SESEN BIO, INC.

FORM 8-K
(Current report filing)

Filed 05/01/17 for the Period Ending 05/01/17

Address 245 FIRST STREET
          SUITE 1800
          CAMBRIDGE, MA, 02142

Telephone 617-444-8550
CIK 0001485003
Symbol SESN
SIC Code 2834 - Pharmaceutical Preparations
Industry Biotechnology & Medical Research
Sector Healthcare
Fiscal Year 12/31
CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 1, 2017

ELEVEN BIOThERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction of Incorporation)

001-36296
(Commission File Number)

245 First Street, Suite 1800
Cambridge, MA
(Address of principal executive offices)

26-2025616
(IRS Employer Identification No.)

02142
(Zip code)

Registrant’s telephone number, including area code: (617) 444-8550

None
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:
☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☑

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

☑
Item 8.01 Other Events

Attached as Exhibit 99.1 is a presentation that Eleven Biotherapeutics, Inc. will post on its website on May 1, 2017 and may use from time to time in presentations or discussions with investors, analysts and other parties.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits.

<table>
<thead>
<tr>
<th>Exhibit No.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.1</td>
<td>Eleven Biotherapeutics, Inc. Presentation</td>
</tr>
</tbody>
</table>
SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ELEVEN BIOThERAPEUTICS, INC.

Date: May 1, 2017    By: /s/ John J. McCabe

John J. McCabe
Chief Financial Officer
<table>
<thead>
<tr>
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</table>
Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, clinical development of our protein therapies, potential milestone and royalty payments under the Roche license agreement, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make as a result of various important factors, including: the occurrence of any event change or other circumstances that could give rise to the termination of the Roche license agreement, the uncertainties inherent in receiving future payments pursuant to the Roche license agreement, the uncertainties inherent in the initiation and conduct of clinical trials, our ability to successfully develop our product candidates and complete our planned clinical programs, our ability to obtain marketing approvals for our product candidates, expectations regarding our ongoing clinical trials, availability and timing of data from clinical trials, whether interim results from a clinical trial will be predictive of the final results of the trial or results of early clinical studies will be indicative of the results of future studies, the adequacy of any clinical models, expectations regarding regulatory approvals, our ability to obtain, maintain and protect our intellectual property for our technology and products, availability of funding sufficient for the Company’s foreseeable and unforeseeable operating expenses and capital expenditure requirements, other matters that could affect the financial performance of the Company, other matters that could affect the availability or commercial potential of the Company’s product candidates and other factors discussed in the “Risk Factors” section of the Company’s Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and other reports on file with the Securities and Exchange Commission (SEC). The forward-looking statements contained in this presentation are made as of the date hereof, and Eleven assumes no obligation to update any forward-looking statements whether as a result of new information, future events, or otherwise except as required by applicable law.
How We Got Here: Eleven Biotherapeutics

• Cambridge, Massachusetts-based company founded in 2010 by Flagship Pioneering and Third Rock Ventures to engineer protein therapeutics for a wide variety of disorders
  – Formed with $55 million in venture capital; raised $57.5 million in 2014 IPO

• In August 2016, granted Roche exclusive license to EBI-031, a humanized monoclonal antibody that binds interleukin-6 (IL-6) and inhibits all forms of IL-6 cytokine signaling
  – Received $30 million in upfront and milestone payments
  – Eligible for additional $240 million upon achievement of future regulatory, development and commercialization milestones
  – Entitled to tiered royalties on net sales of future products containing EBI-031 and any future products containing other Eleven IL-6 compounds

• In September 2016, acquired Viventia Bio Inc.
  – Create targeted protein therapeutics oncology company
  – Pipeline of late-stage TPTs, including Vicinium and Proxinium
Investment Rationale

Proprietary Targeted Protein Therapeutics designed specifically to improve upon and overcome challenges of existing ADCs
- Dual action: direct killing of cancer cells promotes a systemic anti-tumor immune response
- Effective against quiescent cancer cells as well as cancer cells with multidrug resistance (MDR)

Lead drug candidate Vicinium™ in Phase 3 registration study for treatment of high-grade non-muscle invasive bladder cancer (NMIBC); initial data expected 2018
- In Phase 2 study, demonstrated complete response rate of 40% at 3 months

Broad pipeline of locally and systemically-administered product candidates
- Proxinium™, in development for squamous cell head and neck (SCCHN)
  - Demonstrated anti-tumor activity in prior Phase 1 and Phase 2 studies
  - Plan to initiate a Phase 1/2a trial in combination with a checkpoint inhibitor in 2H 2017
- VB6-845d, systemically-administered TPT, utilizes proprietary deBuogangin payload
  - Plan to file IND with FDA in Q1 2018

Strong corporate and financial position
- Management team and Board of Directors with extensive experience in oncology
- Over $25 million of cash at end of 2016; funds operations into early 2018
# Product Pipeline

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Payload</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
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<tbody>
<tr>
<td><strong>Locally-administered TPTs</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Vicinium</td>
<td>ETA</td>
<td>BCG refractory high-grade NMIBC</td>
<td></td>
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</tr>
<tr>
<td>Proxinium (combination with checkpoint inhibitor)</td>
<td>ETA</td>
<td>Late-stage SCCHN</td>
<td></td>
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</tr>
<tr>
<td><strong>Systemically-administered TPTs</strong></td>
<td></td>
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</tr>
<tr>
<td>VB6-845d</td>
<td>deBoug</td>
<td>Solid tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Partnered Assets</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>EBI-031 (Roche)</td>
<td>n/a</td>
<td>Diabetic Macular Edema</td>
<td></td>
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</tbody>
</table>
Targeted Protein Therapeutics: Overcoming the Limitations of Existing ADCs

- Deliver a greater amount of drug to tumor bed with deeper penetration
  - Engineered utilizing antibody fragments (single chains and Fabs) vs. intact Mabs

- Kill a broader array of cancer cell types within a targeted tumor
  - Powerful protein synthesis inhibitors designed to kill both rapidly proliferating and slower growing cancer cells potentially including cancer “stem cells”
  - Payload not subject to multidrug resistance (MDR)

- Clinical and pre-clinical data suggest targeted cell killing promotes cell-mediated anti-tumor immune responses
  - Immunogenic cell death signaling from dying cancer cells activates tumor-specific T cells
  - Potential combinations with checkpoint inhibitors and other I/O products
  - Unlike chemotherapy targeted to cancer - no damage to critical immune cell populations\(^1\)

- Potentially improved safety profile due to stable, genetically-engineered linkers
  - Product candidates are fusion proteins which are designed to remain intact until internalized into targeted cancer cell

- One-step manufacturing
  - More efficient than existing ADC manufacturing
  - E. Coli system lowers cost of goods
  - Single protein product candidates

\(^1\)Rébé & Ghiringhelli. Future Oncol. 2015 Sep 17
Fit for Purpose Design

Fully biologic constructs that are designed through recombination of key components as single gene-fused proteins

One Targeting Moiety + Linker + Protein toxin

- scFv
- Fab
- Diabody
- Furin Cleavable

or

- Non-Cleavable

- ETA
  (Pseudomonas Exotoxin A)

or

- DeBouganin

Designed for loco-regional delivery: Vicinium and Proxinium

De-immunized toxin designed for systemic delivery: VB6-845d
In Phase 3 for the Treatment of High-Grade NMIBC
Vicinium: Targeting High-Grade NMIBC

A Single Protein anti-EpCAM Antibody Fragment Fused With *Pseudomonas* Exotoxin A

**EpCAM target on NMIBC**
- EpCAM over-expressed in >98% of high grade NMIBCs – no companion diagnostic needed
- Minimal to no EpCAM expression on normal bladder cells
- Vicinium binds specifically to EpCAM+ cells

**Truncated *Pseudomonas* exotoxin A (ETA)**
- Potent payload (subpicomolar IC$_{50}$)
- Requires antibody binding to enter into a cell
- Induces Immunogenic Cell Death

**Designed specifically for Loco-Regional Delivery**
- Administered via intratumoral injection; mirrors standard of care
- Enters cell only after binding to EpCAM
Vicinium: Mechanism of Action

1. Vicinium targets EpCAM antigen
2. Vicinium is internalized once bound to EpCAM
3. Furin within endosome cleaves proteolytic site, releasing ETA
4. ETA hydrolyzes NAD, freeing ADP-R
5. ADP-R ribosylates diphthamide residue on EF-2
6. Modified EF-2 blocks protein synthesis and induces cell death
Significant Unmet Need in NMIBC

- Bladder Cancer - 2nd most common cancer of genitourinary system
  - Ninth most common cancer diagnosed worldwide (~430,000 new patients/year)\(^1\)
  - There are 79,000 new diagnoses of bladder cancer in the U.S. each year and an estimated 765,000 bladder cancer survivors
  - In the U.S., bladder cancer has the highest per patient treatment costs
    - Estimated overall cost of $3.9 billion annually

- Non-muscle invasive bladder cancer (NMIBC) is treated by urologists, accounts for 70-80% of all bladder cancers

- Bacillus Calmette-Guerin (BCG) with or without transurethral resection of the bladder tumor (TURBT) is first-line treatment for high-grade NMIBC
  - High failure rates in high-grade disease (50% within 1 year, 90% percent within 5 years)
  - Significant intolerant population

- No major advances in 40 years

\(^1\)World Cancer Research Fund (http://www.wcrf.org/int/cancer-facts-figures/worldwide-dataInternational)
NMIBC: Recent Events Underscore Unmet Medical Need

- In November 2016, Sanofi announced plans to stop producing BCG in mid-2017 due to manufacturing challenges
- In November 2016 the FDA released draft guidance:

BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment Guidance for Industry\(^1\)

The natural history of BCG-unresponsive NMIBC (CIS with or without resected disease) is that, in the absence of a pharmacologic intervention or cystectomy, CIS will almost always persist. In this setting, a single-arm clinical trial with complete response rate as the primary endpoint can provide primary evidence of effectiveness to support a marketing application.

- Our Phase 3 design is consistent with the draft guidance for providing primary evidence of effectiveness to support a marketing application
- Suggested the potential for Full Approval instead of Conditional Approval
Vicinium: Phase 1 Clinical Results

- 64 NMIBC patients with Grade 2 or 3 BCG refractory or intolerant
  - 95% of the patients had two or more bladder cancer recurrences
  - 55% had 2 or more BCG cycles
  - Only 5 of 64 were intolerant

- **Trial design**
  - Treated weekly x 6 weeks: Dose escalation (0.1 - 30.16 mg)
  - Efficacy assessment: Cystoscopy, Biopsy (Random and Directed), Urine Cytology

<table>
<thead>
<tr>
<th>Safety and Exploratory Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CIS population Complete Response (CR) rate at 3 months:</td>
</tr>
<tr>
<td>• Low Dose (0.1 mg - &lt;1.0mg): 1/6 (17%)</td>
</tr>
<tr>
<td>• High Dose (≥ 10.0mg): 4/11 (36%)</td>
</tr>
<tr>
<td>• Papillary patients: 19/44 (43%)</td>
</tr>
<tr>
<td>• No dose limiting toxicities (DLTs) reported. Well tolerated at these doses.</td>
</tr>
<tr>
<td>• No maximum tolerated dose (MTD) was reached.</td>
</tr>
<tr>
<td>• Significant difference (p-value 0.042) in the CR rate of the combined middle and highest dose group vs. the lowest dose group</td>
</tr>
</tbody>
</table>

Source: Kowalski et. al., Drug Design, Development and Therapy 4: 313, 2010
Vicinium: Phase 2 Clinical Results

- A total of 46 patients received 1 induction cycle of 6 (cohort 1) or 12 (cohort 2) weekly intravesical instillations of 30 mg
  - BCG refractory or intolerant carcinoma in situ (CIS) subjects
    - CIS is most aggressive form and toughest to treat NMIBC population
  - Refractory or intolerance to one or more courses of BCG
  - Maintenance cycle (1 x per week for 3 weeks) every 3 months in responders

- Primary endpoint: CR at 3 mo; assessed every 3 months up to 12 months

<table>
<thead>
<tr>
<th>Safety and Exploratory Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR rates</td>
</tr>
<tr>
<td>3 months: 40.9% (cohort 1) and 39.1% (cohort 2)</td>
</tr>
<tr>
<td>12 months: 13.6% (cohort 1) and 17.4% (cohort 2)</td>
</tr>
<tr>
<td>All patients that achieved CR at 1 year on 12 week arm remained disease-free at last follow-up visit (18-25 months)</td>
</tr>
<tr>
<td>Median time to recurrence: 408 days (12 week arm) vs. 274 days (6 week arm), p = 0.17</td>
</tr>
<tr>
<td>No significant toxicity or tolerability issues</td>
</tr>
</tbody>
</table>

Vicinium: Phase 2 Clinical Results

- Amount of prior BCG had no impact on responses
  - 12 week arm had the highest number of patients that had 2 or more courses of BCG
    - 10 of 22 patients in cohort #1 had ≥2 courses of BCG
      - 4 (40%) were CR at 3 months and 2 (20%) were a CR past 18 months
    - 16 of out 23 in cohort #2 had ≥2 courses of BCG
      - 7 (43.8%) were CRs at 3 months and 3 (18.8%) were CRs past 18 months

- Evidence supporting more frequent dosing:
  - A more durable response at 12 months was observed in cohort #2 (17.4%) versus cohort #1 (13.6%)
  - The median time to recurrence was greater for cohort #2 (408 days) versus cohort #1 (274 days)
  - Two patients in cohort 1 with persistent CIS at week 12 after a single induction treatment achieved a CR after first 3 week maintenance dosing

- Low Grade Disease:
  - Two patients (1 patient each cohort) remained free of CIS but developed low grade disease. As per Phase 2 protocol design, these patients were considered non-responders and were removed from the study.
  - Per our discussion with the FDA, development of low grade disease will not be considered a failure in our Phase 3 trial

- 73% of the non CRs showed reduction in tumor or stable disease

Vicinium: Phase 2 Clinical Results

6 Week Induction
CIS with or without Ta, T1

12 Week Induction
CIS with or without Ta, T1

Treatment Arm A Subjects (N=20)
Of the 46 subjects enrolled, 27 subjects (58.7%) had failed at least two rounds of BCG treatment (Only subjects (40/46) with baseline and 3 months bladder map data are included)
Adverse Events: Phase 1 and 2 Trials

• No significant toxicity or tolerability issues
  - Generally well tolerated
  - No subjects unable to complete treatment

• Phase 1 Trial
  - 31% of subjects experienced an AE related to treatment
  - 98% of all AEs were Grade 1 or 2
  - Incidence of AEs did not increase with dose
  - No treatment-related SAEs were reported

• Phase 2 Trial
  - 65% of subjects had an AE related to treatment
    - The majority being local bladder
    - Distribution of AEs similar in both treatment arms
  - 6 subjects reported SAEs. None of the SAEs were determined to be study drug related.

• AEs regardless of causality
  - Renal and urinary disorders were the most common adverse events
    - Hematuria, dysuria, pollakiuria, micturition urgency, urinary tract infections, nocturia, incontinence and bladder pain and spasms
  - The most frequent systemic adverse events
    - Fatigue and Dizziness
VISTA: Vicinium Phase 3 Registration Study

- Enrolling 134 patients (including 77 patients CIS) with BCG refractory or relapsed high-grade NMIBC (CIS and/or Papillary Tumors) at over 65 centers in the U.S. and Canada
- Increased induction and maintenance treatments
- Primary endpoint: CR for CIS subjects
- Secondary endpoints include: time to disease recurrence and event free survival
- Complete enrollment targeted 2H 2017, Initial data expected 2018

**Induction Phase**
- Weeks 1-6
  - Twice Weekly Dosing
- Weeks 7-12
  - Once Weekly Dosing

**Maintenance Phase**
- Up to Week 104
  - Every Other Week Dosing

Subjects with no evidence of high-grade disease
Treatment of Late-Stage SCCHN
Phase 1/2a Initiation Expected in 2H 2017
Proxinium: Targeting Late-Stage SCCHN

• Single chain anti-EpCAM antibody fragment fused with ETA
• Late-stage SCCHN is dominated by the primary tumor
  - 40-60% of deaths result from local or regional disease\(^1\)
  - 90% of patients with disseminated disease die as a result of uncontrolled disease at the primary site or in the neck\(^2\)
• The annual incidence of head and neck cancers worldwide is more than 650,000 cases with around 350,000 deaths each year\(^3\)
  - 2016 estimate of 46,330 new cases of oral cavity, pharyngeal and laryngeal tumors in the U.S. with ~9,570 deaths\(^4\)
• Surgery highly invasive and associated with significant morbidity
  - Five year survival rate of only 40-50%, depending on stage of advancement
  - Up to 70% of patients present with advanced disease
  - Recurrent disease often not suitable for additional surgery or radiation
• Standalone chemo/biologics have limited benefit
  - 2\(^{nd}\) line chemotherapy median survival is 103 days\(^2\); best supportive care median survival is 56 days\(^2\)
• Potentially complementary to checkpoint inhibitors

\(^{1}\)Cayman & Drewing, Injectable Monoclonals as Local and Regional Strategies for Head and Neck Cancer
\(^{3}\)Herold et al. Manistica. 2013; 8(1), 80-85
# Proxinium: Phase 1 Trials

<table>
<thead>
<tr>
<th></th>
<th>VB4-101</th>
<th>VB4-101A</th>
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<tbody>
<tr>
<td><strong>Location</strong></td>
<td>Russia</td>
<td>Brazil</td>
</tr>
<tr>
<td><strong>Schedule</strong></td>
<td>Daily x 5 q 28 days</td>
<td>Weekly x 4</td>
</tr>
<tr>
<td><strong>MTD</strong></td>
<td>200 μg</td>
<td>700 μg</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td><strong>EpCAM+</strong></td>
<td>17</td>
<td>18</td>
</tr>
</tbody>
</table>
| **Response Criteria – based on target lesion(s)** | - Investigator’s measurements  
- Investigator’s overall assessment including qualitative changes  
- Independent 3rd party assessment of available radiologic data |
| **Evaluable for Response** | 14                  | 16                  |
| **Antitumor Activity** | 43%                 | 62.5%               |
| **Dose-Limiting Toxicity** | LFT elevations  | LFT elevations      |
Proxinium: Phase 1 Clinical Trial Results

- EpCAM expression was not an inclusion criterion
  - EpCAM+ subjects were 71% (Russia) and 90% (Brazil)
  - None of the evaluable EpCAM- subjects (n=8) from either trial responded
- Three out of the four patients with complete responses had regression or complete resolution of noninjected lesions adjacent to the injected tumors
- Mean OS for EpCAM+ subjects was 196 days vs. 101 days for EpCAM- subjects
- Proxinium was generally well-tolerated
- The results from these two Phase 1 studies suggest that Proxinium may be effective in the treatment of EpCAM+ SCCHN
  - Weekly dosing chosen to move forward based on safety and efficacy profile

Sources: MacDonald et al. Drug Design, Development and Therapy 2: 105, 2008; MacDonald et al., Medical Oncology 26: 257, 2009
Proxinium: Responses in Targeted & Non-Targeted Tumors

Targeted tumor cell cytotoxicity may lead to cross-priming and immune therapy (T cell-mediated killing) of non-targeted tumors.
**Proxinium: Phase 2 Trial**

- Small study performed in N. America to verify safety of recommended dose
  - 15 EpCAM+ radiation and chemotherapy refractory late-stage SCCHN subjects

- Proxinium administered weekly at 500 µg or 700 µg via intratumoral injection
  - Confirmed 700µg as the recommended dose.

- Proxinium was generally well-tolerated with pain at the injection site as the most common AE

- Reduction in the bidirectional size of the principle targeted tumor observed in 71% (10/14) of the evaluable subjects
  - RECIST criteria not employed

- In 5 subjects with multiple tumors, growth control of the initial treated tumor was achieved in 4/5 subjects leading to treatment of additional tumors

(One non-evaluable subject who received a single dose not included in graph)
Proxinium + BSC vs. BSC summarized Phase 2 and Phase 3 data\(^1\)

REGIST criteria not employed

\(^1\)Only subjects with baseline and post-treatment tumor measurements are included (N = 36 for Proxinium + BSC; N = 26 for BSC only).
Immune Checkpoint Combinations

- Clinical trials suggest that Proxinium may be promoting host anti-tumor immune responses

- Immune checkpoint therapy requires an ongoing immune response
  - Effective in “hot” (inflamed) tumors often associated with somatic mutations

- Immunogenic Cell Death (ICD)$^1$
  - Promotes a pro-inflammatory environment
  - Release of tumor neoantigens from dying cells into this environment could drive adaptive cellular immune responses

- ICD by TPTs releases Damage Associated Molecular Patterns (DAMPs)
  - Cell death signals recognized by APCs (M1 phenotype)
  - Key DAMPs – calreticulin cell surface expression, active ATP release from the cell, passive release of high mobility group box 1 protein (HMGB1)
    - Not all cytotoxins mediate cell death equally - Mitomycin C – poor activator, doxorubicin is a good activator

Proxinium: ICD-induced DAMPs

Proxinium mediates ICD and induces DAMPs suggesting that it could promote host cellular anti-tumor immune responses

ATP release

*In vitro* ATP release from SW-480 tumor cells was observed following Proxinium treatment but not with a non-specific control (VB4-4B5)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Proxinium</th>
<th>VB4-4B5</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 hrs</td>
<td>5.7 ± 0</td>
<td>8.8 ± 0.1</td>
<td>5.8 ± 0.3</td>
</tr>
<tr>
<td>18 hrs</td>
<td>10.3 ± 0.3</td>
<td>17.05 ± 0.35</td>
<td>10.5 ± 0.1</td>
</tr>
<tr>
<td>36 hrs</td>
<td>9.75 ± 0.25</td>
<td>21.65 ± 0.55</td>
<td>11.5 ± 0.1</td>
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*measured by quinacrine using flow cytometry*

Cell Surface Calreticulin expression

*In vitro* expression of calreticulin on the cell surface was observed following Proxinium-mediated killing of SW-480 tumor cells

<table>
<thead>
<tr>
<th></th>
<th>NT</th>
<th>Proxinium</th>
<th>VB4-4B5</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 hours</td>
<td>22.5 ± 1.6</td>
<td>41.6 ± 1.9</td>
<td>16 ± 0.6</td>
</tr>
</tbody>
</table>

*measured by flow cytometry*

Source: R.L. Dillon, et al., AACR Annual Meeting, 2017
Proxinium: Robust Clinical Development Plan

- Observed responses in non-injected tumors during prior clinical trials and evidence from preclinical *in vitro* and animal studies suggest that Proxinium generates a host anti-tumor immune response that may improve the efficacy of checkpoint inhibitors

- Two checkpoint inhibitors that act by blocking PD-1, Opdivo and Keytruda, have been approved for treatment of SCCHN

- Plan to initiate Phase 1/2a trial evaluating Proxinium in combination with checkpoint inhibitors in patients with SCCHN in 2H 2017
De-Immunized Systemic Product Pipeline

deBouganin toxin

Bougainvillea sp.
deBouganin: Next Generation Payload

• Highly potent plant toxin
  – Picomolar killing, avoidance of MDR, potentially effective against cancer stem cells
  – Safety profile provides broad therapeutic window

• Engineered a de-immunized variant for systemic delivery

• Type 1 ribosome inactivating protein
  – RNA N-glycosidase causes deacylation of the 28S ribosome
  – Blocks translation inducing apoptotic cell death

• Cell cycle independent
  – Potentially effective against cancer stem cells

• Pilot Phase 1 study showed significant reduction in payload immunogenicity

• Plan to file IND in Q1 2018 for deimmunized TPT, VB6-845d
Corporate
## Experienced Leadership Team

### MANAGEMENT TEAM

**Steve Hurly**  
President, CEO, and Director

**Arthur DeCillis, MD**  
Chief Medical Officer

**John McCabe, CPA**  
Chief Financial Officer

**Greg Adams, PhD**  
Chief Scientific Officer

**Glen MacDonald, PhD**  
Chief Technology Officer

### BOARD OF DIRECTORS

Wendy L. Dixon, PhD - Chair

Abbie C. Celniker, PhD

Paul Chaney

Leslie L. Dan, BSc Phm, MBA, CM

Dan Lynch

Jay S. Duker, MD

Barry J. Gertz, MD, PhD

Jane V. Henderson
## Upcoming Milestones

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Timeframe</th>
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</thead>
<tbody>
<tr>
<td>Initiate Proxinium / Checkpoint SCCHN Phase 2 trial</td>
<td>2H 2017</td>
</tr>
<tr>
<td>Vicinium NMIBC Phase 3 complete enrollment</td>
<td>2H 2017</td>
</tr>
<tr>
<td>Submit IND to FDA for systemic product candidate VB6-845d</td>
<td>Q1 2018</td>
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<tr>
<td>Vicinium NMIBC Phase 3 topline data</td>
<td>2018</td>
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