

Payload Licensing Opportunity

VIVENTIA Biotechnologies Inc.

TARGETING CANCER WITH
POWER + PRECISION



De-Bouganin

- Highly potent, de-immunized protein payload for targeted cell therapy
- Suitable for fusion protein construction or chemical conjugation
- Excellent preclinical safety profile
- First-in-man clinical experience

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De-Bouganin Highlights

- **De-immunized payload with preliminary clinical validation**
- **Highly potent and well-defined mechanism of action**
- **Unaffected by MDR mechanisms unlike antibody drug conjugates**
- **Fusion protein engineering provides a stable linkage between payload and targeting molecule**
 - ◊ Also amenable to chemical conjugation
- **Scalable manufacturing process**
- **Simple single-stream production process translates to a more favorable cost of goods**
- **Exploratory clinical study**
 - ◊ Evidence of tumor response in 5 of 7 patients
 - ◊ Majority of treatment-related AEs were transient and assessed as mild or moderate

Overview

Native antibodies as monotherapies are often not sufficiently potent to be therapeutically effective. As such, Viventia Biotechnologies Inc. has developed a toxin payload technology that when coupled to an antibody is capable of increasing its therapeutic potential.

De-Bouganin Payload Technology

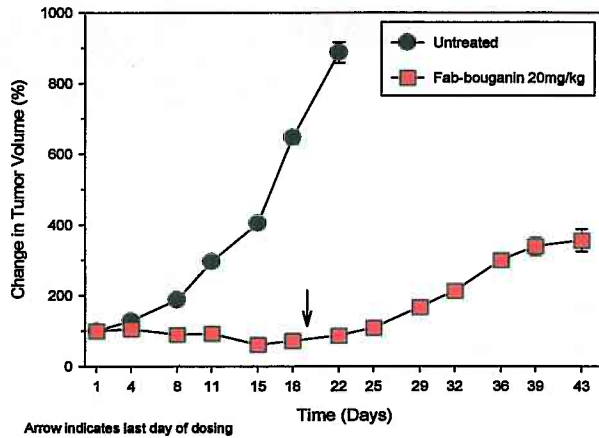
Bouganin is a plant-derived toxin that is unable to enter a cell unless attached to a targeting molecule like an antibody. Once inside the cell it blocks protein synthesis and ultimately induces cell death. As Bouganin is a protein foreign to the human body, Viventia has engineered a de-immunized form of the toxin, De-Bouganin, through the removal of T-cell epitopes. De-Bouganin has proven pre-clinical efficacy when attached to a targeting antibody as well as an excellent safety profile in animal models. At Viventia, De-Bouganin was added to an EpCAM-targeting Fab fragment to create the immunotoxin VB6-845 for clinical evaluation.

Clinical Experience

A first-in-man study was performed to evaluate the safety and tolerability of VB6-845 in patients with advanced solid tumors of epithelial origin. VB6-845 was administered as a monotherapy IV fusion, once weekly at two dose levels (1.0 and 2.0 mg/kg). In total, 13 patients were enrolled into 2 cohorts. Overall, VB6-845 was well tolerated and exploratory efficacy ranged from stable disease to evidence of tumor reduction. The lack of anti-De-Bouganin titers in patient samples confirmed the successful de-immunization of De-Bouganin.

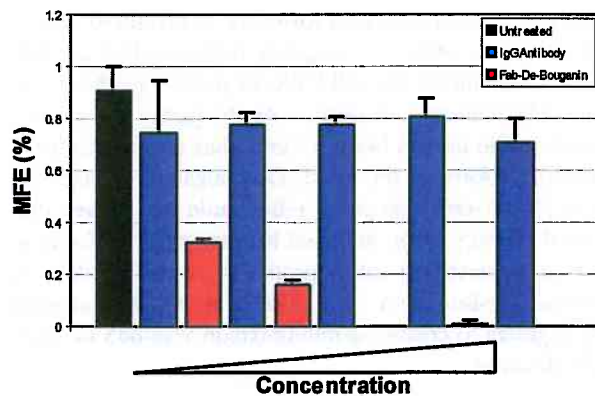
Preclinical Experience

Change in mean volume of untreated MCF-7 tumors versus tumors treated 5x per week for 3 consecutive weeks with 20mg/kg Fab-bouganin.

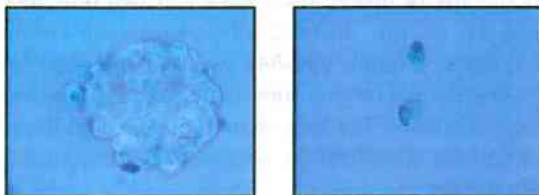


De-Bouganin vs. Cancer Stem Cells

De-Bouganin linked to a cancer stem cell targeting antibody fragment is superior to the corresponding IgG antibody in inhibiting stem cell mammosphere forming efficiency (MFE).



Vital cell staining shows De-Bouganin-linked Fab fragments block MFE by killing cancer stem cells.



Business Opportunities

Viventia holds world-wide rights to the development of De-Bouganin. Direct access to De-Bouganin technology can be achieved through licensing and technology transfer. Viventia has the in-house expertise to co-develop molecules with the licensee to expedite drug development by:

- Molecular engineering of different drug formats for rapid assessment
- Knowledge of process development strategies for De-Bouganin-conjugated drugs
- Research grade production of drug to support preclinical development
- cGMP manufacture of drug to support clinical trials
- CMC, Regulatory and Clinical experience with De-Bouganin-conjugated drugs

Publications

1. Cizeau J, Grenkow D, Brown J, et al. (2009) Engineering and Biological Characterization of VB6-845, an Anti-EpCAM Immunotoxin Containing a T-cell Epitope-depleted Variant of the Plant Toxin Bouganin. *Journal of Immunotherapy* 32 (6): 574-584
2. Chaboureau A, Ragon I, Stibbard S, et al. (2008) Intracellular trafficking of VB6-845, an immunocytotoxin containing a de-immunized bouganin. *AACR*
3. Entwistle J, MacDonald G, Glover N. (2005) Epitope-Depleted Bouganin: An innovative, antibody-directed, cytotoxic payload for a safer and more efficacious treatment of cancer. *AACR*
4. Rasamoeliso M, Cizeau J, Bosc D, et al. (2005) Functional and biological characterization of VB6-845, a recombinant Ep-CAM-specific Fab antibody genetically-linked with de-immunized Bouganin (de-bouganin). *AACR*
5. Cizeau J, Bosc D, Rasamoeliso M, et al. (2005) Recombinant engineering of an Ep-CAM-specific Fab antibody (VB6-845) with de-immunized bouganin. *IBC Protein Engineering*

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