BACKGROUND: BriaVax™ (formerly GEMI-MG) is a breast cancer cell line transfected to release GM-CSF. Under FDA BB-IND 10312, 35 patients received 20 million viable cells ID x 4 sites 40-72 hours after low-dose cyclophosphamide, 350 mg/m². Mean cell count was 22.8 x10^6 (18.8-27.6). Interferon-alpha (10,000 million viable cells ID at 4 sites) was injected into each inoculation site after 48 and 72 hrs. The protocol permitted 3 inoculations at 2 week intervals, then, if not showing clearly progressive disease, 3 more inoculations monthly. All patients were stable after 3 inoculations (2 months). However, BI A002 exhibited complete tumor regression of a progressing lung metastasis and near-complete resolution of widespread brain metastases (20). These results prompted the final and final inoculation per protocol. After obtaining FDA permission to inoculate, 15 tumours, including BriaVax™, again showed prompt and subtotal regression after 3 inoculations (see Wiseman C and Kharazi A. The Breast Journal 2006). Toxicity was minimal and the overall survival of the 4 patients was 35 months.

TRIAL DESIGN: 9 patients will be accrued, toxicity (and also response) will be reviewed; unless there are toxic serious adverse events, 15 patients will then be treated. ELIGIBILITY Inclusion Criteria Patients must have histological confirmation of breast cancer with recurrent/metastatic disease and ECOG 0-2. Patients with new or progressive breast metastasis to brain will be eligible if they meet other conditions. Patients must be 18 years of age or older, have expected survival of at least 4 months, adequate performance status (ECOG 0-2). Patients must be 18 years of age or older, have expected survival of at least 4 months, adequate performance status (ECOG 0-2). Patients may be maintained on hormonal therapy provided there is clear evidence of tumor progression and have provided written informed consent.

In a nutshell:

- **Trial Objectives:**
  - Inclusion: 9 patients will be accrued, toxicity (and also response) will be reviewed; unless there are toxic serious adverse events, 15 patients will then be treated.
  - Eligibility:
    - Inclusion Criteria: Patients must have histological confirmation of breast cancer with recurrent/metastatic disease and ECOG 0-2.
    - Patients with new or progressive breast metastasis to brain will be eligible if they meet other conditions. Patients must be 18 years of age or older, have expected survival of at least 4 months, adequate performance status (ECOG 0-2).
    - Patients may be maintained on hormonal therapy provided there is clear evidence of tumor progression and have provided written informed consent.

### Clinical Data To-Date

<table>
<thead>
<tr>
<th>Lesion 1</th>
<th>Lesion 2</th>
<th>Lesion 3</th>
<th>Lesion 4</th>
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<tbody>
<tr>
<td>Baseline</td>
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<tr>
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**Response in Patient A002 and CD40L**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Tumor Type</th>
<th>Tumor Status</th>
<th>Months Effective</th>
<th>CD40L Levels</th>
<th>CD40L Changes</th>
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<tbody>
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<td>A001</td>
<td>Breast</td>
<td>Progressive</td>
<td>4 months</td>
<td>High</td>
<td>Increase</td>
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<tr>
<td>A002</td>
<td>Breast</td>
<td>Stable</td>
<td>3 months</td>
<td>Low</td>
<td>Decrease</td>
</tr>
<tr>
<td>A003</td>
<td>Breast</td>
<td>Stable</td>
<td>2 months</td>
<td>Moderate</td>
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</tr>
</tbody>
</table>

**Notes:** BriaVax™ and Subcut A002 with tumor regressions even at metastatic sites reported in Wiseman and Kharazi, 2006 share both MHC class I (HLA-A) and class II (HLA-DR) alleles.

**HLA Alleles**

- BriaVax™ cell line displays both HLA Class I and II alleles, & the responding patient matched in both categories.

**Molecular Biology Findings**

- BriaVax™ cell line contains both HLA Class I and II alleles, & the responding patient matched in both categories.
- BriaVax™ expresses tumor-associated antigens, including HER2/neu, PRAME, and others.

**Response to BriaVax™**

- **Antigenic Expression:** Cancer/Testis AG
  - **Cancer/Testis Antigens (CTAs):** A class of cancer tissue specific antigens
    - **PRAME** is expressed in several malignancies, including some breast cancers.
  - **FRAME** is also expressed in BriaVax™.
  - **BriaVax™** injection may activate PRAME-specific T cells and thereby cause destruction of PRAME-expressing tumors.

**Experimental Plan**

1. **Initial Phase I:**
   - Up to 4 stage IV breast cancer patients
   - 3 re-inoculations (wk 0,2,4) at 3 sites
   - Non-progressive disease after month 6

2. **Second Phase I:**
   - Up to 24 stage-IV breast cancer patients
   - 3 re-inoculations (wk 0,2,4) at 3 sites
   - Non-progressive disease after month 6

### Pending Trials To Come

- Combination with Checkpoint Inhibitors
- Dose-Ranging exploration
- Schedule variations

In Appreciation

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**CFO:** Cancer Insight, Inc. San Antonio, TX

**Acknowledgements:** Dr. Gerhard Bauer, Dr. Saeid Babaei, Dr. William Williams, St. Vincent Medical Center, Dr. Alex Kharazi, Dr. George Peoples for advice and guidance.

**Notes:**

- **Response in CNS Mets**
  - No RECIST response (3 vaccines/4 weeks) to multiple metastatic sites
  - Complete response to re-treatment
  - One robust responder with 95% regression during treatment, subsequent relapse (upon halting treatment) responded to re-treatment.