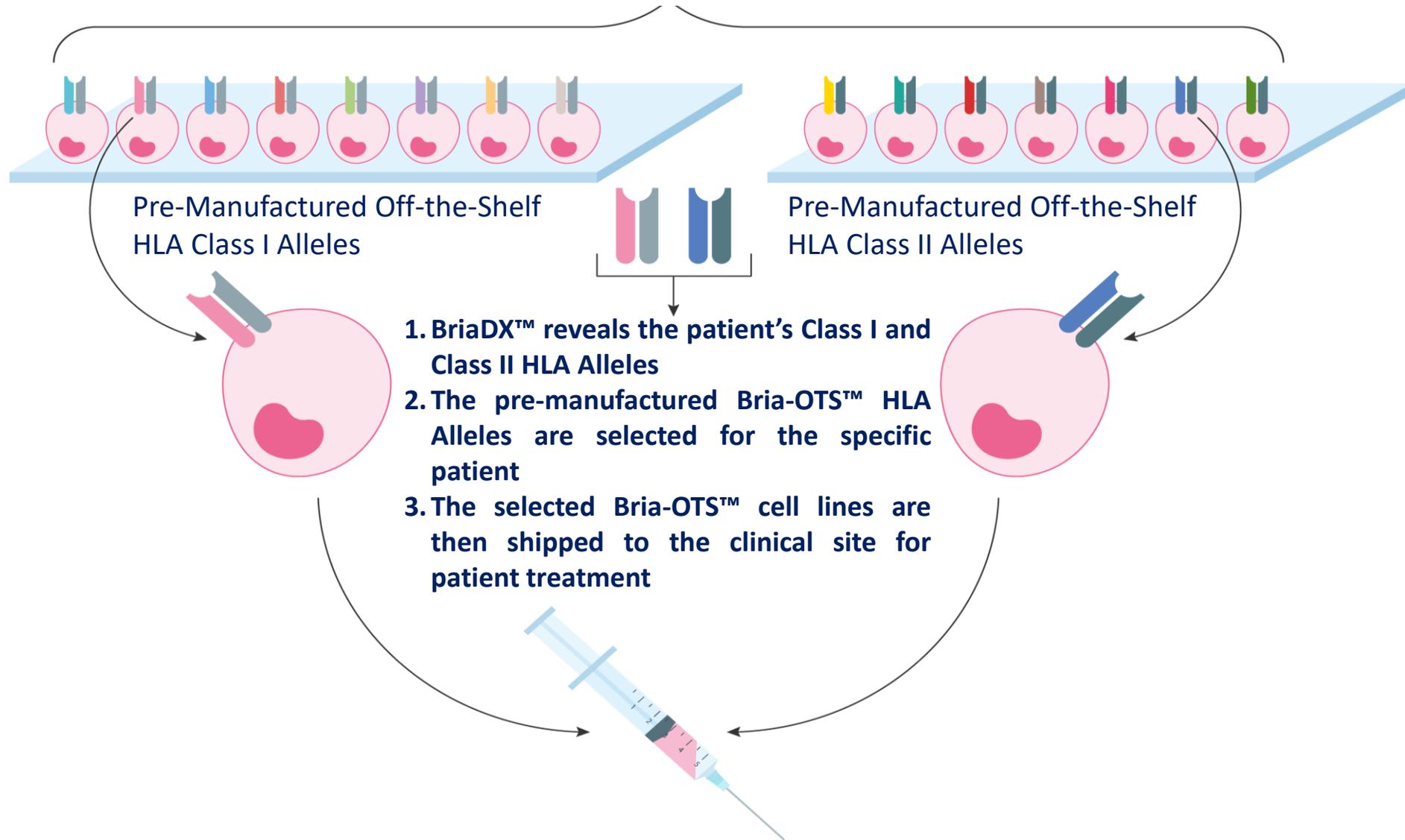
So far, excellent safety profile of Bria-IMT™ and targeted anti-tumor immune response has been demonstrated.

Bria-IMT™ & Bria-OTS™ should synergize with the following:

- Existing approved immunotherapies, especially PD-1 and PD-L1 inhibitors
- Immunotherapies under development
- Targeted therapies (tyrosine kinase inhibitors, breast cancer targeting antibodies or ADCs, etc.)



These allele combinations cover/match with ~90% of the advanced breast cancer population



**Our main priority will be the development of Bria-OTS™, BriaCell's off-the-shelf personalized immunotherapy – expected to double match 90% of the patient population and in the clinic by 2019**

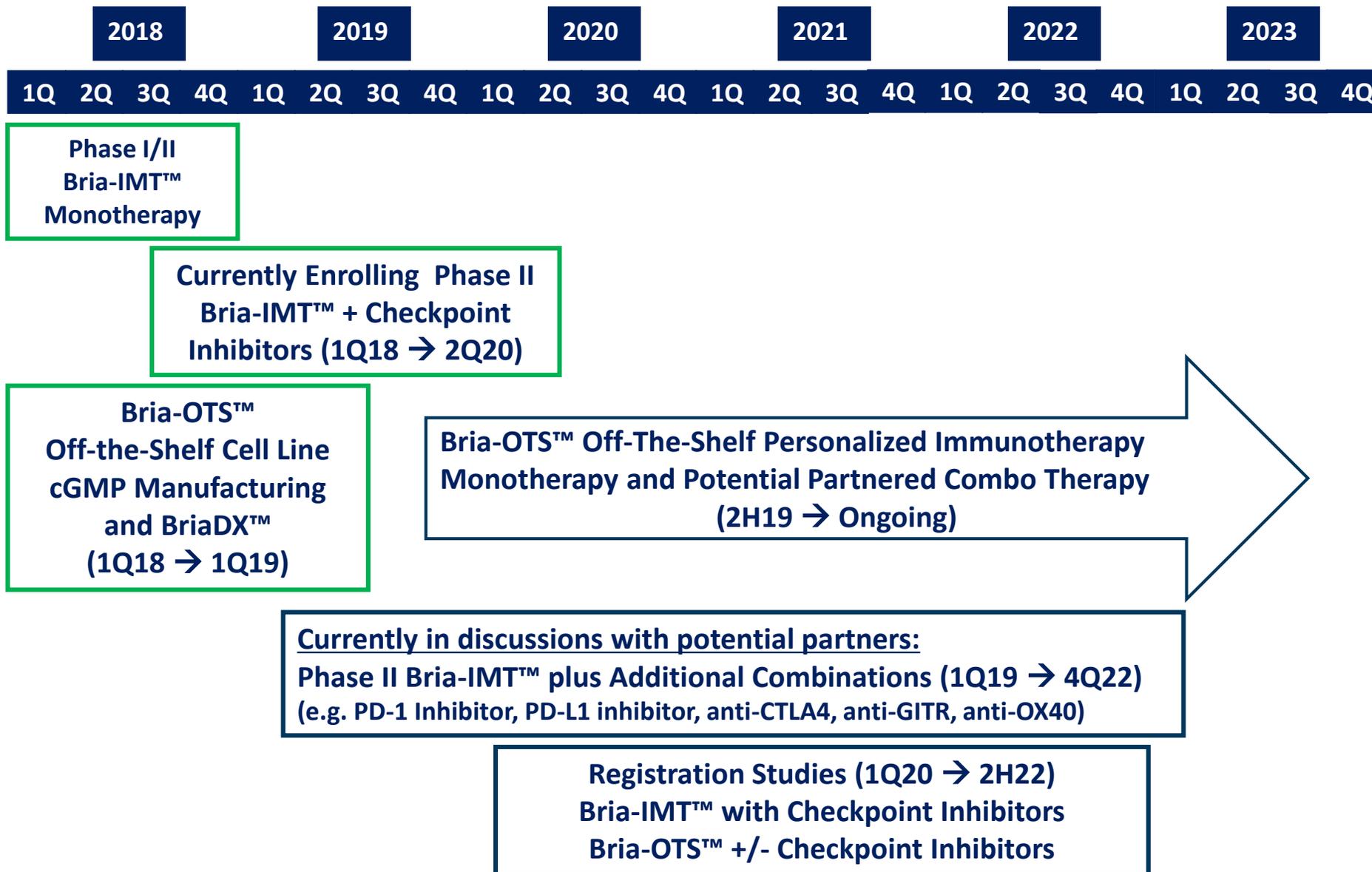
- Bria-OTS™ engineering requires 3 stages:
  - ✓ Knock-out endogenous HLA genes
  - Transfect in GM-CSF and IFN $\alpha$  genes
  - Transfect in HLA genes that match more patients
- We have successfully completed Stage 1
- Stage 2 and Stage 3 genes have been developed and are being introduced into SV-BR-1 cells
- Anticipate completion of engineering and beginning of GMP manufacturing in 1Q 2019
- On track to begin clinical study in 2019

- Completed enrollment of MBC patients in the Phase I/IIa “monotherapy” study of Bria-IMT™

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# Development Timeline – Breast Cancer



# Upcoming Milestones & Catalysts

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- ✓ Q3 2018: Data on first 20 Patients
  
- ❑ Q3 2018: Initiate Combination Study of Bria-IMT™ with Keytruda or Yervoy
- ❑ Q4 2018: Switch to a novel frozen Bria-IMT™ formulation
- ❑ Q4 2018: Safety Data (6 patients) of the Combination Study (San Antonio Breast Cancer meeting)
- ❑ Q4 2018: Ongoing Corporate Partnership/Collaboration Discussions
  
- ❑ Q1 2019: Efficacy Data (6 patients) of the Combination Study
- ❑ Q2 2019: Additional Safety and Efficacy data for Monotherapy and Combination Study (AACR meeting)
- ❑ Q2 2019: Final data for Monotherapy and Additional Data for the Combination Study (ASCO meeting)
- ❑ H2 2019: Bria-OTS™ Authorization from FDA; First Patient Dosed



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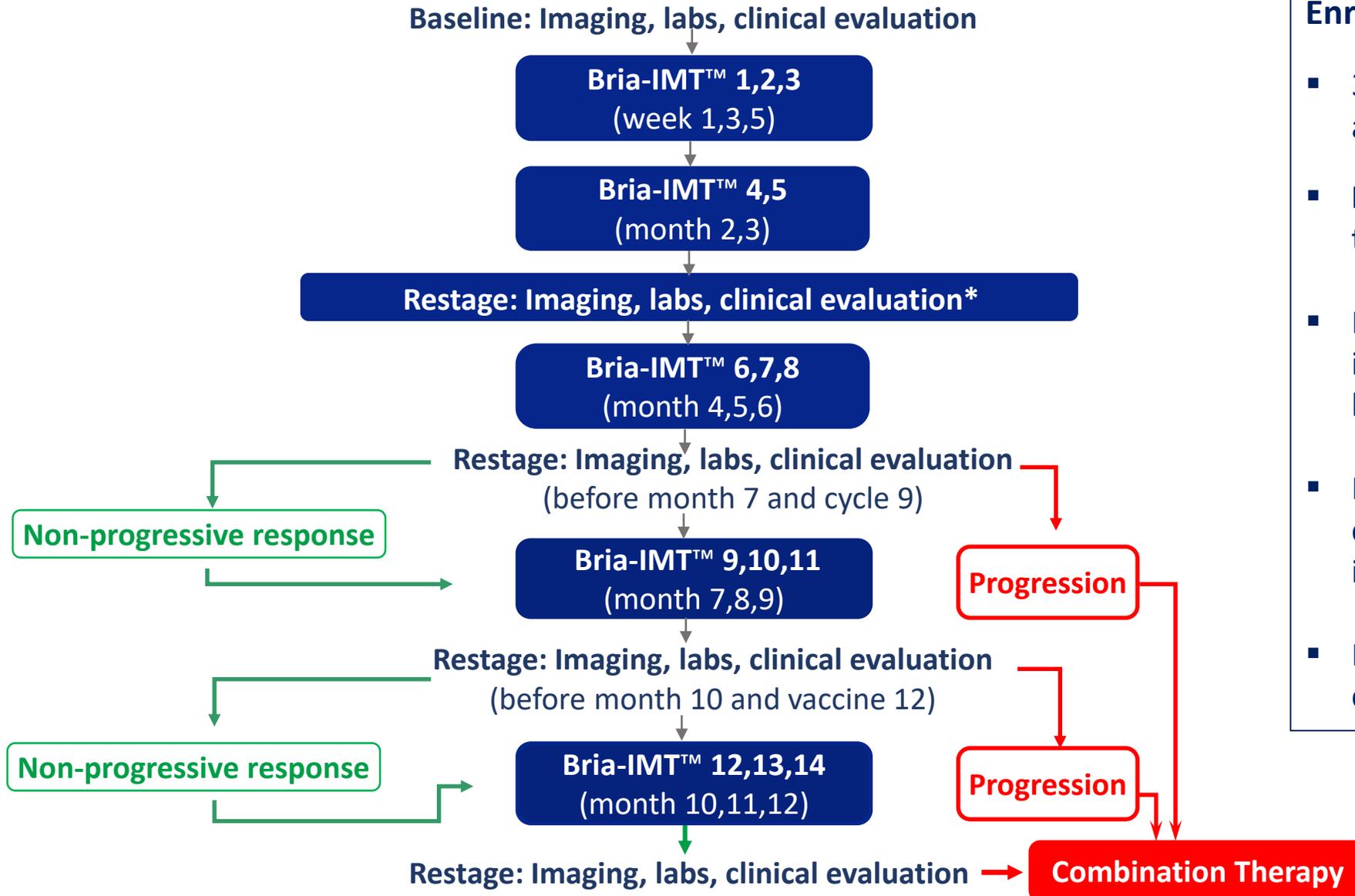
## **Clinical Development Update- Appendix**

**September 2018**

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# Bria-IMT™ Phase IIa Monotherapy Trial



- Enrollment Completed:**
- 30 MBC patients screened and 20 dosed
  - **Primary objectives:** Safety & tumor response
  - Exploratory objectives include immune response to tumor, biomarkers, Quality of Life
  - Pre-dose low dose cyclophosphamide to reduce immune suppression
  - Post-dose IFN- $\alpha$ 2b to boost cell mediated immunity

## Bria-IMT™ Non-Personalized Immunotherapy – Given as Monotherapy

- Patient A002 was the only patient matching a key HLA type with Bria-IMT™ and experienced tumor regression and complete remission at some metastatic sites

	Tumor Type	Survival (months)	Tumor regression	HLA-A Alleles		HLA-B Alleles		HLA-DRB3 Alleles	
<b>Bria-IMT™</b>	<b>Breast</b>			<b>11:01</b>	<b>24:02</b>	<b>35:08</b>	<b>55:01</b>	<b>01:01</b>	<b>02:02</b>
Patient A001	Breast	40.7	No	02:01	24:02	13:02	41:01	03:01	-
Patient A002	Breast	33.7	<b>YES</b>	02:01	11:01	18:03	44:02	<b>02:02</b>	-
Patient A003	Ovarian	35.6	No	02:01	03:01	07:02	13:02	Negative	-
Patient B001	Breast	7.0	No	11:01	-	35:01	40:01	Negative	-

- We compared the interim data of Ph I/IIa study of Bria-IMT™ in advanced breast cancer with the data in the early stage clinical studies of recently approved breast cancer drugs, and one fast tracked product candidate.

**Apples to apples comparison:** Early Stage Clinical Studies in oncology are typically done in patients with no other therapeutic options. Thus, the patients have very advanced disease and response rates are typically quite low.

The patients in our Ph I/IIa study have been heavily pre-treated (median 4.5 prior regimens)

Some recent studies of relevance in breast cancer are noted in the following slides

# Breast Cancer Market Opportunity

The market for breast cancer drugs is a multibillion dollar market with new drugs being approved in an ongoing basis indicating the shortage of safe and effective treatments for this deadly disease

Drug	Technology	Approved for	Market (US)
Ibrance (palbociclib)	CDK 4/6 Inhibitor	HR+/HER2- MBC in combination with fluevestrant or aromatase inhibitor	\$933M in 1Q2018; \$3,126M in 2017
Kisqali (ribociclib)	CDK 4/6 Inhibitor	2017: HR+/HER2- MBC in combination with fluevestrant or aromatase inhibitor	Peak sales projected at \$2.5B
Verzenio (abemaciclib)	CDK 4/6 Inhibitor	2017: HR+/HER2- MBC in combination with fluevestrant or aromatase inhibitor	Peak sales projected at \$2B
Lynparza (olaparib)	Poly (ADP-ribose) polymerase (PARP) inhibitor	2017: ovarian & breast cancer	\$997M in 2017
Halaven (eribulin mesylate)	Tubulin-based antimetabolic	2H2017: 3rd line MBC & liposarcoma	\$181M in 2017
balixafortide	CXCR4 antagonist	Fast track designation in 2018 for HER2- MBC who have failed 2 prior regimens	

# Competitors- Phase I/II Clinical Data

**Bria-IMT™ shows superior safety and similar to superior efficacy data compared with those of the multi-billion dollar drugs when they were at a similar early stage of development**

Drug	Patient # (n)	Safety	Efficacy
Ibrance (palbociclib)	41 & 18	20%-61%: Gr3/4 Neutropenia 23%-39%: Gr3/4 Leucopenia	0% response rate (n=41); 11% PR (n=18) but only with letrozole (0% for monotherapy)
Kisqali (ribociclib)	132	27%: Gr3/4 Neutropenia 17%: Gr3/4 Leucopenia	2.3% PR – included 1 in breast cancer (5% of breast cancer patients)
Verzenio (abemaciclib)	12	17%: Gr3/4 Neutropenia 33%: Gr3/4 Leucopenia	17% PR – included 1 in breast cancer
Lynparza (olaparib)	28	11%: Gr3+ Neutropenia 8%: Gr3+ Thrombocytopenia 18%: Gr3 Fatigue 25%: Gr3 Hypertension	0% response rate for breast cancer (8 patients)
Halaven (eribulin mesylate)	12	100%: Gr3/4 Neutropenia 83%: Gr3/4 Leukopenia 25%: Gr3/4 Lymphopenia 8%: Gr3/4 Febrileneutropenia	8% PRs
balixafortide	56	41%: Gr3/4 Neutropenia 11%: Gr3/4 Leucopenia 11%: Gr3/4 Febrileneutropenia 2: Related mortalities	30% PRs in combination with Halaven
<b>Bria-IMT™</b>	<b>20</b>	<b>Injection site reactions No related SAEs or SUSARs</b>	<b>Tumor vol. ↓, &amp;/or ↓ circul. tumor cells) All Comers: 21%(4/19), 26%(5/19) One or More HLA matches: 27%(4/15), 33%(5/15) Two or More HLA matches: 50% (2/4), 75% (3/4)</b>



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