Forward Looking Statements

The statements in this presentation that relate to future plans, events or performance are forward-looking statements, which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended. Such forward-looking statements involve significant risks and uncertainties, and actual results, events and performance may differ materially from those expressed or implied in this presentation. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements include, but are not limited to, statements concerning the following: (i) estimates of our expenses, future revenue and capital requirements; (ii) our ability to obtain additional funding on terms acceptable to us, or at all; (iii) our ability to advance product candidates into, and successfully complete, clinical trials; (iv) the initiation, timing, progress and results of future preclinical studies and clinical trials, and our research and development programs; (v) the timing or likelihood of regulatory filings and approvals; (vi) our expectations regarding the results of our Phase 3 clinical trials of bremelanotide for hypoactive sexual desire disorder (HSDD), a type of female sexual dysfunction (FSD); (vii) our expectation regarding the timing of regulatory submissions for approval of bremelanotide for HSDD in the United States and other jurisdictions; (viii) the potential for commercialization of bremelanotide for HSDD and our other product candidates, the potential market size and market acceptance for bremelanotide for HSDD for FSD and our other product candidates, if approved for commercial use; (ix) our expectations regarding performance of our exclusive licensee of bremelanotide for North America, AMAG Pharmaceuticals, Inc. (AMAG), and our licensees in other jurisdictions; (x) our ability and the ability of our licensees, including AMAG, to compete with other products and technologies similar to our product candidates; (xi) the ability of third party collaborators to timely carry out their duties under their agreements with us and our licensees, including AMAG; (xii) the ability of contract manufactures to perform their manufacturing activities in compliance with applicable regulations; (xiii) our ability to recognize the potential value of our licensing arrangements with third parties; (xiv) the potential to achieve revenues from the sale of our product candidates; (xv) our ability to maintain product liability insurance at a reasonable cost or in sufficient amounts, if at all; (xvi) the retention of key management, employees and third-party contractors; (xvii) the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology; (xviii) our compliance with federal and state laws and regulations; (xix) the timing and costs associated with obtaining regulatory approval for our product candidates; (xx) the impact of legislative or regulatory healthcare reforms in the United States; and (xxi) other risks disclosed in our SEC filings. The forward-looking statements in this presentation do not constitute guarantees of future performance. We undertake no obligation to publicly update these forward-looking statements to reflect events or circumstances that occur after the date of this presentation.
Company Profile

Palatin Technologies, Inc. (NYSE MKT: PTN) is a biopharmaceutical company developing targeted, receptor-specific peptide therapeutics for the treatment of diseases with significant unmet medical need and commercial potential.
Corporate/Development Milestones

- **Vyleesi™ (bremelanotide) for Hypoactive Sexual Desire Disorder**
  - NA license agreement with AMAG 1Q2017
  - China license agreement with Fosun Pharma 3Q2017
  - South Korea license agreement with Kwangdong Pharma 4Q2017
  - FDA NDA submission & acceptance 2Q2018
  - PDUFA date 6/23/2019
  - Additional ROW partnerships 2019

- **Melanocortin Anti-Inflammatory Programs**
  - IBD – PL-8177
    - Phase 1 SAD/MAD data 4Q2018
    - Phase 1 oral pk & biodistribution study completed / data 1Q2019
    - Phase 2a PoC study initiation 3Q2019
  - Ocular indication
    - PL-8331 IND submission and initiation clinical studies (dry eye) 2H2019

- **Melanocortin 4 receptor selective agonists**
  - PL-9610 orally active small molecule clinical development candidate
    - IND submission and initiation of Phase 1 clinical study 1H2020

- **Natriuretic Peptide System – Cardiovascular Disease**
  - Academic collaborations ongoing – pursuing partnerships 2019

- **Multiple Orphan Drug designations anticipated** 2019
## Financial Snapshot

### Financial Highlights as of September 30, 2018

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and Cash Equivalents</td>
<td>$32.6 million</td>
</tr>
<tr>
<td>Total Debt</td>
<td>$5.2 million</td>
</tr>
</tbody>
</table>

### Summary Capitalization as of September 30, 2018

<table>
<thead>
<tr>
<th>Description</th>
<th>Common Equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Stock</td>
<td>203.0 million shares</td>
</tr>
<tr>
<td>Preferred</td>
<td>0.1 million shares</td>
</tr>
<tr>
<td>Warrants</td>
<td>23.4 million shares</td>
</tr>
<tr>
<td>Options</td>
<td>12.5 million shares</td>
</tr>
<tr>
<td>RSUs</td>
<td>8.8 million shares</td>
</tr>
<tr>
<td>Fully Diluted Shares</td>
<td>247.8 million shares</td>
</tr>
</tbody>
</table>
Focused chemistry and biology expertise on two receptor families:

- Natriuretic peptide receptors – NP receptors A, B, C
- Melanocortin receptors - MC receptors 1, 4, 5

Multiple related targets provides synergy in chemistry, biology, pharmacokinetics and safety

Disease indications are chosen based on the commercial opportunities which result from our receptor focused efforts

- Orphan indications evaluated
Palatin Technologies Overview

**Platform technology for the design of GPCR agonists**
- MIDAS Technology
- Diverse Compound Libraries
- Rational Design

**Melanocortin Peptide Agonists**
- **Female Sexual Dysfunction**
  - Vyleesi™ NDA filed
  - Partnerships - North America
  - Plus select ROW regions
- **Autoimmune/Anti-Inflammatory**
  - MC1 & 5 selective agonists
  - PL-8177 inflammatory bowel disease
  - PL-8331 ocular inflammation

**Natriuretic Peptide Agonists**
- **Heart Failure**
  - NPR A & C agonists
  - PL-3994
  - PL-5028 preclinical
- **Fibrotic Disease**
  - NPR C agonists
  - PL-5028 preclinical

**Rare Genetic Metabolic and Obesity Disorders**
- MC4r selective agonists
  - PL-8905
  - PL-9610 oral small molecule

- Demonstrated expertise/competence to move programs from discovery to collaboration to NDA
- Strategy leverages our chemistry and biology research across multiple therapeutic opportunities
- Activating endogenous pathways known to reverse disease processes
- MOAs with the potential to modify underlying disease pathologies - not just treat symptoms
- Vyleesi™ (bremelanotide) partnerships provide financial resources to unlock the potential of our pipeline assets
## Clinical Pipeline

<table>
<thead>
<tr>
<th>PIPELINE</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>FDA APPROVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanocortin Receptor Programs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vyleesi™ (bremelanotide) MC4r Agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoactive Sexual Desire Disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PL-8177 MC1r Agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBD &amp; Autoimmune Indications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PL-8331 MC1/5r Agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-Inflammatory Ocular Indications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MC4r Agonist Peptide &amp; Small Molecules</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rare Genetic Metabolic and Obesity Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natriuretic Peptide Receptor Programs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PL-3994 NPR-A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular Diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PL-5028 NPR-A/C Agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac Hypertrophy and Fibrosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Helping Premenopausal Women with Hypoactive Sexual Desire Disorder (HSDD)
Female Sexual Dysfunction (FSD) is defined as persistent or recurring problems during one or more of the stages of sexual response with associated distress

- Hypoactive Sexual Desire Disorder (HSDD) is the most common FSD

HSDD has a significant impact on patient self-image, relationships and general well-being

Bremelanotide Indication: Premenopausal women with HSDD

- The treatment of premenopausal women with acquired generalized HSDD as characterized by low sexual desire that causes marked distress or interpersonal difficulties and is NOT due to:
  - A co-existing medical or psychiatric condition
  - Problems with the relationship, or
  - The effect of a medication or other drug substance
Self-administered auto-injector, taken on demand ~30 min. before sexual activity

Treatment effect up to 8-10 hours

Activates endogenous pathways involved in sexual desire and arousal

Does not interact with alcohol (alcohol interaction study completed)

No Box Warning or restrictive REMS program anticipated

Two successful Phase 3 studies completed

- Randomized 1,267 pre-menopausal women with acquired HSDD
- Includes 12 month open label safety extension study
- Co-primary efficacy endpoints met
  - Statistically & clinically significant improvements in sexual desire and decrease in distress associated with low sexual desire

NDA filed and accepted for review by FDA 1H2018

PDUFA date June 23, 2019
Significant Market Opportunity

~10M pre-menopausal women in U.S. with HSDD¹

15M U.S. women with HSDD³

4.4M pre-menopausal women with HSDD (not primary symptom)

5.8M² pre-menopausal women with HSDD (primary symptom)

0.6M treated

1.5M diagnosed not treated

3.7M undiagnosed

5.5M post-menopausal women with HSDD

Potential initial patient population

Low desire/libido with associated distress affects 1 in 10 premenopausal women³,⁴

¹ Survey data from West (2008); Shifren (2008); Leiblum (2006)
² Burke Institute: patient and economic flow study, April 2016
³ Survey data from Shifren (2008); 2014 U.S. census data
North American Vyleesi Licensing Agreement

- AMAG Pharmaceuticals - specialty pharmaceutical company focused on developing and commercializing innovative healthcare solutions
  - Annual sales > $600M
- Dedicated sales, marketing and commercial teams focused on female health
- Committed and capable partner to commercialize Vyleesi
- Exclusive licensing agreement covers NA market – February 2017
  - $60M upfront payment
  - $25M in cost reimbursements
  - $80M upon regulatory milestones
    - $20M FDA NDA acceptance
    - $60M FDA approval
  - Up to $300M in sales milestones and tiered royalties from high single to low double digits
  - AMAG responsible for pre-launch, launch and commercial activities
ROW Vyleesi Licensing Agreements

- Fosun Pharma – Chinese pharmaceutical company focused on developing and commercializing innovative healthcare solutions with >$2B in annual sales
  - Exclusive licensing agreement covers China, Hong Kong, Taiwan and Macau markets
  - $5M upfront payment, $7.5M regulatory milestone
  - Up to $92.5M in sales milestones plus tiered royalties from high single digits to low double digits
  - Fosun responsible for all development, regulatory and commercial activities

- Kwangdong Pharmaceutical Co. – Republic of Korea leading pharmaceutical company with >$900M in annual sales
  - Exclusive licensing agreement for the Republic of Korea
  - $500,000 upfront, ~$40M in regulatory and sales milestones plus royalties on sales
  - Kwangdong responsible for all development, regulatory and commercial activities
Vyleesi™ Program Milestones/Timelines

- NA Phase 3 top-line results / co-primary endpoints met 4Q2016 ✓
- NA license agreement closed with AMAG 1Q2017 ✓
- China license agreement closed with Fosun 3Q2017 ✓
- South Korea license agreement closed with Kwangdong 4Q2017 ✓
- FDA NDA accepted for review 2Q2018 ✓
- PDUFA date 6/23/2019
  - 11/2018 - FDA requested data from a small Phase 1 study with premenopausal volunteers assessing 24-hour ambulatory blood pressure with short term daily use of Vyleesi 1Q2019

- cFDA approval for China anticipated 1H2020
- South Korean approval anticipated 1H2020
- EU partnership anticipated 2019
- EU phase 3 trial start TBD
- Additional ROW partnerships anticipated 2019
Melanocortin
Autoimmune
&
Anti-Inflammation Programs
Melanocortin system is up-regulated by and integral to the resolution of inflammation and autoimmune pathologies

α-MSH and MC1&5 receptors expressed by monocytes, macrophages, neutrophils, lymphocytes, dendritic cells, podocytes and mast cells. MC1r agonism also down-regulates fibroblast function and fibrosis

Melanocortin agonism activates resolution of proinflammatory processes
  - Inhibition of NF-κB and other proinflammatory cytokines (IL-1, IL-2, IL-4, IL-6, IL-13, TNF-α, IFN-γ)
  - Increased production of IL-10, an anti-inflammatory cytokine
  - Mediates antigen specific T-cell and macrophage responses from pro-inflammatory to regulatory

MC1r specific peptides and small molecules have demonstrated *in vivo* activity in numerous disease models of inflammation.

Goal: Design and develop selective MC1r & MC1/5r agonists for treating a variety of inflammatory and autoimmune indications
  ◦ Rational design and synthesis of selective MC1r & MC1/5r agonists
    - PL-8177: cyclic peptide selective MC1r agonist
    - PL-8331: cyclic peptide selective MC1/5r agonist

PL-8177 and PL-8331 demonstrated reversal of pathology in multiple inflammatory and autoimmune disease models
  ◦ Including inflammatory bowel disease, dry eye, uveitis and diabetic retinopathy

PL-8177 Clinical development candidate
  ◦ Phase 1 SAD/MAD SC formulation completed
  ◦ Phase 1 Micro-dose study for oral formulation - data January 2019
  ◦ Phase 2A proof-of-mechanism scheduled 1H2019 start

PL-8331 dry eye (Ora is product development and clinical CRO)
  ◦ Topical eye drop formulation developed
  ◦ IND enabling activities initiated
Dry Eye Overview

- Dry eye syndrome or keratoconjunctivitis symptoms include irritation, redness, discharge and blurred vision.

- **Aqueous-Deficient**
  - Autoimmune disease (e.g. Sjögren’s Syndrome)

- **Lipid-Deficient**
  - Meibomian gland dysfunction, hormonal changes

- **Mucin-Deficient**
  - Goblet cell loss

- **Neural Loop-Associated**
  - Blink disorders, abnormal corneal sensitivity

- **Environmentally-Induced / Exacerbated**
PL-8331 Pre-Clinical Scopolamine Dry Eye Model

Mouse model of Scopolamine-induced dry eye, established disease, topical application

- PL-8331 as good as or better (no level 4 disease) than Restasis
- Xiidra showed no improvement in fluorescein staining
PL-8331 Ocular Clinical Development

- PL-8331: cyclic peptide agonist at the MC1 and 5 receptors
- Single use aqueous eye drop formulation developed
- Ora, Inc., world-leading ophthalmic CRO, managing dry eye development program
  - Preclinical IND enabling activities complete 2H2019
  - IND submission and initiation of phase 2 dry eye clinical trial 2H2019
    - Establish clinical proof of concept
    - Double-blind placebo-controlled study - placebo and 2 doses of PL-8331
    - Data anticipated 1H2020
By 2050, the number of Americans with diabetic retinopathy is expected to nearly double, from 7.7 million to 14.6 million.

Approximately 22 million Europeans have diabetic retinopathy.

DME affects ~10% of people with diabetic retinopathy.
- ~750,000 in the USA & 2.2 million people in the EU

DME is the most common cause of vision loss in patients with diabetes.

IVT VEGF antagonists and steroids are the only pharmaceutical treatments for DME.

There is a high need for additional treatments.
- Novel MOA to improve visual acuity alone or when used adjunctively with a VEGF antagonist.
- Replacement for steroids without glaucoma or cataract side effects.

Current market – Eylea and Lucentis global annual sales for DR/DME estimated at $1.85b.
- VEGF and TNF-α levels are similar to healthy mice even though the diabetic mice remain hyperglycemic throughout the study
- IL-10 is a marker of inflammation resolution
PL-8331 Diabetic Retinopathy Retinal Histopathology

Healthy  Diabetic mice  PL-8331 treated  Untreated

NEL  GCL  IPL  INL  OPL  ONL  Phr

![Histopathological images of retina](image)

![Graph showing RCG (cells/mm)](graph)

*P < 0.05
NS = No significant difference
PL-8331 Diabetic Retinopathy Conclusions

- PL-8331 therapy promoted preservation of retinal structure seen by RGC survival and histology of the retinas
- PL-8331 suppressed VEGF production in the diabetic retinas
- PL-8331 treatment could block vascular leakage and neovascularization
- RPE from PL-8331-treated diabetic mice suppress inflammation and promotes anti-inflammatory activity by activated macrophages
- PL-8331 treatment helps preserve ocular immune privilege and prevents inflammatory activity in the diabetic retina
- Optimal dosing regimens are being investigated
Non-Infectious uveitis (NIU) is a potentially blinding intraocular inflammatory disease that arises without a known infectious trigger and is often associated with immunological responses to unique retinal proteins.

Prevalence of NIU in N. America:
- Adults: ~72,000
- Pediatric: ~21,000

NIU causes bilateral legal blindness in 6% of patients and unilateral blindness in 18% of patients.

Only 2 FDA approved treatment options:
- Ozurdex (dexamethasone intravitreal implant)
- Humira (adalimumab)
- Significant off-label treatments – steroids, Infliximab, methotrexate, azathioprine etc.

There remains a high need for new safer treatments:
- Use of steroids leads to glaucoma and cataracts and has systemic toxicities
- Humira increases rates of serious infection and has substantial contraindications
Mouse Experimental Autoimmune Uveitis (EAU)

- PL-8177 is a potent selective MC1 receptor agonist
- Palatin collaborated with Dr. Andrew Taylor (Boston University) to evaluate PL-8177 in a mouse model of uveitis
- EAU induced by immunizing C57BL/6 mice with an emulsion of complete Freund’s adjuvant (CFA) with additional 5 mg/mL desiccated *M. tuberculosis* and 2 mg/ml IRBP peptide amino acids 1-20
- Course of EAU evaluated every 3-4 days by fundus examination
- EAU mice injected i.p. with PL-8177 on the first day of clinically positive uveitis (uveitis score of at least 2) and two days later
- Native α-MSH injected at 50 µg/mouse as positive control
MC1r agonism has significant effects in reversing uveitis
Conducted in collaboration with Dr. A. Taylor at Boston University School of Medicine
PL-8177 Experimental Autoimmune Uveitis

Cross section of the eye

- Treatment with PL-8177 results in reversal of the disease process with return to normal phenotype
- Reversal of immune cell infiltration and restoration of tissue morphology
MC1r agonism is an endogenous mechanism that downregulates inflammatory/immune responses.

MC1r are upregulated in IBD and expressed on the cell surface of intestinal epithelia.

Numerous animal models have demonstrated that the endogenous pan-agonist α-MSH prevents and reverses intestinal inflammation.
MC1r Antibody Staining Human Colon Tissue

A-C Normal human colon samples
A Sample # D35887
B Sample # D35885
C Sample # D35879

D-E Ulcerative colitis samples
D Sample # D35786
E Sample # D35784

F Negative control (no primary Ab)

Staining using antibody against MC1r showed mostly strong staining in all samples - both normal and UC. In cases of crypts loss, the epithelial cells covering the ulcer showed similar strong staining.
Crucial Role of MC1r in Experimental Colitis

Mean Gross Pathology (Groups 1-5)
* p<0.05 vs. Vehicle (Group 2) using T-test

- PL-8177 delivered topically to the colon. Budesonide oral delivery.
- PL-8177 0.5 µg/rat is 60X more potent than budesonide 0.125mg/kg.
Melanocortin Receptor-4 Agonist
For Genetic Obesity
MC4r Agonists for Genetic Obesity

- Obesity is a multifactorial condition with numerous biochemical components relating to satiety (feeling full), energy utilization and homeostasis.

- Mutations in the Leptin-Melanocortin pathway represent some of the most prevalent forms of monogenetic obesity in humans.

- The Leptin-Melanocortin signaling pathway plays a key role in regulating food intake and energy homeostasis.

- Estimates suggest all forms of genetic obesity that can be effected by MC4r agonist therapy are approximately 28,000 patients (US).
PL-9610 causes weight loss in wild-type DIO mice but not in MC4r knockout mice
PL-9610 was dosed orally twice a day

PL-9610 in Leptin-Deficient (ob/ob) Mice

Weight loss in Leptin-deficient mice

- Vehicle PO
- 30mg/ml PL9610 PO

Study Day

% change in BW

-5 0 5

0 1 2 3 4 5 6

- PL-9610 was dosed orally twice a day
MC4 Receptor Obesity Program Summary

- MC4r selective agonists, peptide and oral small molecules
  - Efficacy established in DIO and leptin-deficient animal studies
  - No effect seen in MC4r knock-out model, establishing weight loss effect as MC4r based
  - Two phase 2a clinical trials established proof of concept
  - Limited effects on blood pressure (excellent therapeutic window)

- PL-9610 orally-active small molecule clinical development candidate
  - IND enabling activities started 2H2018
  - IND submission and initiation of phase 1 targeted 2H2019

- Program is under evaluation for Orphan Drug designations for treatment of rare genetic metabolic and obesity disorders
Natriuretic Peptide Receptor Program
Heart Failure Overview

- Heart failure (HF) is a common, progressive disorder in which impaired cardiac pump function leads to inadequate systemic perfusion required to meet the body's metabolic demands
  - 5M US patients (Circulation. 2013;127(1):e6)
  - > 1M annual US hospitalizations (Circulation. 2010;121(7):e46)

- High unmet medical need:
  - Decrease re-hospitalization rates
  - Decrease morbidity and mortality

---

### Classification

<table>
<thead>
<tr>
<th>NYHA I</th>
<th>NYHA II</th>
<th>NYHA III</th>
<th>NYHA IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of HF Patients</td>
<td>~25%</td>
<td>~29%</td>
<td>~35%</td>
</tr>
<tr>
<td>Annual Mortality Rate</td>
<td></td>
<td>~0.3%</td>
<td>10.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Remodelling</th>
<th>Chronic HF</th>
<th>Acute Episode (AHF)</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Myocardial Infarction</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1-yr Mortality: ~30%\(^1\)

Increases dramatically with every acute episode & disease progression

5-yr Mortality ~50%\(^2\)
Rate comparable to cancers & other deadly diseases

Increasing Frequency of Acute Decompensation Resulting in Hospitalization
Natriuretic Peptide System (NPS)

Neuropeptide hormone system plays an important role in the regulation of cardiovascular homeostasis

**Physiological Effects**

- Downregulate RAAS (renin-angiotensin-aldosterone system)
- Suppression of cardiac hypertrophy, fibrosis & remodeling
- Stimulation of diuresis & natriuresis
- Increased myocardial perfusion
- Vasodilation & decreased blood pressure
- Bronchodilation
The natriuretic peptide system represents an underexploited mechanism for treating HF and other CV diseases

- Proprietary natriuretic peptide library
  - Compounds selective for NPR-A, NPR-B, NPR-A/B & NPR-C
  - Comprehensive IP portfolio with composition of matter and methods of use patent and patent applications

- PL-3994 selective for NPR-A clinical candidate
  - Two phase 1 clinical studies completed
  - In preclinical models significant reductions in cardiac hypertrophy and fibrosis
  - Once daily SC patient self-administration
  - Phase 2A ready

- PL-5028 NPR-C/A agonist preclinical candidate
  - NPR-C agonism increases effects on reducing cardiac fibrosis
  - Potential for superior efficacy with reduced potential for hypotension
PL-3994 Cardiac cGMP and pKG

- 14 day continuous infusion of PL-3994
- PL-3994 had no effect on systemic blood pressure
- Systemic PL-3994 activated NPR-A & pKG in cardiomyocytes
- PL-3994 rescued cardiac hypertrophy and reduced cardiac fibrosis

Mouse TAC model in cardiomyocyte conditional corin gene KO mice

Collaboration with Dr. Daniel Dries, Temple Cardiovascular Research Center

Samples are from LV apical region
PL-3994 in Corin “Cardiac-KO” HF Model

- Rescues cardiac hypertrophy
  - KO vs. PL-3994 p=0.03

- Reduces cardiac fibrosis
  - KO vs. PL-3994 p=0.005

- Reduces TGF-β expression
  - KO vs. PL-3994 p=0.03

- Reduces aldosterone expression
  - KO vs. PL-3994 p=0.04
NPS Development Program

- PL-3994 - Two phase 1 trials completed
  - Well tolerated and dosing range established
- PL-3994 phase 2A (open label trial) in HF-pEF patients starts 1H2019
  - N=50, with ascending IV dosing
  - Objectives
    - Characterization of systemic and pulmonary blood pressure effects
    - Cardiac biopsy to evaluate NPS pathway activation in HF-pEF patients
    - Characterization of duration of drug effect
  - Preliminary data anticipated 2H2019
- PL-5028 NPR-A & -C Agonist
  - Efficacy established in heart failure preclinical models
  - Efficacy established in bleomycin pulmonary fibrosis model
  - Preclinical IND enabling activities to initiate 1H2019
Pipeline Development Milestones

- Melanocortin Anti-Inflammatory Programs
  - IBD – PL-8177
    - IND submission cleared 4Q2017 ✓
    - Phase 1 SAD/MAD 1Q2018 ✓
    - Phase 1 SAD/MAD data 4Q2018 ✓
    - Phase 1 oral pk & biodistribution study data 1Q2019
    - Phase 2a PoC study 3Q2019
  - Ocular indication – PL-8331
    - IND submission and initiation clinical studies (dry eye) 2H2019

- Melanocortin 4 receptor selective agonists
  - PL-9610 orally active small molecule clinical development candidate
    - IND submission and initiation of Phase 1 clinical study 1H2020

- Natriuretic Peptide System – Cardiovascular Disease
  - Academic collaborations ongoing – pursuing partnerships 2019

- Multiple Orphan Drug designations anticipated 2019
Thank You