Multidisciplinary Program
November 2016
Cellceutix Corporation
100 Cummings Center
Suite 151B
Beverly, MA 01915
Safe Harbor; Forward-Looking Statements

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Corporate Focus and Management Team

Established in 2007, Cellceutix is a clinical-stage biopharmaceutical company dedicated to discovering and developing innovative compounds with dermatology, oncology, anti-inflammatory and antibiotic applications.

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Title</th>
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<tbody>
<tr>
<td>Leo Ehrlich</td>
<td>Chief Executive Officer, Chief Financial Officer</td>
<td>Co-Founder; Investor</td>
</tr>
<tr>
<td>Krishna Menon, PhD, DVM</td>
<td>Chief Scientific Officer</td>
<td>Co-Founder</td>
</tr>
<tr>
<td>Arthur P. Bertolino, MD, PhD, MBA</td>
<td>President, Chief Medical Officer</td>
<td>[Lilly]</td>
</tr>
<tr>
<td>Jane Harness, MS, MP</td>
<td>VP, Clinical Sciences and Portfolio Management</td>
<td>[Novartis, Pfizer]</td>
</tr>
<tr>
<td>LaVonne Lang, DrPH</td>
<td>VP, Regulatory Affairs</td>
<td>[Pfizer]</td>
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**Board of Directors:** Leo Ehrlich; Krishna Menon, PhD, DVM; Barry Schechter, MD; Zorik Spektor, MD; Mark Tobin, MBA
First-in-Class Drug Candidates

Cellceutix has **three lead drug candidates**, each with **first-in-class potential** across a number of therapeutic areas and clinical indications, advancing in mid-to-late stage clinical trials under various special FDA designations.

**Prurisol**

*Orally-delivered psoriasis* drug candidate in a Phase 2b trial utilizing advantages of the 505(b)(2) development approach

**Kevetrin**

*p53-modulating* drug candidate with three Orphan Drug designations starting a Phase 2a trial for *ovarian cancer*

**Brilacidin**

*Drug candidate in a new antibiotic class* with unique immunomodulatory properties advancing in clinical trials under Fast Track designations
Pipeline—Clinical Asset by Therapeutic Area

**Dermatology**
- Psoriasis*
  - [Atopic Dermatitis**]

**Infectious Disease**
- ABSSSI
  - [Acne]
  - [HS]

**Gastrointestinal**
- Inflammatory Bowel Disease (IBD)
  - Ulcerative Colitis (UC)
    - (Proctitis/Proctosigmoiditis)**
    - [Crohn’s Disease]

**Cancer**
- Ovarian Cancer
  - [Renal Cancer]
  - [Pancreatic Cancer]
  - [Pediatric Retinoblastoma]

**Oral Mucositis**

**Biologics**

**Prurisol**
- Potential future indications
- [Biofilms]

**Kevetrin**
- Hidradenitis Suppurativa
- ABSSSI - Acute Bacterial Skin and Skin Structure Infection

**Brilacidin**

---

*Utilizing advantages of FDA 505(b)(2) development approach for Prurisol (shortens development time, reduces costs)

**A type of Ulcerative Colitis (UC) characterized by mucosal inflammation of unknown cause involving only the rectum and the sigmoid

***Both oral Prurisol and a topical formulation of Brilacidin may prove beneficial in treating atopic dermatitis

---

**Pipeline—Clinical Asset by Therapeutic Area**

**Dermatology**
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***Both oral Prurisol and a topical formulation of Brilacidin may prove beneficial in treating atopic dermatitis

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Pipeline—Clinical Asset by Stages of Development

Exceptionally strong pipeline, novel mechanisms of action

<table>
<thead>
<tr>
<th>Drug Candidate</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<tbody>
<tr>
<td>Prurisol</td>
<td>Psoriasis&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
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<tr>
<td>Kevetrin</td>
<td>Ovarian Cancer&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td>Brilacidin</td>
<td>ABSSSI&lt;sup&gt;3,4&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Oral Mucositis&lt;sup&gt;5&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>IBD: UC (UP/UPS)&lt;sup&gt;6&lt;/sup&gt;</td>
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- Planned to enter clinic

<sup>1</sup> Utilizing advantages of 505(b)(2) development approach; a Phase 2 trial evaluated Prurisol in mild-to-moderate psoriasis, with the ongoing Phase 2b trial—a randomized, double-blind, parallel-group, placebo-controlled study with approximately 189 patients to be enrolled—evaluating Prurisol in moderate-to-severe psoriasis

<sup>2</sup> Awarded Orphan Drug Designation

<sup>3</sup> ABSSSI - Acute Bacterial Skin and Skin Structure Infection

<sup>4</sup> Awarded Qualified Infectious Disease Product (QIDP) Designation (qualifies for Fast Track and Priority Review)

<sup>5</sup> Awarded Fast Track Designation

<sup>6</sup> Inflammatory Bowel Disease (IBD); UC - Ulcerative Colitis (UP/UPS - Ulcerative Proctitis/Ulcerative Proctosigmoiditis)

Leveraging data from clinical studies in other indications to expedite development
Pipeline—Clinical Asset by Status of Trial

Three lead drug candidates in mid-to-late stage clinical trials; company has yet to fail a clinical trial

<table>
<thead>
<tr>
<th>Clinical Trials</th>
<th>Brilacidin</th>
<th>Prurisol</th>
<th>Kevetrin</th>
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</thead>
<tbody>
<tr>
<td><strong>Completed</strong></td>
<td>ABSSSI* (Phase 2b)</td>
<td>Psoriasis (Pso)*** (Phase 2)</td>
<td>Solid Tumors (Phase 1)</td>
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<tr>
<td><strong>Ongoing</strong></td>
<td>Oral Mucositis (OM) (Phase 2)</td>
<td>Psoriasis (Pso)**** (Phase 2b)</td>
<td></td>
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<tr>
<td></td>
<td>IBD: UC (UP/UPS)** (Phase 2a)</td>
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<tr>
<td><strong>Planned</strong></td>
<td>ABSSSI* (Phase 3)</td>
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<td>Ovarian Cancer (OC) (Phase 2a)</td>
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<tr>
<td></td>
<td>Crohn’s Disease</td>
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<td>Hidradenitis Suppurativa (HS)</td>
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<td></td>
<td>Acne</td>
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<td></td>
<td>Atopic Dermatitis</td>
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* ABSSSI - Acute Bacterial Skin and Skin Structure Infection

** IBD - Inflammatory Bowel Disease; UC - Ulcerative Colitis (UP/UPS - Ulcerative Proctitis/Ulcerative Proctosigmoiditis)

*** In a Phase 2 trial, Prurisol was tested in mild-to-moderate psoriasis

**** In a Phase 2b trial, Prurisol is being tested in moderate-to-severe psoriasis
Pipeline—Clinical Asset by Special FDA Designation

Leveraging designations to expedite development, improve likelihood of drug approval, gain market exclusivity

<table>
<thead>
<tr>
<th>Drug Candidate</th>
<th>Designation Type</th>
<th>Date Granted</th>
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<tbody>
<tr>
<td>Kevetrin</td>
<td>Orphan Drug Designation for Ovarian Cancer</td>
<td>July 2015</td>
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<tr>
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<td>Orphan Drug Designation for Retinoblastoma</td>
<td>November 2015</td>
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<td>Rare Pediatric Disease Designation for Retinoblastoma</td>
<td>November 2015</td>
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<td></td>
<td>Orphan Drug Designation for Pancreatic Cancer</td>
<td>January 2016</td>
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<td>Brilacidin</td>
<td>QIDP* Fast Track Designation for ABSSSI**</td>
<td>December 2014</td>
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<td>Fast Track Designation for Oral Mucositis</td>
<td>November 2015</td>
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*QIDP – Qualified Infectious Disease Product  
**ABSSSI – Acute Bacterial Skin and Skin Structure Infection
Brilacidin Franchise

A First-in-Class Host Defense Protein (HDP) Mimic
Host Defense Protein (HDP) Mimics

Background & Rationale

Small, non-peptidic, fully synthetic mimics of HDPs developed as a systemic or topical agent*

- **HDPs are Small Antimicrobial Peptides**
  - Expressed widely in the animal kingdom
  - Produced in skin, mucosal surfaces, neutrophils
  - Target microbial membrane
- **First Line of Defense Against Foreign Invasion**
  - Part of innate immunity
  - Maintenance of epithelial barrier function
  - Regulate microbiota
  - Immunomodulatory – innate and adaptive immunity
  - Anti-inflammatory properties
- **Addresses Global Problem of Antimicrobial Resistance**
  - Gram-positive (e.g., MRSA) and Gram-negative (e.g., CRE) programs (identified by CDC and FDA as high priority pathogens)

*Note: Brilacidin, as an arylamide foldamer and unlike peptidic-based small molecules (e.g., Pexiganan), is not subject to the traditional shortcomings of antimicrobial peptide (AMP)-based compounds, including rapid proteolytic degradation. Instead, by using sophisticated coarse-grain computer modeling that mimicked the actions of natural defensins (electrostatics, lipophobicity, etc.), it was designed to be smaller (one-tenth the size) and then fine-tuned to exhibit enhanced pharmacological properties—more easily and much less expensively synthesized, more stable (a rigid backbone), more potent (by a 100-fold) and more selective (by a 1000-fold). This biocomputational aspect of Brilacidin’s development has resulted in the drug candidate having much better exposure and efficacy in terms of its pharmacokinetics.

Sources:
- “New Weapons for the Germ Wars: Inexpensive Polymers can Extend the Range of Nature’s Germ-Fighter Arsenal.” (pdf)
- http://www.pnas.org/content/99/8/5110.long
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2646611/
- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2808429/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2153456/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2667368/
- https://deepblue.lib.umich.edu/bitstream/handle/2027.42/100268/mabi201300126.pdf
- https://deepblue.lib.umich.edu/bitstream/handle/2027.42/94848/1199_Htp.pdf
Brilacidin
First-in-Class Anti-Inflammatory/Anti-Microbial Drug Candidate

Brilacidin is the first of a completely new class of anti-inflammatory antibiotics. A small, non-peptidic, fully synthetic mimetic of Host Defense Proteins (HDPs): uniquely functions in an immunomodulatory capacity, (lessening inflammation and promoting healing) and, in addition, kills bacteria quickly.

Mechanism of Action

- Immunomodulatory and anti-inflammatory
  - Inhibits the production of TNF-α, IL-1β, IL-6, IL-8, MIP2-α, MCP-1, MMP-9
  - HDP dysfunction implicated in inflammatory disorders of skin and mucosal surfaces
    - Inflammatory bowel disease (IBD), atopic dermatitis, acne, skin infections, cystic fibrosis…
  - Brilacidin functions as an anti-microbial, piercing the cell walls of bacteria (bactericidal)

Unique Mechanism of Action Fundamentally Different from ALL Current Systemic Antibiotics

Note:
- Received FDA QIDP Fast Track designation for ABSSSI (additional 5 years of market exclusivity in the U.S.)
- Strong IP/Patent protections
"The most relevant biological role of host defense peptides is immunomodulation." (source)

"Despite the success of biologic therapies in many areas in the autoimmune and autoinflammatory disease field, there is growing interest in effective and orally available small-molecule approaches." (source)

**Brilacidin**

**Clinical Literature Supporting Therapeutic Potential (Immunomodulation, Inflammation)**

- "Antimicrobial Peptides: Do They Have a Future as Therapeutics?" Part of the series Birkhäuser Advances in Infectious Diseases pp 147-154 Date: 25 December 2015.

Source: http://www.cell.com/trends/immunology/abstract/S1471-4906%2809%2900005-2
Brilacidin
Inhibits PDE4 and Suppresses Cytokines/Chemokines, Lessening Inflammation and Promoting Healing

Beyond its antimicrobial properties—which itself can play a major role in treating certain inflammatory diseases given the association between pathogens and host organisms, inflammation and infection (e.g., see the link between Enterobacteriaceae and IBD; the link between Crohn’s and E. coli [against which HDP-Mimics have shown activity]; and the link between Crohn’s and infections)—Brilacidin functions through the cyclic AMP/cyclic GMP pathways to suppress pro-inflammatory cytokines and chemokines, such as TNF-α, IL-1β, IL-6, IL-8, MIP2-α, MCP-1 and MMP-9.

Brilacidin’s inhibition of PDE4—a predominant phosphodiesterase expressed in neutrophils, T cells, macrophages and keratinocytes—leads to an increase in the intracellular cAMP concentration, thereby reducing the production of pro-inflammatory mediators and increasing anti-inflammatory mediators.

Additional research is underway to determine Brilacidin’s role in regulating IL-17, a central driver most inflammatory diseases, including many skin diseases.

Sources:
http://discoverpde4.com/
http://www.sinobiological.com/Proinflammatory-cytokines-list.html
Brilacidin

Inhibition of PDE4B2 and PDE3A

Phosphodiesterase inhibition assays demonstrated that Brilacidin inhibits both PDE4B2 (IC$_{50}$ of 2.5 ± 0.21µM; n=5) and PDE3A (IC$_{50}$ of 1.5 ± 0.2µM; n=4) in a dose dependent manner.

The PDE-Glo phosphodiesterase assay was performed using 8ng of PDE4B2 and 2.75ng of PDE3A, respectively, with 1µM cAMP substrate and indicated amount of Brilacidin.

Brilacidin and PDE4B2 and PDE3A, respectively, were mixed and pre-incubated at room temperature for 15 minutes. Substrate was added and the reaction was incubated for 7 minutes at room temperature.
Brilacidin reduced the severity of Ulcerative Colitis (UC) induced by DSS administered through drinking water in mice. Brilacidin 400mg/kg were given intra-rectally once per day for 5 days. 5-amino salicylic acid (5-ASA) was used as a positive control. At the end of experiments, animals were anaesthetized. Their abdomens were opened and colons were washed directly with cold PBS (pH7) and immediately cut into small 1cm piece (distal portion) and transferred to liquid nitrogen container for further study. Frozen colon tissues were lysed and protein concentrations were measured and all samples were diluted to equal concentration. IL-6 and IL-1β were measured according to manufacturer’s instruction.

**Mouse Ulcerative Colitis: IL-1β**

Effects of Brilacidin on DSS-induced IL-1β. The data were normalized to the total proteins. Levels of IL-1β levels presented as treated UC with Brilacidin (400mg/kg) relative to untreated UC. 5-ASA were used as positive control.

**Mouse Ulcerative Colitis: IL-6**

Effects of Brilacidin on DSS-induced IL-6. The data were normalized to the total proteins. Levels of IL-6 levels presented as treated UC with Brilacidin (400mg/kg) relative to untreated UC. 5-ASA were used as positive control.
Gastrointestinal

Inflammatory Bowel Disease (IBD):
Ulcerative Proctitis/Ulcerative Proctosigmoiditis (UP/UPS)

Dermatology/Cancer

Oral Mucositis (OM)
Brilacidin for IBD

Inflammatory Bowel Disease (IBD)—A Difficult-to-Treat Chronic Condition

- **Group of inflammatory conditions of colon & small intestine**
  Principle types: *Ulcerative colitis (UC)* and *Crohn’s disease (CD)* ([Ulcerative proctitis (UP) and Ulcerative Proctosigmoiditis (UPS) are subcategories of UC)]

- **Autoimmune etiology**

- **Main GI symptoms**: abdominal pain, vomiting, diarrhea, rectal bleeding, severe internal abdominal/pelvic cramps/muscle spasms and weight loss

- **Recurrences are common**: disease also associated with increased risk of co-morbidities

- **Medications for treatment include**: Aminosalicylates, corticosteroids, immune modifiers, anti-TNF agents (*biologics*), and antibiotics

Sources:
- http://tmedweb.tulane.edu/pharmwiki/doku.php/inflammatory_bowel_disease_ibd
- http://www.slideshare.net/afzalhaqasif/inflammatory-bowel-disease2014; Cellceutix research
Study Design

- Open-label, sequential dose escalation
- Brilacidin (N=6 per cohort) retention enema once daily for 42 days
  - Cohort A: 50 mg
  - Cohort B: 100 mg
  - Cohort C: 200 mg

Objectives

Primary:
- Assess frequency of clinical and endoscopic remission
  - Brilacidin retention enema administered per rectum in subjects with active UP or UPS
  - 6 weeks of treatment

Interim Results in First Study Cohort

All 4 subjects evaluated demonstrated a clinical response, measurable by the Modified Mayo Disease Activity Index (MMDAI)

- Partial MMDAI (Day 42)
  - 2 of 4 subjects achieved full response (100% reduction)
  - 2 of 4 subjects had notable improvement (50% reduction)

- MMDAI (Day 42; 3 of 4 subjects completed endoscopy)
  - 1 of 3 subjects achieved full response (100% reduction)
  - 2 of 3 subjects had notable improvement (50% reduction)

- Patient Quality of Life, as measured by the Short Inflammatory Bowel Disease Questionnaire (SIBDQ)
  - Improved after 6-week treatment with Brilacidin

- Safety
  - Generally well-tolerated
  - Subjects had stable normal vital signs

- Drug Concentrations in Plasma
  - All levels at all time points below the lower limit of quantification (ie, <100 ng/mL),
  - Consistent with very limited systemic exposure from administration per rectum by enema
Brilacidin for IBD
Market Opportunity, Competitive Landscape

BioWorld: IBD: As Biosimilars Advance, Players Jockey for Position (February 2016)
“Although TNF alpha inhibitors still lead the list of clinical trials for drugs targeting IBD, UC and Crohn’s, and glucocorticoid agonists appear in the top 10, biopharmas are quickly moving on to other mechanisms.”
“Many in the field cited a new spirit of openness about GI disorders for bringing deserved attention to the unmet medical need in the space.”
“The science emerging in IBD is changing.”

*In trials, not yet approved for general use. Biosimilars of infliximab are not considered in this review.


The Global Burden of IBD: from 2015 to 2025
Latest GED-0301 Results
From Celgene Generating a Mixed Reaction
Motley Fool
The Street
Xconomy
EP Advantage
In The Pipeline
Reflecting Earlier Skepticism
Endpoints; The Street; FierceBiotech

Ozanimod in UC only slightly better than placebo
Biogen backs out of its SP1 modulator
Brilacidin for OM
Oral Mucositis—a Painful Complication of Chemoradiation Afflicting Hundreds of Thousands

**Clinical Overview**

- Frequent complication of chemoradiation for head and neck tumors
- Painful and debilitating inflammation & ulceration; increases susceptibility to bacterial infections
- Patients unable to speak or eat (often requires insertion of feeding tube)
- Can be dose-limiting leading to reduction/cessation of radiation and chemotherapy for cancer
- Severe cases require hospitalization
- No currently approved medications for prevention of OM in this population

Brilacidin for OM
Oral Mucositis—Animal Model Results (Phase 2 Trial in Progress)

Pre-Clinical

Study Design:
• Brilacidin-OM administered 3x/day as topical rinse @ doses of 0.3, 1, 3 or 10 mg/ml over 28 days
• Reduced animal days w/ ulcerative oral mucositis by >90%
  • From 42.7% to 2.4%
  • High statistical significance

Results seen with Brilacidin-OM:

Primary Endpoints
• Control and prevent oral mucositis in patients receiving chemoradiation therapy for Head and Neck Cancer
• Efficacy of topically-applied Brilacidin vs placebo in delaying the onset of severe OM (WHO Grade ≥ 3)
• Safety and tolerability of topically-applied Brilacidin administered three times daily for approximately 7 weeks

For study details, see https://clinicaltrials.gov/ct2/show/NCT02324335

Phase 2 Trial

Study Design
• Phase 2, Multi-center, Randomized, Double-blind, Placebo-controlled (10 sites in US expanding to up to 20)
• 60 subjects – 30 each of drug or placebo (Water for Injection)
• “Swish and spit” Brilacidin 3x/daily for 7 weeks – 16 ml oral rinse
• Interim analysis after 36 subjects (18 per treatment group) by a Data Monitoring Committee (DMC); will review safety and efficacy results

Clinical Predictability of the Hamster Oral Mucositis Models

Studies by Dr. Stephen Sonis, Harvard

Effect in animal model vs Effect in Clinic
% reduction % reduction

ActoGenix
AG018 (HIF-1)
33% 30%

SciClone
SCV-07
33% 30%

Volafermin
(bFGF-20)
37% 51%

*Cellceutix Clinical Advisor

BRLACIDIN 94%

Interim Phase 2 Results Anticipated Q2 2017
Brilacidin for OM

Oral Mucositis—Market Opportunity, Competitive Landscape

- Significant Market
  - ~400,000-450,000 patients/year in U.S. alone\(^1\)
  - ~167,000 patients in US at risk for ulcerative oral mucositis
  - 80-100% of head and neck cancer patients develop ulcerative oral mucositis

- Cost of Mucositis
  - 4-fold increased risk for septicemia in oral mucositis\(^2\)
  - 62% of patients require hospitalization; 70% with grade 3 or 4 require gastric feeding tubes\(^2\)
  - Oral mucositis adds ~$18,500 to the cost of treatment\(^3\)
  - 2010 Red Book price of Kepivance: $9,900 per treatment cycle (six infusions)

- Limited Competition
  - Only one drug available (Kepivance for IV infusion; limited label); some medical devices with no or little relevant efficacy data (e.g., Gelclair)
  - Limited treatment alternatives and development pipeline

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Brilacidin’s low level of systemic exposure, as revealed in the ongoing Phase 2 trial in Ulcerative Proctitis (UP)/Proctosigmoiditis (UPS)—measurements of concentrations of Brilacidin in plasma showed all levels, across all time points, to be below the lower limit of quantification, i.e., <100 ng/mL—suggests that multiple inflammatory conditions might be treated locally and efficaciously with the drug.

“Understanding and controlling inflammation has become a central goal of modern medical investigation.”

Dr. Jerome Groopman

Sources: “How Cytokine Networks Fuel Inflammation: Toward a Cytokine-Based Disease Taxonomy” (Nature Medicine 19, 833-824 2013);
“The Immunology of Host Defence Peptides: Beyond Antimicrobial Activity” (Nat Rev Immunol 2106 May; 16(5):321-34.)
Host Defense Protein (HDP) Mimics
Gateway Concept/Platform Potential

**Innate Immunity**

<table>
<thead>
<tr>
<th>Direct Antimicrobial Activity</th>
<th>Barrier Function</th>
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<tbody>
<tr>
<td><strong>Bacterial</strong></td>
<td><strong>Respiratory Mucosa</strong></td>
</tr>
<tr>
<td>• <em>ABSSSI (skin)</em></td>
<td>• Cystic Fibrosis</td>
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<tr>
<td>• Bone and Joint</td>
<td>• Asthma</td>
</tr>
<tr>
<td>• DFIs</td>
<td>• Chronic Bronchitis</td>
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<td>• Respiratory</td>
<td>• Lung-ARS</td>
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<td>• Blood Stream</td>
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<td><strong>GI Mucosa</strong></td>
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<tr>
<td>• Ulcerative Proctitis **</td>
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<td>• IBD</td>
<td>• Burns/Abrasions</td>
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<tr>
<td>• Oral Mucositis</td>
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<tr>
<td>• IBS</td>
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<tr>
<td>• GI-Acute Radiation Sickness</td>
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<td>• Periodontitis</td>
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**Parasitic**
- Malaria
- Sleeping Sickness
- Giardiasis

**Viral**
- Influenza
- Herpes
- RSV

*ABSSSI is gateway for antibiotic opportunities
**Ulcerative Proctitis is gateway for anti-inflammatory opportunities
## Brilacidin Franchise

### Intellectual Property and Patent Overview

<table>
<thead>
<tr>
<th>Patent Title</th>
<th>Status</th>
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| **Ophthalmic And Otic Compositions Of Facially Amphiphilic Polymers And Oligomers And Uses Thereof** | United States: allowed  
Europe: issued 03/04/15  
Japan: issued 04/04/14; 05/15/15  
Australia: issued 11/28/13  
China: issued 12/07/11; 10/01/14  
Pending: Canada, India, Australia  
Patents Expire: 2027 | Category 1 – **Brilacidin**  
Brilacidin compound; compositions; methods of treating bacterial otic and ophthalmic infections |
| **Synthetic Mimetics Of Host Defense And Uses Thereof** | United States: issued 10/02/12; 03/10/15  
Taiwan: issued 04/01/15  
Australia: issued 11/28/13  
China: issued 01/08/14  
Mexico: issued 09/28/12  
Russia: issued 01/27/15  
Ukraine: issued 03/25/14  
Pending: Europe, Japan, Brazil, Canada, India, Israel, South Korea, Mexico  
Patents Expire: 2029 | Category 1 – Arylamide compounds  
Brilacidin enantiomer; compositions and formulations; methods of preparation of enantiomer; methods of preparation of Brilacidin |
## Brilacidin Franchise
### Intellectual Property and Patent Overview (continued)

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<th>Country</th>
<th>Issuance Dates</th>
<th>Expire Dates</th>
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<td>Brilacidin and related compounds; anti-microbial surfactants and related compounds</td>
<td>United States: issued 02/06/07; 11/18/14</td>
<td>Patents Expire: 2022</td>
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1. Patent family owned by The Trustees of The University of Pennsylvania.
2. Patent family owned by The Trustees of The University of Pennsylvania.
## Brilacidin Franchise

### Intellectual Property and Patent Overview (continued)

<table>
<thead>
<tr>
<th>Category 1</th>
<th>Compounds For Use In Treatment Of Mucositis</th>
<th>United States: issued 08/12/14; allowed Pending: United States, Europe, Japan, Taiwan, Australia, Brazil, Canada, China, Israel, Mexico, New Zealand, Russia, South Korea, Ukraine, South Africa</th>
<th>Category 1 – Brilacidin Methods of treating mucositis with Brilacidin and related compounds; compositions of Brilacidin and palifermin</th>
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<td>Compounds And Methods For Treating Candidiasis And Aspergillus Infections</td>
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<td>Category 1 – Anti-fungal compounds Methods of killing or inhibiting the growth of a Candida or Aspergillus species or preventing or treating a mammal having oral or disseminated candidiasis or an aspergillus infection;</td>
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<td>Compositions Of Arylamide Compounds And Antimicrobial Agents</td>
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<td>Category 1 – Arylamide compounds in combination with anti-microbial agents</td>
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<td>Antimicrobial Compounds</td>
<td>United States: provisional pending</td>
<td>Category 1 – Anti-microbial compounds</td>
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1 Patent family co-owned with the University of Massachusetts Amherst.
1 Patent family co-owned with Rutgers, The State University of New Jersey.
Host Defense Protein (HDP) Mimetics For Prophylaxis And/Or Treatment Of Inflammatory Diseases Of The Gastrointestinal Tract
US 20160243117 A1

ABSTRACT

The present invention provides methods for treating and/or preventing inflammatory diseases of the gastrointestinal tract with one or more compounds, or pharmaceutically acceptable salts thereof, disclosed herein, and the use of compositions comprising the same.

See:
https://www.google.com/patents/US20160243117
USPTO Filing

Source:
Wuerth, Kelli C; Hilchie, Ashley L; Brown, Kelly L; and Hancock, Robert EW (May 2013) “Host Defence (Antimicrobial) Peptides and Proteins.” In: eLS. John Wiley & Sons, Ltd: Chichester.
Additional Information
**Brilacidin**

*Inhibition of TNF-α, IL-1β, IL-6*

![Graph 1](image1.png)

**Fig. 1.** Effects of Brilacidin on LPS-induced TNF-α release in NR8383 cells. Rat macrophages (NR8383) were pretreated with Brilacidin with concentrations shown for 45 minutes, followed by LPS (1µg/ml) treatment for 8 hrs. After 8 hrs, supernatants were collected for TNF-α measurement by ELISA.

![Graph 2](image2.png)

**Fig. 2.** Effects of Brilacidin on LPS-induced IL-6 release in NR8383 cells. Rat macrophages (NR8383) were pretreated with Brilacidin with concentrations shown for 45 minutes, followed by LPS (1µg/ml) treatment for 8 hrs. After 8 hrs supernatants were collected for IL-6 measurement by ELISA.

![Graph 3](image3.png)

**Fig. 3.** Effects of Brilacidin’s on IL-1β production in rat macrophage cells pretreated with the compound. Brilacidin demonstrated a strong inhibition of IL-1β induction after LPS stimulation. There was more than 50% decrease in IL-1β production within 8 hrs of treatment at 2.5µM concentration of Brilacidin.
Brilacidin

Inhibition of IL-8, MIP2-α

Effects of Brilacidin on LPS-induced IL-8 production in THP-1 cells. THP-1 cells were pretreated with Brilacidin with concentrations shown for 45 minutes, followed by LPS (1µg/ml) treatment for 8 hrs. After 8 hours, IL-8 concentrations were determined by ELISA using an immunoassay kit specific for human IL-8 (Thermo Fisher). Brilacidin inhibited the LPS-induced IL-8 production in THP-1 cells in a dose-dependent manner.

Effects of Brilacidin on LPS-induced MIP-2a (Rat CINC-3) release in NR8383 cells. Rat macrophages (NR8383) were pretreated with Brilacidin with concentrations shown for 45 minutes, followed by LPS (1µg/ml) treatment for 8 hrs. After 8 hrs, supernatants were collected for MIP-2a (Rat CINC-3) measurement by ELISA. A 65% decrease in CINC-3 levels at a 2.5µM concentration of brilacidin was observed.
Brilacidin

Inhibition of MCP-1, MMP-9

Effects of Brilacidin on LPS-induced MCP-1 release in NR8383 cells. Rat macrophages (NR8383) were pretreated with Brilacidin with concentrations shown for 45 minutes, followed by LPS (1µg/ml) treatment for 8 hrs. After 8 hrs, supernatants were collected for MCP-1 measurement by ELISA.

Effects of Brilacidin on LPS-induced MMP-9 release in NR8383 cells. Rat macrophages (NR8383) were pretreated with Brilacidin with concentrations shown for 45 minutes, followed by LPS (1µg/ml) treatment for 8 hrs. After 8 hrs, supernatants were collected for MCP-1 measurement by ELISA.