PETRAGEN
novel therapeutics for periodontal disease
Petragen was founded Aug. 2020; Closed on >$1m of seed capital in Mar. 2021
Based on biology developed by Dr. Braddock; also basis for the spinout Inozyme

Demetrios Braddock, MD, PhD
- Associate Professor of Pathology, Yale University
- Scientific Founder, Inozyme (NASDAQ: INZY)
- Founder & CSO, Petragen, Inc.
- Expert in ENPP1 biology (our target)

Martha Somerman, DDS, PhD
- Former Director of the National Institute of Dental and Craniofacial Research (NIDCR) at NIH
- Chief of the Laboratory of Oral Connective Tissue Biology at the National Institute of Arthritis and Musculoskeletal and Skin Diseases
- Co-inventor on Petragen IP

David Kolb, MBA
- 10+ yrs life science investment banking; 3 yrs equity research
- 12 yrs as life science entrepreneur and executive
- Founder of 3 previous university spinouts (2 exited; 1 active)
- Founder & CEO, Petragen, Inc.

Enrique De La Cruz, PhD
- Professor and Chair of Molecular Biophysics and Biochemistry; Head, Branford College
- Co-inventor on Petragen IP
WHAT PROBLEM ARE WE TRYING TO SOLVE?

PERIODONTAL DISEASE: NOT SEXY BUT STILL A BIG PROBLEM

The Disease

<table>
<thead>
<tr>
<th>Mild Periodontitis</th>
<th>Moderate Periodontitis</th>
<th>Severe Periodontitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 MM - 5 MM</td>
<td>5 MM - 7 MM</td>
<td>7 MM and above</td>
</tr>
</tbody>
</table>

- 26.8 million ≥2 tooth/pt
- 7.6 million ≥1 tooth/pt

$5 Billion Est. Opportunity In the U.S. Alone

Standard of Care

Procedure: Scaling & Root Planing (SRP)
- Cost: ~$370; Benefit: ~1mm

Pocket depth = Clinical endpoints

Therapeutic: Arestin® (minocycline)
- Cost: ~$87/tooth; Benefit: ~0.3mm

Lack of care can lead to implants ($10K+), nutritional issues and other diseases.
EXTENDING HUMAN PROOF OF CONCEPT

HUMAN PROOF OF CONCEPT

HUMAN

Healthy Control

GACI Individual

MURINE VALIDATION OF TARGET

Mouse Model

WT

Enpp1-asj

Observed cementum build-up in ENPP1 mutant patients

Missense Mutation of Enpp1 gene leads to severe osteoarthritis but also an observable buildup of cementum

asj = ages with stiffening joints
SO WHAT’S THE THERAPEUTIC STRATEGY?

Replicate the known ENPP1 inhibition phenotype LOCALLY . . .

. . . and drive neocementogenesis in the periodontal pocket

We expect that by avoiding systemic distribution and by using a micro-dose of inhibitor we should avoid any systemic toxicities.
IN A NUTSHELL (WHAT TO REMEMBER)

✓ Human proof of concept
✓ Known inhibitors in hand; optimization ongoing
✓ IP portfolio covers (current/in process) method of use, composition of matter, formulation and dosing
✓ Standard of care not getting it done
✓ $5B U.S. opportunity (+ animal health)
✓ Known regulatory path and endpoints
✓ Limited capital needs; value inflection points near
PETRAGEN
Backup slides
Dr. Braddock’s lab had been focused on an ENPP1-mutated rare disease called GACI which leads to significant calcification of the heart and arteries.

His work led to the founding and funding of Inozyme, now a public company (July 2020) with over $250m in investor funding.

It also led to the discovery that GACI patients had very thick cementum around their teeth which led to strong periodontal ligament (gum) attachment.

He believed this might be an interesting solution for periodontal disease and brought in the dental experts at the NIH to test the hypothesis and help develop a therapeutic.
ARESTIN “EFFICACY” DATA FROM PIVOTAL STUDIES
LOW REGULATORY AND COMPETITIVE BAR TO HURDLE

**Table 1:** Probing Pocket Depth at Baseline and Change in Pocket Depth at 9 Months From 2 Multicenter US Clinical Trials

<table>
<thead>
<tr>
<th>Time</th>
<th>Study OPI-103A (N=368)</th>
<th>Study OPI-103B (N=380)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SRP+ Alone n=124</td>
<td>SRP+ Vehicle n=123</td>
</tr>
<tr>
<td></td>
<td>SRP+ ARESTIN® n=121</td>
<td>SRP + Vehicle n=126</td>
</tr>
<tr>
<td>PD (mm) at Baseline</td>
<td>5.88 ±0.04</td>
<td>5.91 ±0.04</td>
</tr>
<tr>
<td></td>
<td>5.88 ±0.04</td>
<td>5.82 ±0.04</td>
</tr>
<tr>
<td>PD (mm) Change from Baseline at 9 Months</td>
<td>-1.04 ±0.07</td>
<td>-0.90 ±0.54</td>
</tr>
<tr>
<td></td>
<td>-1.20**+++</td>
<td>0.07 ±0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.16 mm</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Change over SRP Alone</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>0.31 mm</strong></td>
</tr>
</tbody>
</table>

SE = standard error; SRP = scaling and root planing; PD = pocket depth.
Significantly different from SRP *(P ≤0.05); ***(P ≤0.001).
Significantly different from SRP + vehicle †(P ≤0.05); ††(P ≤0.001).

In these 2 studies, an average of 29.5 (5-114), 31.7 (4-137), and 31 (5-108) sites were treated at baseline in the SRP alone, SRP + vehicle, and SRP + ARESTIN® groups, respectively. When these studies are combined, the mean pocket depth change at 9 months was -1.18 mm, -1.10 mm, and -1.42 mm for SRP alone, SRP + vehicle, and SRP + ARESTIN®, respectively.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/050781s020lbl.pdf
It is estimated that over 40 million dogs in the U.S. have periodontal disease, leading to a potential therapeutics market of over $3 billion.

Source: VCA Hospitals reports.

Globally the prevalence of moderate/severe periodontal disease is quite significant; India, the EU, China and South America represent large market opportunities.


Data does not include North America.