Dermatology Program
November 2016

First-in-Class Drug Candidates
With dermatology, oncology, anti-inflammatory, and antibiotic applications

100 Cummings Center, Beverly, MA

Ticker: CTIX
Safe Harbor; Forward-Looking Statements

This presentation contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 that involve risks, uncertainties and assumptions that could cause Cellceutix’s actual results and experience to differ materially from anticipated results and expectations expressed in these forward-looking statements. Cellceutix has in some cases identified forward-looking statements by using words such as “anticipates,” “believes,” “hopes,” “estimates,” “looks,” “expects,” “plans,” “intends,” “goal,” “potential,” “may,” “suggest,” and similar expressions. These forward-looking statements include, but are not limited to, statements concerning future drug development plans and projected timelines for the initiation and completion of preclinical and clinical trials; the potential for the results of ongoing preclinical or clinical trials and the efficacy of Cellceutix’s drug candidates; the potential market opportunities and value of drug candidates; other statements regarding future product development and regulatory strategies, including with respect to specific indications; any statements regarding Cellceutix’s future financial performance, results of operations or sufficiency of capital resources to fund its operating requirements; any statements relating to Cellceutix’s planned uplisting or use of proceeds; and any other statements that are not statements of historical fact. Forward-looking statements involve risks and uncertainties, which may cause Cellceutix’s actual results, performance or achievements to be materially different from those expressed or implied by forward-looking statements. Such forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions and uncertainties. Among other factors that could cause actual results to differ materially from those expressed in forward-looking statements are Cellceutix’s need for, and the availability of, substantial capital in the future to fund its operations and research and development, including the amount and timing of the sale of shares of common stock to Aspire Capital; Cellceutix’s ability to continue to fund and successfully progress internal research and development efforts and to create effective, commercially-viable drugs; and the fact that Cellceutix’s compounds may not successfully complete pre-clinical or clinical testing, or be granted regulatory approval to be sold and marketed in the United States or elsewhere. A more complete description of these risk factors is included in Cellceutix’s filings with the Securities and Exchange Commission. You should not place undue reliance on any forward-looking statements. Forward-looking statements speak only as of the date on which they are made. Cellceutix undertakes no obligation to release publicly the results of any revisions to any such forward-looking statements that may be made to reflect events or circumstances after the date of this presentation or to reflect the occurrence of unanticipated events, except as required by applicable law or regulation.
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>Co-Founder; Investor</th>
</tr>
</thead>
<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>Novartis, Pfizer</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>
</tr>
</tbody>
</table>

Board of Directors: Leo Ehrlich; Krishna Menon, PhD, DVM; Barry Schechter, MD; Zorik Spektor, MD; Mark Tobin, MBA
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]
  - [Biofilms]

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

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

**Potential future indications**

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* 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

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**Cellceutix**

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6
**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>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prurisol</strong></td>
<td>Psoriasis&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Kevetrin</strong></td>
<td>Ovarian Cancer&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
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<tr>
<td><strong>Brilacidin</strong></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>
<td></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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<tr>
<td>Crohn’s Disease</td>
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<tr>
<td>Hidradenitis Suppurativa</td>
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<tr>
<td>Acne</td>
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<tr>
<td>Atopic Dermatitis</td>
<td></td>
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</tbody>
</table>

Planned to enter clinic  

Leveraging data from clinical studies in other indications to expedite development

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<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)
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>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Completed</strong></td>
<td>ABSSSI*</td>
<td>Psoriasis (Pso)***</td>
<td>Solid Tumors (Phase 1)</td>
</tr>
<tr>
<td></td>
<td><em>(Phase 2b)</em></td>
<td><em>(Phase 2)</em></td>
<td></td>
</tr>
<tr>
<td><strong>Ongoing</strong></td>
<td>Oral Mucositis (OM)</td>
<td>Psoriasis (Pso)****</td>
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<tr>
<td></td>
<td><em>(Phase 2)</em></td>
<td><em>(Phase 2b)</em></td>
<td></td>
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<tr>
<td><strong>Planned</strong></td>
<td>ABSSSI*</td>
<td></td>
<td>Ovarian Cancer (OC)</td>
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<tr>
<td></td>
<td><em>(Phase 3)</em></td>
<td></td>
<td><em>(Phase 2a)</em></td>
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<tr>
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</tr>
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</table>

* 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>
</tr>
</thead>
<tbody>
<tr>
<td>Kevetrin</td>
<td>Orphan Drug Designation for Ovarian Cancer</td>
<td>July 2015</td>
</tr>
<tr>
<td></td>
<td>Orphan Drug Designation for Retinoblastoma</td>
<td>November 2015</td>
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<tr>
<td></td>
<td>Rare Pediatric Disease Designation for Retinoblastoma</td>
<td>November 2015</td>
</tr>
<tr>
<td></td>
<td>Orphan Drug Designation for Pancreatic Cancer</td>
<td>January 2016</td>
</tr>
<tr>
<td>Brilacidin</td>
<td>QIDP* Fast Track Designation for ABSSSI**</td>
<td>December 2014</td>
</tr>
<tr>
<td></td>
<td>Fast Track Designation for Oral Mucositis</td>
<td>November 2015</td>
</tr>
</tbody>
</table>

*QIDP – Qualified Infectious Disease Product

**ABSSSI – Acute Bacterial Skin and Skin Structure Infection
Prurisol for Psoriasis

A First-in-Class Oral Psoriasis Drug Candidate
84% of those with moderate to severe psoriasis report suffering discrimination and humiliation.

Psoriasis
Debilitating Chronic Disease That Affects Millions

- 7.5 million people afflicted
- Most common autoimmune disease in the U.S.
- Large unmet therapeutic need
- Patient survey (Lebwohl et al., 2014):
  - 46% feel that therapies worse than disease itself
  - 85% state that there is need for better therapies

Sources:
http://apps.who.int/iris/bitstream/10665/204417/1/9789241565189_eng.pdf
http://www.uptodate.com/contents/treatment-of-psoriasis
http://www.cytherapharm.com/
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0052935
Psoriasis
A Multibillion Dollar Market

Biologics continue to flare up the psoriasis market, indicating opportunities in the larger dermatology space.

Sources:
http://www.nature.com/nrd/journal/v14/n11/full/nrd4763.html
Prurisol for Psoriasis

*The Goal: A Best-in-Class Oral Drug...*

...that treats many types of psoriasis, regardless of disease severity and with an efficacy approaching that of biologics but without the harmful side effects.

**Prurisol**

Prurisol for Psoriasis
Market Opportunity, Competitive Landscape

Otezla® (apremilast), the main potential oral competitor, demonstrates only moderate efficacy by week 16.*

Celgene expects Otezla® to earn revenue of up to $1 billion in 2016 and in the range of $1.5 billion–$2 billion in 2017.

Recent Psoriasis Deals

$490 million
Monomethylfumarate prodrug

$640 million
RORγt IL-17 modulation

$595 million
Anti-IL-23 mAb

Source: [http://www.baystreet.ca/articles/research_reports/lifesci/Can-Fite%20BioPharma041216.pdf](http://www.baystreet.ca/articles/research_reports/lifesci/Can-Fite%20BioPharma041216.pdf); Cellceutix research
Prurisol for Psoriasis

MOA and Attributes

**Mechanism of Action (MOA)**

- Acts through immune modulation and PRINS* reduction
  - Reduces IL-20
  - Reduces skin cell proliferation rate

**Attributes**

- NCE with strong Intellectual Property (IP) and patent protections
- **Accelerated development plan** utilizing advantages of 505(b)(2) development approach [reference drug: Abacavir]
- **Efficacy in Phase 2 trial in mild-to-moderate chronic plaque psoriasis**
- Oral dosing
- Small-molecule (<500 MW) (an ester of Abacavir)
- Bioavailable
- Excellent in-vivo and in-vitro activity
- Efficacy in xenograft model

*PRINS – Psoriasis-associated non-protein coding RNA induced by stress

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**Molecular formula:** $\text{C}_{16}\text{H}_{20}\text{N}_6\text{O}_3$

**Molecular weight:** 344.37

[Abacavir (α-hydroxy) acetate; abacavir glycolate]
New Imiquimod-induced Psoriasis Mouse Model for In Vivo Efficacy Screening


Imiquimod-Induced Psoriasis Efficacy Studies - The Jackson Laboratory
https://www.jax.org/...mice.../imiquimod-induced-psoriasis

- BALB/C mice treated daily with IMQ cream or control cream on the back of the animal close to the tail
- 16 days of treatment; assessed every 2nd day for erythema, scales and thickness; Scale 0 to 4
- Calculated a cumulative score of erythema + scaling + thickness of the skin
- 2 daily doses of Prurisol 10mg/kg had greatest reduction in cumulative score (94% compared to IMQ cream alone)
- Ziagen® (Abacavir) similar to IMQ cream alone
Human psoriatic skin xenograft model; SCID mice received 350 rad total body irradiation, then transplanted with psoriatic human tissue.

Four groups:
- 10 mg/kg Prurisol orally once per day for 21 days
- 10 mg/kg Prurisol orally twice per day for 21 days
- 7.5 mg/kg methotrexate (MTX) intraperitoneally daily for 5 days
- Saline control

96% reduction in PRINS with 2 daily doses of Prurisol compared to controls.

Single daily doses of Prurisol reduced levels of PRINS to comparable extent as MTX.

IL-20 reduced by 69% and 87% after treatment with one or two daily doses of Prurisol; 46% reduction with MTX.
Prurisol for Psoriasis

CTIX-0001: Prurisol Bioequivalence Trial

- AUC values were comparable for both Prurisol and Ziagen, within 80% to 125% equivalence window, indicating equivalent systemic exposure
- No serious adverse events, or other significant adverse events occurred over the course of the study

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>Prurisol 350 mg</th>
<th>Ziagen 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/mL)</td>
<td>2.816 ± 703 (16)</td>
<td>3.617 ± 885 (16)</td>
</tr>
<tr>
<td>Tmax (hr)</td>
<td>0.88 (16)</td>
<td>0.75 (16)</td>
</tr>
<tr>
<td>AUC(0-t) (hr×ng/mL)</td>
<td>7.781 ± 2,072 (16)</td>
<td>8,420 ± 2,573 (16)</td>
</tr>
<tr>
<td>AUC(0-∞) (hr×ng/mL)</td>
<td>7.901 ± 2,079 (16)</td>
<td>8,523 ± 2,582 (16)</td>
</tr>
<tr>
<td>1/2 (l/hr)</td>
<td>0.3854 ± 0.1103 (16)</td>
<td>0.4033 ± 0.1183 (16)</td>
</tr>
<tr>
<td>t½ (hr)</td>
<td>2.00 ± 0.84 (16)</td>
<td>2.02 ± 1.30 (16)</td>
</tr>
<tr>
<td>CL/F (L/hr)</td>
<td>46.0 ± 12.8 (16)</td>
<td>38.5 ± 12.2 (16)</td>
</tr>
<tr>
<td>Vz/F (L)</td>
<td>136 ± 78.1 (16)</td>
<td>109 ± 67.5 (16)</td>
</tr>
</tbody>
</table>

*Arithmetic mean ± standard deviation except for Tmax for which the median range is reported. (N) Number of subjects.

For study details, see [https://clinicaltrials.gov/ct2/show/NCT02101216](https://clinicaltrials.gov/ct2/show/NCT02101216)

**[Abacavir (α-hydroxy) acetate; abacavir glycolate]**
### Primary Efficacy Endpoint:

Percentage of subjects with ≥ 2 point improvement in IGA rating at 84 days (12 weeks).

Investigator Global Assessment (IGA) rating: clear (0), almost clear (1), mild (2), moderate (3), severe (4), very severe (5).

- Randomized, double-blind, parallel-group, placebo-controlled.
- 4 treatment groups, 1:1:1:1 randomization, 12 weeks treatment.
  - Prurisol:
    - 50 mg daily (50 mg AM)
    - 100 mg daily (50 mg AM & 50 mg PM)
    - 200 mg daily (100 mg AM & 100 mg PM)
  - Placebo AM & PM

- Trial conducted at 9 sites in U.S.
- 115 subjects, 4 arms, ~29 per arm.
- Efficacy, Safety & PK

For study details, see [https://clinicaltrials.gov/ct2/show/NCT02494479](https://clinicaltrials.gov/ct2/show/NCT02494479)
Individually with mild-to-moderate chronic plaque psoriasis

- Clinical diagnosis of stable (at least 6 months) plaque psoriasis, not including scalp or intertriginous areas
- Body surface area (BSA) affected by plaque psoriasis of 10% to 20% inclusive
- Investigator Global Assessment (IGA) score of “mild” (2) or “moderate” (3) (using IGA rating scale; 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, 5=very severe)
- Identification of a target psoriatic lesion with a score of at least “moderate” (3) on the Target Lesion Assessment for Scaling (TLA) scale

*(HLA-B*5701-negative patients)*
## Prurisol for Psoriasis

### CTIX-0002: Patient Demographics

Characteristics at Baseline were similar for all 4 treatment groups

<table>
<thead>
<tr>
<th>ITT Population Baseline Characteristic</th>
<th>Prurisol 50 mg (N=29)</th>
<th>Prurisol 100 mg (N=28)</th>
<th>Prurisol 200 mg (N=28)</th>
<th>Placebo (N=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), Mean (SD)</td>
<td>57.7 (11.11)</td>
<td>55.2 (13.55)</td>
<td>56.9 (15.02)</td>
<td>55.9 (11.25)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>48.3</td>
<td>60.7</td>
<td>64.3</td>
<td>53.3</td>
</tr>
<tr>
<td>Female (%)</td>
<td>51.7</td>
<td>39.3</td>
<td>35.7</td>
<td>46.7</td>
</tr>
<tr>
<td>Hispanic or Latino (%), [ethnicity]</td>
<td>89.7</td>
<td>89.3</td>
<td>89.3</td>
<td>90.0</td>
</tr>
<tr>
<td>White (%), [race]</td>
<td>93.1</td>
<td>89.3</td>
<td>92.9</td>
<td>93.3</td>
</tr>
<tr>
<td>Weight (kg), Mean (SD)</td>
<td>80.66 (17.75)</td>
<td>81.41 (16.84)</td>
<td>83.43 (18.65)</td>
<td>80.44 (16.98)</td>
</tr>
<tr>
<td>BSA Affected (%), Mean (SD)</td>
<td>14.19 (3.57)</td>
<td>14.23 (3.56)</td>
<td>14.11 (3.56)</td>
<td>14.42 (3.44)</td>
</tr>
<tr>
<td>Baseline IGA=2, n (%)</td>
<td>12 (41.4)</td>
<td>8 (28.6)</td>
<td>9 (32.1)</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td>Baseline IGA=3, n (%)</td>
<td>17 (58.6)</td>
<td>20 (71.4)</td>
<td>18 (64.3)</td>
<td>23 (76.7)</td>
</tr>
<tr>
<td>Baseline IGA Missing, n (%)</td>
<td>-</td>
<td>-</td>
<td>1 (3.6)</td>
<td>-</td>
</tr>
</tbody>
</table>
Prurisol for Psoriasis

CTIX-0002: Primary Efficacy Endpoint (Percentage of Subjects ≥ 2-point improvement in IGA at Week 12)

At Week 12 (200 mg group), 25.9% subjects (ITT) and 35.0% subjects (PP) achieved ≥ 2-point improvement in IGA

<table>
<thead>
<tr>
<th>Week 12 Analysis</th>
<th>Prurisol 200 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT population (LOCF imputation)</td>
<td>n/N1, (%)</td>
<td>7/27 (25.9)</td>
</tr>
<tr>
<td>Difference in % vs placebo</td>
<td></td>
<td>+12.6 (p=0.3179)</td>
</tr>
<tr>
<td>PP population</td>
<td>n/N1, (%)</td>
<td>7/20 (35.0)</td>
</tr>
<tr>
<td>Difference in % vs placebo</td>
<td></td>
<td>+18.3 (p=0.2778)</td>
</tr>
</tbody>
</table>

Note: The p-values generated from this study were for informational purposes only and statistical significance was not a criterion for study success (cf protocol section 9.8)

n = number of subjects with ≥ 2-point improvement in IGA, with missing IGA scores imputed with LOCF
N1 = number of subjects with available IGA score
p-value from Fisher's exact test comparing proportions in Prurisol and Placebo group
Prurisol for Psoriasis

CTIX-0002: ≥ 2-point Improvement in IGA Over Time

- Clinical improvement observed in 200 mg group as early as 4 weeks
- ≥ 2-point IGA improvement (200 mg group) at Week 12 was 25.0% subjects (ITT) and 35.0% subjects (PP)

* ITT population denominator for % calculation based upon subject population at baseline
Prurisol for Psoriasis

CTIX-0002: IGA Scores Over Time (200 mg group) & Topline Results

- IGA changes noted as soon as Week 2
- Progressive decrease of IGA scores to lower values over 12 weeks
- Time-based transition of original moderate & mild population to less psoriasis activity with emergence of almost clear and clear groups
  - At Week 12: 42.8% subjects (ITT) [and 55.0% subjects (PP)] achieved “clear” (0) or “almost clear” (1) in IGA

*Where % subject total <100%, basis is attrition without data imputation

Prurisol 200 mg* (ITT Population)

Prurisol met the primary endpoint (a 2-point IGA reduction) in 35% of all patients who received a dose of 200 mg per day (Per Protocol).

- Prurisol was well-tolerated—just one Serious Adverse Event (SAE) occurred and it was in the 50 mg dose group
- PK results showed a dose-dependent increase in drug exposure and maximum plasma concentration

Among patients with the severest form of psoriasis in study, those having a baseline IGA score of 3 (“moderate”), the primary endpoint was met in 46% of patients who received 200 mg per day. These data were derived from analyses of all patients.
Prurisol for Psoriasis
CTIX-0002: Safety Summary (Generally Well-Tolerated)

• Adverse Events
  For the Prurisol dose groups combined:
  • Headache was the most frequently reported AE (6 AEs, 7.1%)
  • One Serious Adverse Event (preferred term “hepatic enzyme increased”) reported in 50 mg dose group
  • Liver function test increases reported as AEs, with following frequency:
    • Aspartate Aminotransferase (AST) increased, 4 AEs; Alanine Aminotransferase (ALT) increased, 3 AEs; Hepatic enzyme increased, 1 AE

• Clinical Laboratory Review
  • Blood chemistry changes of clinical significance observed for a small number of subjects, most notable in AST and ALT
  • Seven (7) subjects had on-treatment ALT and/or AST elevations >2xULN
  • Elevations in ALT and/or AST do not appear dose related; n=2 in each active group, n=1 in placebo group
  • No associated increases noted for bilirubin
  • Hematology changes were generally not clinical significant, no trending (increasing or decreasing) noted
  • Urinalysis findings were not clinically significant

• Vitals Signs Assessments were without clinically significant changes
Prurisol for Psoriasis

CTIX-0002: Pharmacokinetics of Abacavir

Dose-related increase in exposure and plasma concentrations observed

- Comparable plasma concentrations expected for 50 mg AM and 50 mg AM & PM doses due to short t½ (1.24 hr and 1.27 hr, respectively); however values higher for the AM & PM regimen

- Less than dose proportional increase in mean plasma concentrations, Cmax and AUC, between 50 mg AM & PM (100 mg daily) and 100 mg AM & PM (200 mg daily)

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>Prurisol Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50 mg AM</td>
</tr>
<tr>
<td>Cmax (n g/mL)</td>
<td>209 ± 87.6 (8)</td>
</tr>
<tr>
<td>Tmax (hr)</td>
<td>1.00 (8)</td>
</tr>
<tr>
<td>AUC(0-t) (hr×ng/mL)</td>
<td>[0.50 - 4.00]</td>
</tr>
<tr>
<td>AUC(0-∞) (hr×ng/mL)</td>
<td>522 ± 228 (8)</td>
</tr>
<tr>
<td>Vz (L/hr)</td>
<td>462 ± 161 (6)</td>
</tr>
<tr>
<td>t½ (hr)</td>
<td>0.5801 ± 0.1340 (6)</td>
</tr>
<tr>
<td>CL/F (L/hr)</td>
<td>1.24 ± 0.24 (6)</td>
</tr>
<tr>
<td>Vz/F (L)</td>
<td>107 ± 62.5 (6)</td>
</tr>
<tr>
<td></td>
<td>194 ± 120 (6)</td>
</tr>
</tbody>
</table>

*Arithmetic mean ± standard deviation (N) except for Tmax for which the median (N) [Range] is reported.

- Median Tmax, ranged from 0.5 hr to 1.0 hr
- Mean t½, ranged from 1.24 hr to 1.40 hr, appears to be independent of dose or regimen
- Small numbers of subjects per group
  (Note: larger sample size planned in next study for more definitive PK parameter calculations)
Prurisol for Psoriasis

Summary Observations, Looking Ahead

- The primary efficacy endpoint of percentage of subjects with ≥ 2-point improvement in IGA was met with the 200 mg Prurisol dose group achieving highest magnitude of effect.
- A clear progressive decrease of IGA scores to lower values was seen as early as 2 weeks and further improved out through 12 weeks (200 mg group).
- Sufficient clinical improvement was observed to warrant more detailed examination of clinical responses to treatment at 200 mg and higher dosing levels.
- Prurisol was generally well-tolerated.
- As ⅔rd of these subjects (200 mg group) had Baseline IGA=3 (“moderate” psoriasis), their favorable responses serve as a bridge to investigate Prurisol in a moderate-to-severe psoriasis population.
- A Phase 2b trial has begun 4Q16 evaluating higher dosing regimens (300 mg and 400 mg) in moderate-to-severe psoriasis, using proportion of subjects achieving PASI75 at Week 12 as the primary endpoint.

Press Releases


Prurisol for Psoriasis
Phase 2b Clinical Trial in Moderate-to-Severe Plaque Psoriasis (Currently Enrolling Patients)

- Randomized, double-blind, parallel-group, placebo-controlled

- Treatment Groups
  - Prurisol 300 mg: Pbo: Prurisol 400 mg
  - 3:3:1

- Number of Subjects
  - ~189

- Treatment Duration
  - 12 weeks (interim readout 2Q17)

- Number of Sites (U.S.)
  - ~30

For study details, see https://clinicaltrials.gov/ct2/show/NCT02949388
Prurisol for Psoriasis
Intellectual Property and Patent Overview

Granted Patents

United States (Patent No 8895569) (Composition of Matter claim)

“Carbocyclic Nucleosides and Their Pharmaceutical Use and Compositions”

Abstract: Abstract of the Disclosure Disclosed are compounds of the formula and the pharmaceutically acceptable salts of such compounds. Also disclosed are Aprocesses for the preparation of such compounds, intermediates used in the preparation of such compounds, and the uses of such compounds in treating inflammatory skin diseases.

Australia (Patent No 2012363635)
Singapore (Patent No 11201404291T)
Taiwan (Patent No 1481611)

Pending Patents

Argentina, Bangladesh, Brazil, Canada, China, E Patent Office, Hong Kong, India, Israel, Japan, Malaysia, Mexico, Pakistan, South Korea, Thailand

Patents Expire 2032
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, lipophilicity, 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/PMC2908429/
- 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_fbp.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)

Note:
- Received FDA QIDP Fast Track designation for ABSSSI (additional 5 years of market exclusivity in the U.S.)
- Strong IP/Patent protections
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/Pro-inflammatory-cytokines-list.html
Host Defense Protein (HDP) Mimics
Gateway Concept/Platform Potential

**Innate Immunity**

**Direct Antimicrobial Activity**
- **Bacterial**
  - ABSSSI (skin)*
  - Bone and Joint
  - DFI
  - Respiratory
  - Blood Stream
  - STDs

- **Fungal**
  - Oral Candidiasis
  - Disseminated Candidiasis
  - Aspergillosis

- **Parasitic**
  - Malaria
  - Sleeping Sickness
  - Giardiasis

- **Viral**
  - Influenza
  - Herpes
  - RSV

**Barrier Function**
- **GI Mucosa**
  - Ulcerative Proctitis **
  - IBD
  - Oral Mucositis
  - IBS
  - GI-Acute Radiation Sickness
  - Periodontitis

- **Respiratory Mucosa**
  - Cystic Fibrosis
  - Asthma
  - Chronic Bronchitis
  - Lung-ARS
  - Chronic Sinusitis

- **Skin/Eye**
  - Hidradenitis Suppurativa
  - Acne
  - Atopic Dermatitis
  - Diabetic Ulcers
  - Keratitis
  - Burns/Abrasions

---

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

**ABSSSI Phase 2b Clinical Trial Results**

#### Early Clinical Response at 48-72 hours

<table>
<thead>
<tr>
<th></th>
<th>Brilacidin 0.6 mg/kg IV x 1 day (N=53)</th>
<th>Brilacidin 0.8 mg/kg IV x 1 day (N=53)</th>
<th>Brilacidin x 3 days (N=53)</th>
<th>Daptomycin X 7 days (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number assessed</td>
<td>51</td>
<td>48</td>
<td>52</td>
<td>48</td>
</tr>
<tr>
<td>Clinical Response (%)</td>
<td>47 (92.2)</td>
<td>46 (95.8)</td>
<td>51 (98.1)</td>
<td>45 (93.8)</td>
</tr>
<tr>
<td>95% C.I.</td>
<td>(84.8, 99.5)</td>
<td>(90.2, 100)</td>
<td>(94.3, 100)</td>
<td>(86.9, 100)</td>
</tr>
</tbody>
</table>

#### Current Perspectives

- Safe and effective in three Phase 2 studies
- Convenient single-dose regimen
  - Pharmacoeconomic advantages
- Efficacy comparable to 7-day regimen of robust comparator (daptomycin x 7 days)
- QIDP designation (Nov 2014) under the GAIN Act
  - Eligible for Fast Track and Priority Review
- Minimal potential for development of resistance
  - Novel class, with no cross-resistance
  - Novel mechanism of action confers fitness disadvantage for bacterial resistance
  - Single dose removes non-compliance as driver for resistance
- Phase 3 planning in progress
  - Response to Special Protocol Assessment (SPA) comments from FDA in process

*Acute Bacterial Skin and Skin Structure Infections*
**Hidradenitis Suppurativa** (acne inversa):

- A debilitating inflammatory skin disease characterized by recurrent abscesses and formation of sinus tracts, typically where skin rubs together, e.g., armpits, groin, between the buttocks and under the breasts.

- The etiology of the disease, which causes significant physical and psychosocial distress to both men and women, remains largely not understood (though a bacterial component may be at work, as might a similar pathogenic mechanism to that of Chron’s disease), with no cure and only limited treatment options.

- Reports of prevalence range widely from approximately one-half a percent up to approximately four percent of the general population.

- Beyond its well-documented antimicrobial properties, Brilacidin also has a broad range of anti-inflammatory effects on various key effector cells that may be involved in Hidradenitis Suppurativa.

Brilacidin for Acne, Atopic Dermatitis (Eczema)
Other Potential Future Indications (Topical Application)

“...inflammation in skin diseases while avoiding unwanted adverse effects.” (source)

Activity of brilacidin and comparators against evaluated Propionibacterium spp.¹

<table>
<thead>
<tr>
<th>MIC (μg/mL)</th>
<th>Brilacidin</th>
<th>Erythromycin</th>
<th>Clindamycin</th>
<th>Minocycline</th>
<th>Doxycycline</th>
<th>Metronidazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIC₅₀</td>
<td>0.5</td>
<td>0.03</td>
<td>0.03</td>
<td>0.06</td>
<td>0.12</td>
<td>&gt;64</td>
</tr>
<tr>
<td>MIC₉₀</td>
<td>1</td>
<td>&gt;128</td>
<td>1</td>
<td>0.25</td>
<td>0.5</td>
<td>&gt;64</td>
</tr>
<tr>
<td>MIC range</td>
<td>0.25 to 2</td>
<td>0.015 to &gt;128</td>
<td>≤0.015 to &gt;16</td>
<td>0.03 to 2</td>
<td>0.03 to 4</td>
<td>&gt;64</td>
</tr>
</tbody>
</table>

¹Propionibacterium spp. includes: P. jensenii, P. granulosum, P. avidum, P. acnes

Contrasting Brilacidin and Crisaborole

- The human skin microbiome is influenced by bacterial infection in a complex manner.
- It has been hypothesized that increased susceptibility of people with atopic dermatitis to S. aureus infections, which is significantly over-expressed in this skin condition, may arise from the impaired expression of Host Defense Proteins (HDPs).
- Unlike Crisaborole (AN2728), Brilacidin, as an antimicrobial agent, is highly active against S. aureus. It also acts to inhibit numerous pro-inflammatory cytokines and chemokines.
- Brilacidin shows a distinct advantage in that the drug exhibits a strong inhibitory effect on IL-1 whereas Crisaborole shows no such activity. IL-1 is linked to the pathogenesis of numerous diseases, including rheumatic disease and eczema.
- According to the National Eczema Association, 17.8 million Americans have moderate-to-severe atopic dermatitis, contributing to an annual cost burden to society of $5.3 billion.


Pfizer Acquires Anacor

By 2022, $5.6 billion in Global Sales

Eczema Market

$5.2 billion
<table>
<thead>
<tr>
<th>Patent Title</th>
<th>Status</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ophthalmic And Otic Compositions Of Facially Amphiphilic Polymers And Oligomers And Uses Thereof</strong></td>
<td>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</td>
<td>Category 1 – Brilacidin Brilacidin compound; compositions; methods of treating bacterial otic and ophthalmic infections</td>
</tr>
<tr>
<td><strong>Synthetic Mimetics Of Host Defense And Uses Thereof</strong></td>
<td>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</td>
<td>Category 1 – Arylamide compounds Brilacidin enantiomer; compositions and formulations; methods of preparation of enantiomer; methods of preparation of Brilacidin</td>
</tr>
</tbody>
</table>
# Brilacidin Franchise

**Intellectual Property and Patent Overview (continued)**

<table>
<thead>
<tr>
<th>Category 1 &amp; 3 – Brilacidin and related compounds; anti-microbial surfactants and related compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Facially Amphiphilic Polymers As Anti-infective Agents</strong></td>
</tr>
<tr>
<td>United States: issued 02/06/07; 11/18/14 Australia: issued 04/05/07; 04/12/07 Canada: issued 07/16/13 China: issued 07/01/09; 07/02/14 Europe: issued 09/17/08; 05/25/11 Japan: issued 08/15/08 South Korea: issued 06/03/09; 06/16/09</td>
</tr>
<tr>
<td>Patents Expire: 2022</td>
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<tr>
<td><strong>Facially Amphiphilic Polyaryl And Polyarylalkynyl Polymers And Oligomers And Uses Thereof</strong>^3</td>
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<tr>
<td>United States: issued 07/17/12; 05/06/14 Australia: issued 03/08/12 Japan: issued 05/02/13 Taiwan: issued 03/11/13</td>
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<tr>
<td>Pending: Canada, Europe (2)</td>
</tr>
<tr>
<td>Patents Expire: foreign (2025); United States (2028)</td>
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<tr>
<td><strong>Facially Amphiphilic Polymers And Oligomers And Uses Thereof</strong>^3</td>
</tr>
<tr>
<td>United States: issued 08/07/12; 06/04/13 Australia: issued 04/07/11; 03/27/14 Canada: issued 05/20/14 South Korea: issued 03/04/13 Taiwan: issued 05/21/15</td>
</tr>
<tr>
<td>Pending: Australia, China, India, Japan, Taiwan</td>
</tr>
<tr>
<td>Patents Expire: foreign (2024); United States (2027)</td>
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<tr>
<td><strong>Antimicrobial Copolymers And Uses Thereof</strong></td>
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<tr>
<td>Canada: issued 08/26/14</td>
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<tr>
<td>Pending: United States</td>
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<tr>
<td>Patent Expires: 2025</td>
</tr>
</tbody>
</table>

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[^3]: Patent family owned by The Trustees of The University of Pennsylvania.
## Brilacidin Franchise

### Intellectual Property and Patent Overview (continued)

<table>
<thead>
<tr>
<th>Compounds For Use In Treatment Of Mucositis</th>
<th>United States: issued 08/12/14; allowed</th>
<th>Category 1 – Brilacidin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pending: United States, Europe, Japan, Taiwan, Australia, Brazil, Canada, China, Israel, Mexico, New Zealand, Russia, South Korea, Ukraine, South Africa</td>
<td>Methods of treating mucositis with Brilacidin and related compounds; compositions of Brilacidin and palifermin</td>
<td></td>
</tr>
<tr>
<td>Patents Expire: 2032</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Polycyclic Compounds And Methods Of Making And Using The Same</th>
<th>Pending: United States</th>
<th>Category 1 – Polycyclic antimicrobial compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patents (if issued) Expire: 2033</td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cyclic Compounds And Methods Of Making And Using The Same</th>
<th>Pending: United States, Europe, Australia, India, New Zealand, Singapore, South Africa</th>
<th>Category 1 – Cyclic antimicrobial compounds</th>
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<td>Patents (if issued) Expire: 2032</td>
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<table>
<thead>
<tr>
<th>Compounds And Methods For Treating Candidiasis And Aspergillus Infections</th>
<th>United States: issued 11/25/14</th>
<th>Category 1 – Anti-fungal compounds</th>
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</thead>
<tbody>
<tr>
<td>Pending: United States, Europe, Japan, Australia, Brazil, Canada, Chile, China, India, Israel, South Korea, Malaysia, Mexico, New Zealand, Russia, Singapore, South Africa, Hong Kong</td>
<td>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>
<td></td>
</tr>
<tr>
<td>Patents Expire: 2033</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compositions Of Arylamide Compounds And Antimicrobial Agents</th>
<th>United States: provisional pending</th>
<th>Category 1 – Arylamide compounds in combination with anti-microbial agents</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Antimicrobial Compounds</th>
<th>United States: provisional pending</th>
<th>Category 1 – Anti-microbial compounds</th>
</tr>
</thead>
</table>

1 Patent family co-owned with the University of Massachusetts Amherst.
1 Patent family co-owned with Rutgers, The State University of New Jersey.
Additional Information
Psoriasis
Costly to Treat (especially with Biologics), for Patients and Society

The total cost burden of psoriasis is estimated to be between $35 billion and $63 billion.

Insurers are more likely to deny costly biologics ("particularly troubling"); representing 9.8% of all U.S. pharmacy spending in 2015), which experience high treatment-failure rates and are associated with more frequent and more serious adverse events.

Sources:
https://www.aad.org/eposters/GetFile.aspx?id=1108&type=sub
Psoriasis

Complex Pathogenesis with No Known Cure

Key Characteristics

• A chronic, autoimmune disease that exhibits symptoms in the form of irritated, flaky skin.
• Increased proliferation and hyperplasia of the epidermal cells.
• Enhanced proliferation of keratinocytes in the psoriatic plaques.
• Growth cycle of skin cells is accelerated by faulty immune signals.
• Inflammatory skin disease in which neutrophils are associated with psoriatic lesions.
• Psoriasis-associated non-protein coding RNA induced by stress (PRINS) in psoriatic lesions and plasma IL-20 are increased.
• In psoriatic lesions, cyclic adenosine monophosphate (cAMP) levels are decreased, which may result in diminished regulation of cell division due to less activation of protein kinase.

Sources:
Numerous cellular mediators and signaling pathways are activated in psoriatic lesions following diverse triggers. In the background of individuals expressing a favorable genetic predisposition toward a hyperactive immune response (quiescent panel), these mediators drive a proinflammatory response (flare panel). The proinflammatory state progressively overwhelms the immune counter-balancing mechanisms, and skin proliferation becomes uncontrollable by conventional regulatory cells and suppressive mediators (eg, Treg, IL-10, TGFβ; Chronic/recurrent panel). This exacerbated inflammation results in the progressive creation of resident memory self-reactive cells that in-turn contribute to recruiting inflammatory mediators that result in a lifelong recurrent chronic inflammatory skin disease.

Source: https://www.dovepress.com/current-knowledge-on-psoriasis-and-autoimmune-diseases-peer-reviewed-fulltext-article-PTT; also see https://core.ac.uk/download/pdf/43309322.pdf
Psoriasis

Condition Presents with Serious Comorbidities

Psoriasis sufferers are at greater risk of developing infections, experiencing depression, and have a higher association with Inflammatory Bowel Disease.

Sources:
Psoriasis
As Severity Increases, so Too Does Treatment Toxicity...

“Currently available therapies, however, still have many limitations associated with prolonged use. For example, topical therapies are only mildly effective and may increase the risk for skin cancers. Traditional systemic agents (e.g., methotrexate) may cause renal and hepatic toxicities when used long-term. In addition, although biologic agents have proven to be very effective at improving symptoms of psoriasis, they may lose their effectiveness over time. Additional considerations with biologics include patient hesitancy to self-inject and an increased risk of infection and lymphoma. Subsequently, therapeutic options that address these limitations may have a large impact on treatment.” (Source)

Source: National Psoriasis Foundation (random sample of 278 adults with psoriasis)

Source: https://en.wikipedia.org/wiki/Psoriasis#/media/File:Psoriasis_treatment_ladder.svg
Psoriasis

... Even as Systemics, Especially Biologics, Prove Highly Efficacious

<table>
<thead>
<tr>
<th>Agent</th>
<th>Psoriasis</th>
<th>Psoriatic arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Study</td>
<td>N</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>Juncture</td>
<td>676</td>
</tr>
<tr>
<td>Ixekizumab</td>
<td>Uncover 2</td>
<td>1224</td>
</tr>
<tr>
<td>Brodalumab</td>
<td>Amagine 2</td>
<td>1831</td>
</tr>
<tr>
<td>Tildrakizumab</td>
<td>Phase IIb</td>
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<tr>
<td>Gusekumab</td>
<td>Phase II</td>
<td>293</td>
</tr>
<tr>
<td>Apremilast</td>
<td>Esteem 1</td>
<td>844</td>
</tr>
</tbody>
</table>


Psoriasis
Dissatisfied Patients Switch or Discontinue Treatment Altogether

55% of those with moderate to severe psoriasis do not believe “clear” or “almost clear” skin is a realistic goal.

Non-Adherence a Major Challenge

Sources:
**Prurisol for Psoriasis**

**Clinical Literature Supporting Therapeutic Potential**

“Data on the efficacy of new systemic therapies will likely alter future therapeutic concepts in favor of effective biologics or oral immunomodulators.”

---

**PRINS / IL-20 / CD8**

- “Targeting CD8+ T cells prevents psoriasis development.” *ScienceDirect - Journal of Allergy and Clinical Immunology* (January 9 2016; Letter to the Editor).
- “CD8(+) T cells in the lesional skin of atopic dermatitis and psoriasis patients are an important source of IFN-γ, IL-13, IL-17, and IL-22.” Hijnen D, et al. *J Invest Dermatol*. 2013.
- “IL-22 and IL-20 are key mediators of the epidermal alterations in psoriasis while IL-17 and IFN-γ are not.” *Journal of Molecular Medicine*. May 2009, Volume 87, Issue 5, pp 523–536.

Prurisol for Psoriasis
Otezla® Emerging as a Blockbuster Oral Drug

Celgene expects Otezla® to earn revenue of up to $1 billion in 2016 and in the range of $1.5 billion–$2 billion in 2017.

Host Defense Protein (HDP) Mimics

Additional Characteristics

Source: https://pharm.ucsf.edu/degrado/research

Source: “New Weapons for the Germ Wars: Inexpensive Polymers can Extend the Range of Nature’s Germ-Fighter Arsenal.” (pdf)
Host Defense Protein (HDP) Mimics
Modelled on Paneth Cells Secreted in the Gut

- Paneth cells are named for Joseph Paneth (1857–1890), an Austrian physiologist
- Paneth cells are found throughout the small intestine and the appendix at the base of the intestinal glands.
- Paneth cells sense bacteria via MyD88-dependent toll-like receptor (TLR) activation which then triggers antimicrobial action.
- Paneth cells are stimulated to secrete defensins when exposed to bacteria (both Gram-positive and Gram-negative) or such bacterial products as lipopolysaccharide, muramyl dipeptide, and lipid A.

Sources:
“New Targets for Mucosal Healing and Therapy in Inflammatory Bowel Diseases;” Mucosal Immunology (2014) 7, 6–19.
“Regulatory Role of Defensins in Inflammatory Bowel Disease;” OII. Vol.2 No.2, June 2012
Brilacidin
Clinical Literature Supporting Therapeutic Potential (Immunomodulation, Inflammation)

“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)

AbbVie experiencing problems reformulating the world’ s top-selling drug, Humira; discontinues Halozyme formulation

- "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.
- "Antimicrobial Peptides in Host Defense: Functions Beyond Antimicrobial Activity." Part of the series Birkhäuser Advances in Infectious Diseases pp 129-147 Date: 25 December 2015

Source: http://www.cell.com/trends/immunology/abstract/S1471-4906%2809%2900005-2
Brilacidin
Clinical Literature Supporting Therapeutic Potential (Infectious Disease)

“Brilacidin [...] has a high likelihood of reaching commercialization. Antimicrobial peptides appear to be coming of age as therapeutics.”

(Michael Zasloff)

“Brilacidin [...] is perhaps one of the most promising of the current investigational agents in this class.”

(Karen Bush)

- "Short Antimicrobial Peptides and Peptide Scaffolds as Promising Antibacterial Agents." Current Topics in Medicinal Chemistry, Volume 16, Number 11, May 2016, pp. 1217-1230(14)
- "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.
Brilacidin
*Treats Infectious Disease and Disorders of Innate Immunity*

**Maintains Healthy Barrier**
- Anti-inflammatory properties
- Anti-biofilm properties
- Prevents ulceration in OM animal model

**Kills Pathogens**
- Concentration-dependent killing
- Long half-life and post antibiotic effect
- Sub-MIC activity

**Prevents Resistance**
- Single-dose 100% compliance
- Rapidly cidal decreased mutation rate
- Stationary phase activity kills persistent bacteria
Host Defense Protein (HDP) Mimics
Gateway Concept/Platform Potential

**Innate Immunity**

**Direct Antimicrobial Activity**

**Bacterial**
- *ABSSSI (skin)*
- Bone and Joint
- DFI
- Respiratory
- Blood Stream
- STDs

**Fungal**
- Oral Candidiasis
- Disseminated Candidiasis
- Aspergillosis

**Parasitic**
- Malaria
- Sleeping Sickness
- Giardiasis

**Viral**
- Influenza
- Herpes
- RSV

**GI Mucosa**
- Ulcerative Proctitis **
- IBD
- Oral Mucositis
- IBS
- GI-Acute Radiation Sickness
- Periodontitis

**Respiratory Mucosa**
- Cystic Fibrosis
- Asthma
- Chronic Bronchitis
- Lung-ARS
- Chronic Sinusitis

**Skin/Eye**
- Hidradenitis Suppurativa
- Acne
- Atopic Dermatitis
- Diabetic Ulcers
- Keratitis
- Burns/Abrasions

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