



# 2018 and Beyond

*Analyst Day*  
*New York – November 14, 2017*

*NASDAQ: LGND*



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*The following presentation contains forward-looking statements regarding Ligand's prospects, plans and strategies, drug development programs and collaborations. Forward-looking statements include financial projections, expectations regarding research and development programs, and other statements including words such as "will," "should," "could," "plan," etc. Actual events or results may differ from Ligand's expectations. For example, drug development program benefits may not be realized and there can be no assurance that Ligand will achieve its guidance in 2017 or thereafter or that third party research summarized herein is correct or complete.*

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# Today's Agenda

Business Overview and Commercial Assets

John Higgins, *CEO*

OmniAb Technology Overview

Roland Buelow, Ph.D., *VP, Antibody Technologies*

Pipeline and Technology Highlights

Matt Foehr, *President and COO*

Partner Presentations:

Sermonix Pharmaceuticals  
Lasofoxifene

David Portman, M.D., *CEO*

Melinta Therapeutics  
Baxdela

Lyn Baranowski, *SVP, Corp Dev & Strategy*

Viking Therapeutics  
VK5211(SARM) and VK2809(TR- $\beta$ )

Brian Lian, Ph.D., *CEO*

GRA Diabetes Program

Eric Vajda, Ph.D., *VP, Preclinical R&D*

Financial Overview and Outlook

Matt Korenberg, *CFO*

# Shots-on-Goal Business Model

## *The “LIGAND MODEL”*

- Realities of the pharmaceutical industry
  - Most drug research programs fail, but not all
  - Programs are not all of equal value – different time to market, risk, economics
- BUT, the more quality programs you have, the higher likelihood of success
  - Diversified across a full range of industry partners
  - Diversified across a broad spectrum of therapeutic indications
- A shot-on-goal for Ligand is a fully funded partnership
  - Backed by license to Ligand’s patents, know-how and/or data
  - Sharing of future economics based on partner’s success

# The “LIGAND MODEL”

## *The Balance in Our Business*

### *What We Do:*

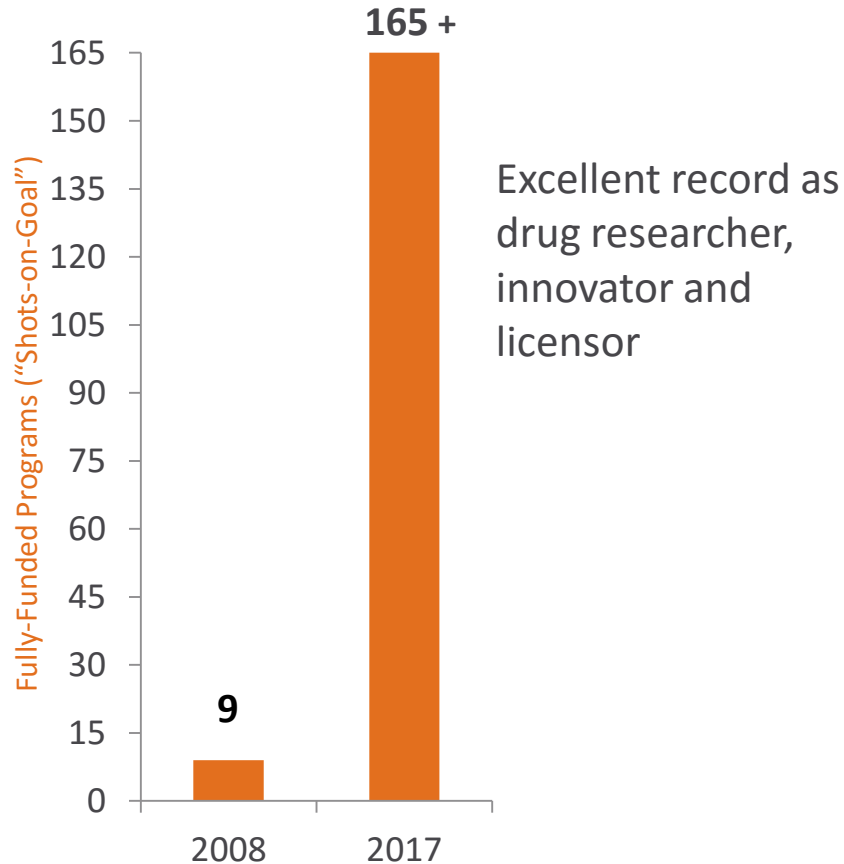
- Conduct early research, discover drugs
- Provide tools that make drugs possible
- License data and patents
- Acquire new technologies and assets
- Operate with low costs and maintain lean sharecount

### *What Our Partners Do:*

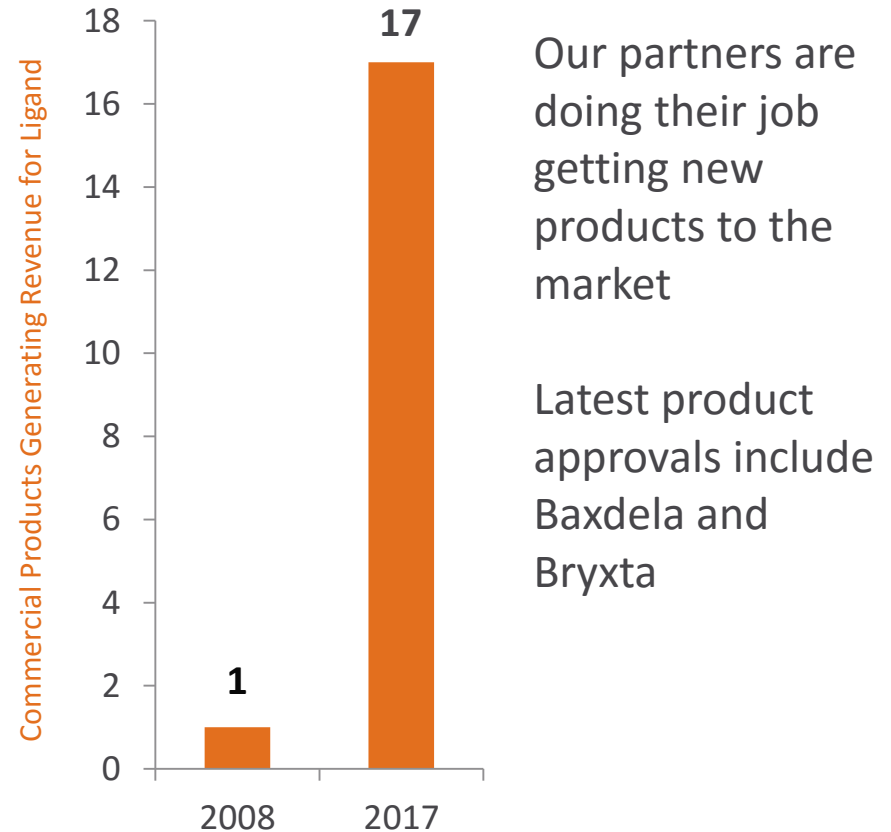
- Decide which indications to pursue
- Design studies; manage regulatory work
- Price drugs and secure reimbursement
- Market drugs
- Fund all development and commercialization

# Ligand's Portfolio Continues to Grow

## Ligand's Achievement: Portfolio Expansion



## Partners' Achievement: Approved Products



# RPT – Ligand's Foundation of Value

*Revenue*

*Pipeline*

*Technology*

# RPT – Ligand's Foundation of Value

*Revenue*



*High Growth*  
*High Margin*  
*Strong Protection*

*Pipeline*



*Large and Growing*  
*High Quality*  
*Many Late Stage*

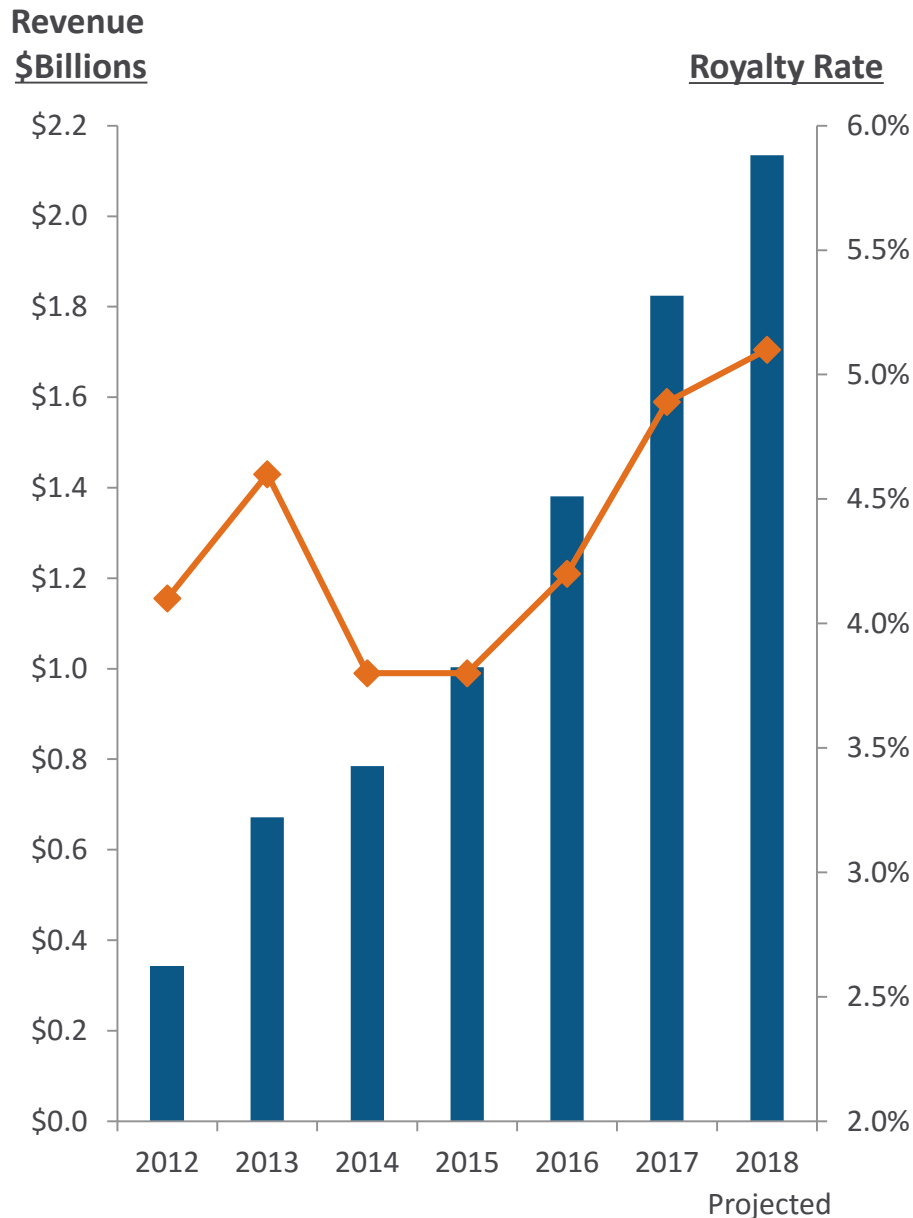
*Technology*



*Best-in-Class*  
*Leverageable*  
*Strong IP*



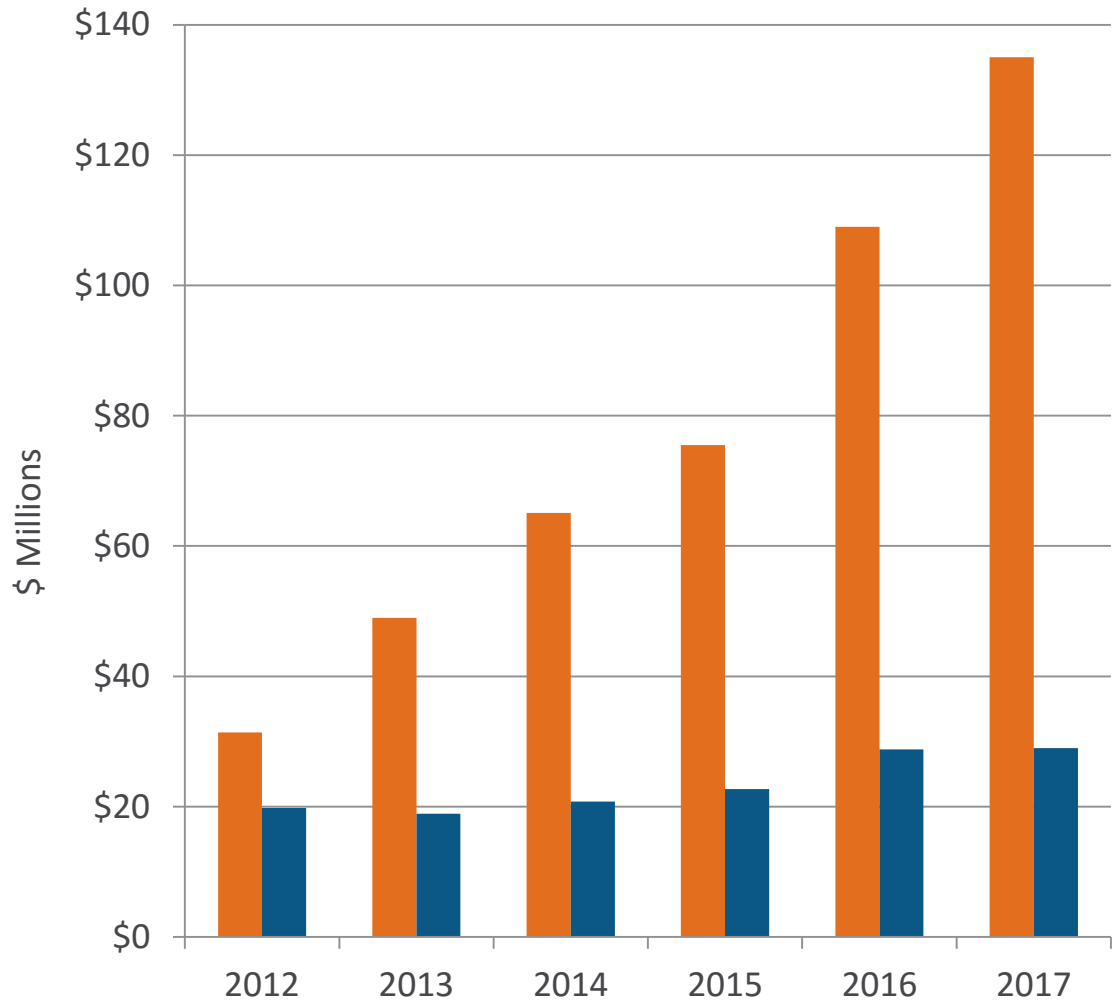
# Underlying Revenue & Effective Royalty Rate



- New approvals and increasing sales of existing partnered products are major drivers for underlying revenue growth
- Average royalty rate increasing due to mix of sales and royalty tiering

Current 2018 outlook, underlying revenue will exceed \$2 billion and average royalty will be ~5%

# Ligand's Cash Generation is Increasing



- Strong revenue growth
  - 95% gross margins
- Cash operating expense levels low and relatively flat
- Significant increase in annual cash flow

Actual Estimated

■ Ligand Revenue ■ Cash Operating Expenses

# Intellectual Property at Ligand

- Over 800 worldwide issued patents
- Significant investment in intellectual property supports licensing and helps further protect existing programs
  - Highly diverse patent portfolio
  - Many programs have layers of IP protection: NCE, formulation, use, etc.
  - Current and emerging programs are well-protected
- Innovation and acquisitions have continued to yield substantial growth in Ligand's patent portfolio

# RPT – Ligand's Foundation of Value

*Revenue*



*High Growth*  
*High Margin*  
*Strong Protection*

*Pipeline*



*Large and Growing*  
*High Quality*  
*Many Late Stage*

*Technology*



*Best-in-Class*  
*Leverageable*  
*Strong IP*

# Pipeline

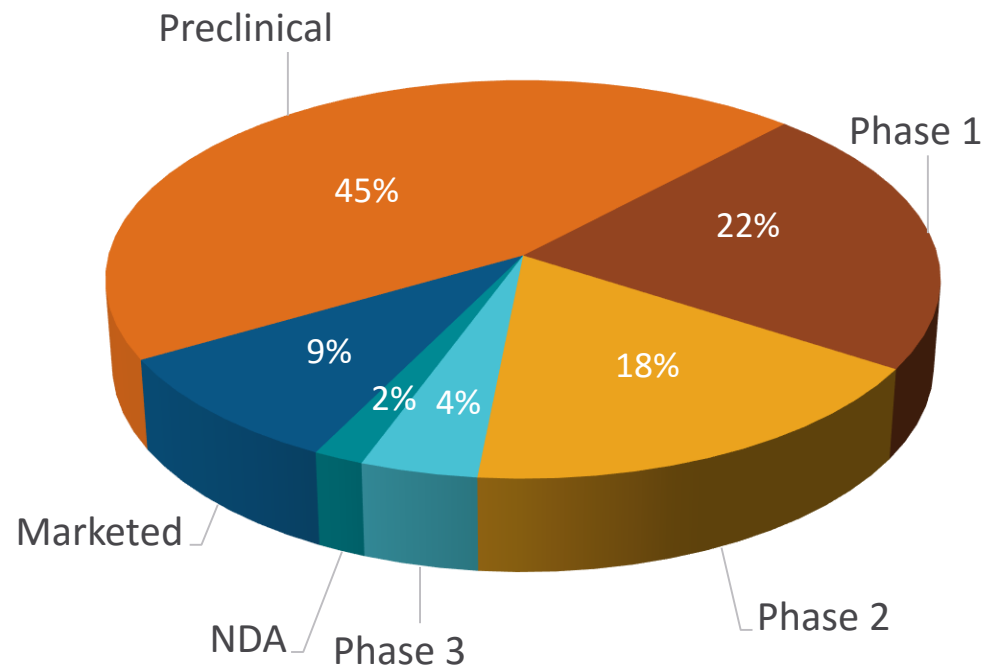
## *Why is Ligand's Pipeline Valuable?*

- In pharmaceuticals, most programs fail; but not **ALL** programs
- Ligand's pipeline is:
  - Large and growing
  - Highly diversified
  - Many programs have top-tier sponsorship
- Unique economic structure of Ligand's pipeline:
  - Our deals are fully funded
  - Ligand is not generating big annual losses OR diluting shareholders to finance its pipeline
- Many of Ligand's major assets are still development-stage

# Ligand's Portfolio Continues to Grow

*Over 165 Partnered Programs*

- Portfolio remains diversified across development stages
- Over 95 different partners
- Nearly 55% of programs in clinical development or later
- 11% marketed or NDA stage



# Ligand Portfolio Highlights

- We estimate our partners will conduct over 200 studies and spend over **\$2 billion** in 2018 on R&D to advance our programs
- Total potential payments under existing contracts for our more than 165 partnerships **exceed \$2 billion**
- Ligand is partnered with major companies for some of the industry's most important potential medicines
- Ligand-based programs are major assets for partners

Foundational for mega-acquisitions

- e.g., Novartis with GSK-Oncology (Promacta), Amgen with Onyx (Kyprolis), BMS with Cardioxyl

Foundational for IPO, reverse mergers or important financings

- e.g., Melinta, Viking, Aldeyra, Retrophin, Sermonix, Marinus, others

# Portfolio Pyramid

**PROMACTA**

**Kyprolis**  
(carfilzomib) for Injection

**Evomela**  
(melphalan) for Injection  
50 mg per vial

**Baxdela IV**  
(Melinta)

**Sparsentan**  
(Retrophin)

**Brexanolone**  
(Sage Therapeutics)

**Lasofoxifene**  
(Sermonix)

**Prexasertib**  
(Lilly)

**BMS986231**  
(BMS)

**APVO436**  
(Aptevo)

**VK5211**  
(Viking Therapeutics)

**Merestinib**  
(Lilly)

**AMG-330**  
(Amgen)

**Pevonedistat**  
(Takeda)

**JNJ-64007957**  
(Janssen/J&J)

**Seribantumab**  
(Merrimack)

**Esaxerenone**  
(Daiichi-Sankyo)

**VK2809**  
(Viking Therapeutics)

**Reproxalap**  
(Aldeyra)

**CHS-0214**  
(Coherus)

**Ganaxolone IV**  
(Marinus)

## The Top 3

*Commercial assets paying significant royalties*

## The Big 6

*Leading pipeline assets based on stage and/or potential value*

## The Next 12


*Assets emerging as next class with high revenue potential*



# Portfolio Pyramid

## *Power of our Pipeline*

### *What the Pyramid Represents*

- **18 companies** with **over 100 trials** conducted and in-progress in 2017
- Estimated **>\$500 million** spent funding the programs partnered with Ligand in 2017 alone
- Leading assets for Ligand  Leading assets for partners
  - Discussed on most quarterly conference calls
  - For many partners, Ligand program is the leading/main program
  - Highly diversified indications and drug types
- Ligand typically contributed drug and technology inventions, and shares in meaningful program economics

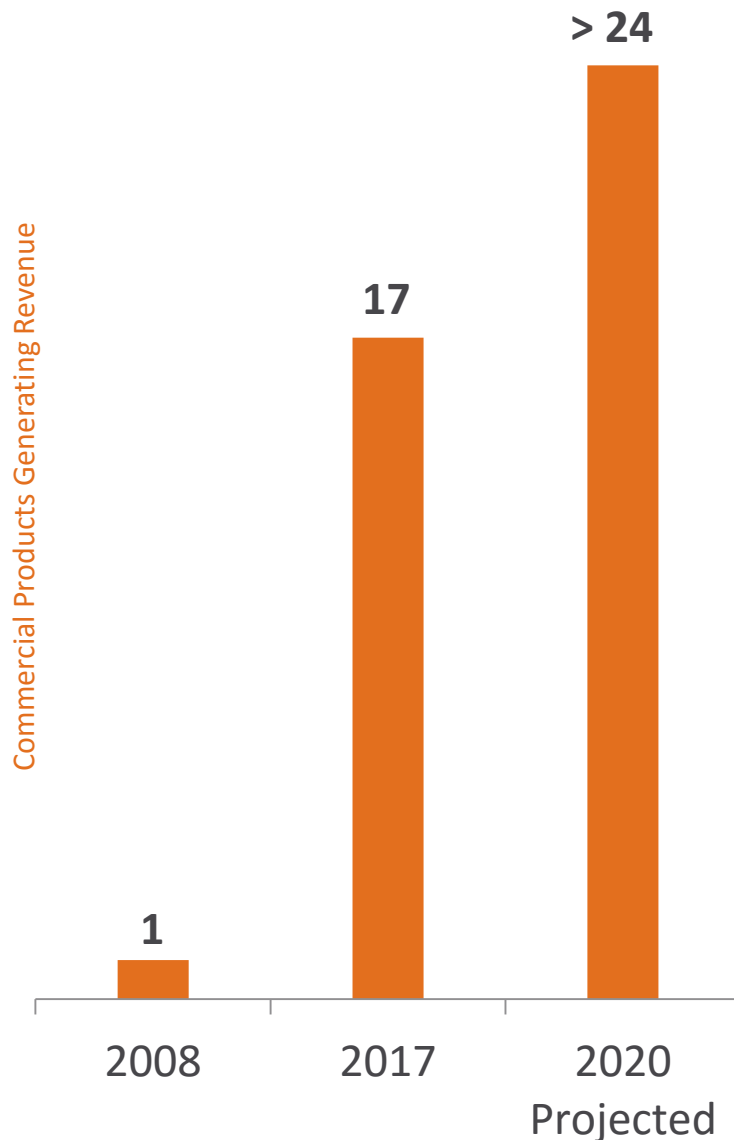
# 24 Commercial Products by 2020

## *Published Industry Success Rates*

- Drug development success rates have been tracked and published through the years
- *BIO* published average rates of success by stage of development as follows:
  - 85% probability of success for compounds with a submitted NDA
  - 50% probability of success for Phase 3 compounds
  - 15% probability of success for Phase 2 compounds
  - 10% probability of success for Phase 1 compounds
  - 7% probability of success for Preclinical compounds
- Applying these current rates of success to Ligand's current portfolio, Ligand projects having over 24 revenue bearing products by 2020

Reference: *Biotechnology Innovation Organization (BIO)* 2016 published averages rates of success by stage of development

# 24 Commercial Products by 2020



- > 24 products projected to be generating commercial revenue for Ligand by the end of this decade
- These revenue-generating assets expected to come from existing portfolio; future deals could be additive to this outlook

# RPT – Ligand's Foundation of Value

*Revenue*



*High Growth*  
*High Margin*  
*Strong Protection*

*Pipeline*



*Large*  
*High Quality*  
*Many Late Stage*

*Technology*



*Best-in-Class*  
*Leverageable*  
*Strong IP*

# Two Major Technology Platforms

*Market Leading, Best-in-Class*

## **CAPTISOL<sup>®</sup>**

*Highly-pure, pharmaceutical grade ingredient with reliable supply*

*Broad, global patent protection*

*Large Drug Master Files*

*Now with most pharma partners, most approved products*

## **OmniAb<sup>®</sup>**

*Only antibody discovery platform with three species*

*Platform with the most partners*

*Strong market protection and long patent coverage for products*

*Fast-growing number of drug candidates moving to the clinic*

# Antibodies: Major Opportunities

Last year, Ligand made a MAJOR strategic investment into antibody discovery by acquiring OMT, Inc. for ~\$178 million

Ligand's continued investment in 2017 has solidified its position with the Best-in-Class antibody discovery platform

## Antibody Technologies

*Like with Captisol, Ligand has made a “right time” investment into a major technology platform to deliver significant returns for the next 20 years*

# Antibodies: Major Opportunities

Antibody treatments are the fastest-growing segment of the pharmaceutical industry

## WHY?

- *“Because they work”<sup>1</sup>*
- Many of the largest drugs on the market are antibodies
- Significant allocation of R&D resources toward antibodies

<sup>1</sup> Janice Reichert, PhD - President, The Antibody Society, 2017

# Antibodies: Major Opportunities

Success rates for antibody drug candidates have been nearly DOUBLE the rate for small-molecule drug candidates...

## WHY?

Antibodies can be highly-targeted and bind very selectively to specific molecules



# Antibodies: Major Opportunities

There is a large and growing demand for antibody research tools

More companies, more dollars than ever

No signs of slowing, given research investments

Industry is shifting to biological-based research

*Ligand is at the right place and right time with a highly-valuable technology platform*

# The OmniAb Platform



***“Three Species – One License”***



**By 2025, platform projected to generate:**

- **>\$300 million of contract revenue**
- **> 40 clinical-stage programs**
- **> 150 research-stage candidates**
- **OmniAb products on the market**



*Roland Buelow, Ph.D.*  
*VP, Antibody Technologies*

# OmniAb® Technology

## Topics

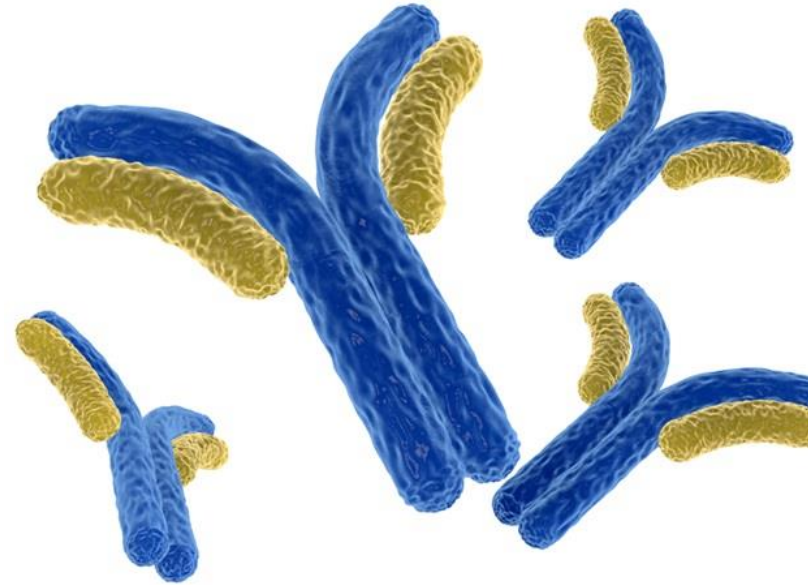
1. The biology, history and success of antibodies
2. OmniAb: A best-in-class technology
3. Our partners' perspectives
4. Future outlook for OmniAb platform



# Biology of Antibodies

## *The Power of the Immune System*

- Antibody therapy leverages an animal's ability to generate proteins that bind **very selectively** to specific molecules
- It is possible to create an antibody that is specific to **almost any cell target**
- Antibodies can **influence the biology** of target cells:
  - As agonists or antagonists
  - Influencing signaling
  - Even facilitating the selective killing of diseased cells

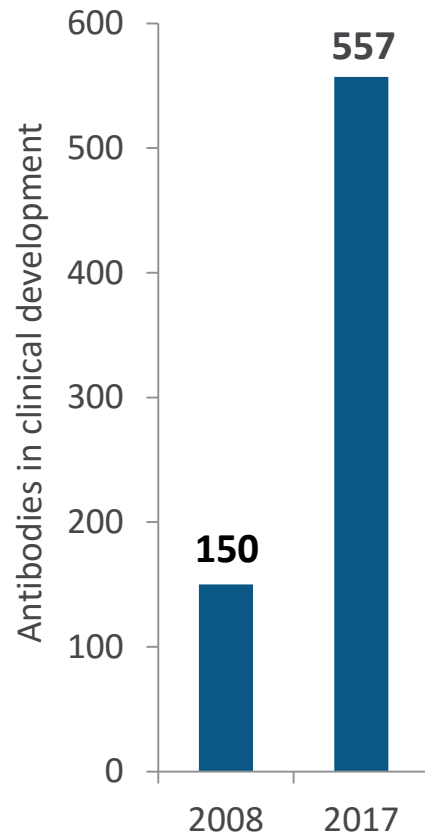


# Antibody Discovery and Research

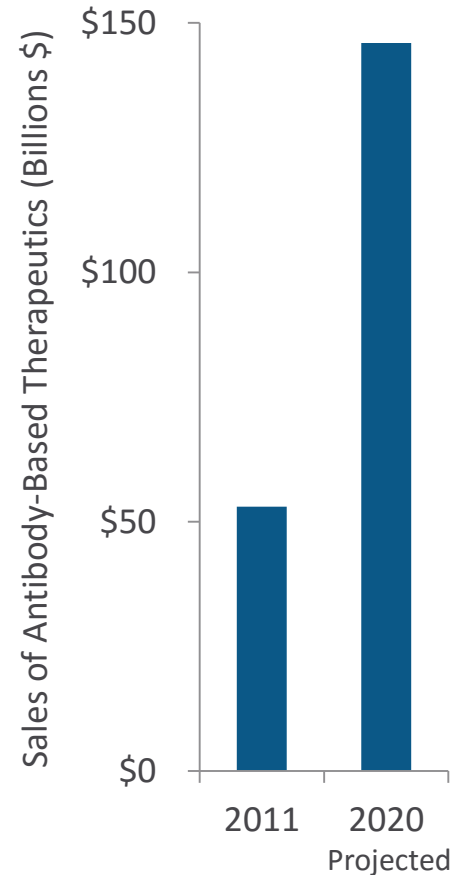
## *History and Facts*

- Display technologies using Phage or Yeast have been used for the discovery of antibodies
  - Lack selectivity that can be achieved with in vivo animal systems
  - It's well established that antibodies from Phage libraries often run into problems with stability, aggregation and other “manufacturability” challenges
- Newer, cutting-edge and the most successful antibody discovery platforms are animal-based technologies that yield fully-human antibodies
  - Antibodies derived from animal systems are optimized *in vivo* and can be referred to as ***naturally optimized human antibodies™***
- Superiority of animal-derived antibodies is clearly illustrated by the fact that the vast majority of antibodies now approved and on the market come from animals

# Antibodies: Major R&D and Sales Growth



- The number of antibodies in clinical development has **more than tripled** since 2008



- Global sales of antibodies in 2020 estimated to approach **\$150 billion in 2020**

# Likelihood of Approval at Phase 1

## *Industry is Recognizing Higher Success Rates for Biologics*

- Success rates for antibody classes is nearly **twice the rate of** small molecules
- Industry continues to make **substantial investment** in novel antibodies

<i>Type of Drug</i>	<i>Likelihood of Approval at Phase 1 Stage</i>
Small molecules	6.2%
Biologics/Antibodies	<b>11.5%</b>

*“Over the past 15 years, it has become clear that antibody therapeutics are both versatile and successful. The industry continues to be very interested in antibody-based therapeutics development, **because they work.**”*

**Janice Reichert, PhD**

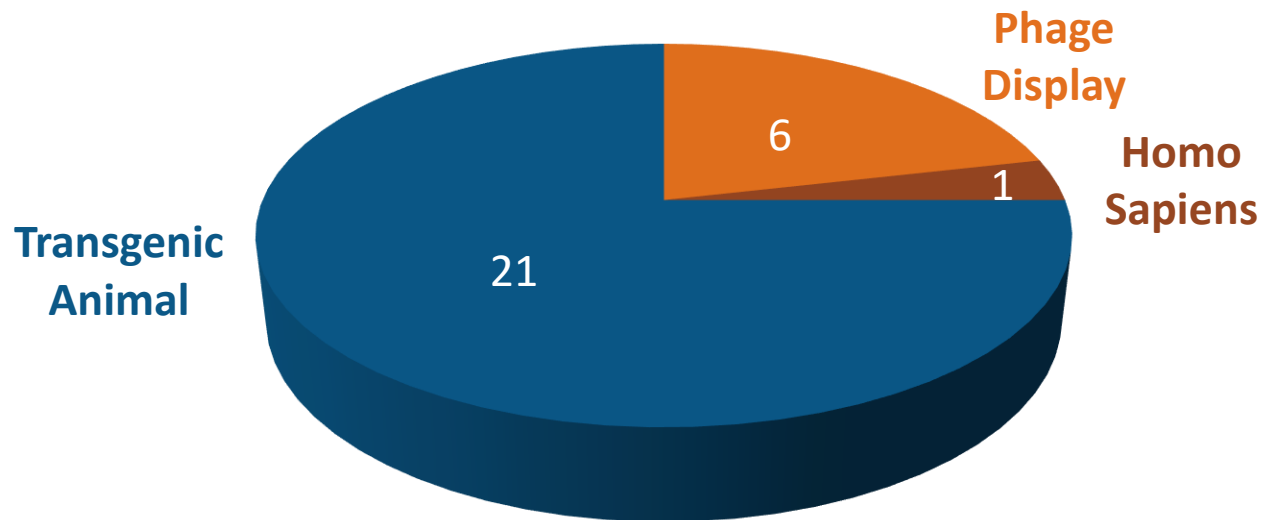
*President, The Antibody Society*



# Discovering Therapeutic Antibodies

## *Success of Genetically-Engineered Animals*

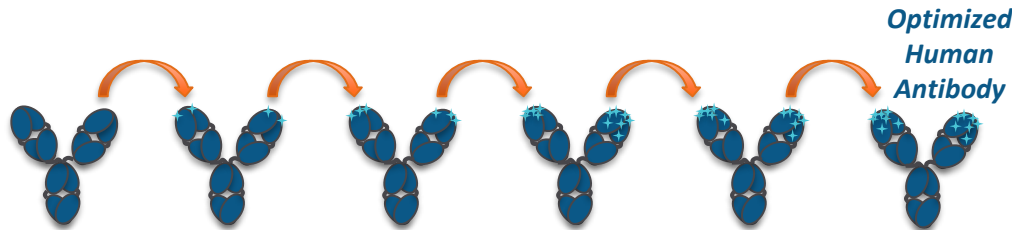
*Genetically-engineered animals have been more successful in development*



*28 FDA-approved fully human antibodies*

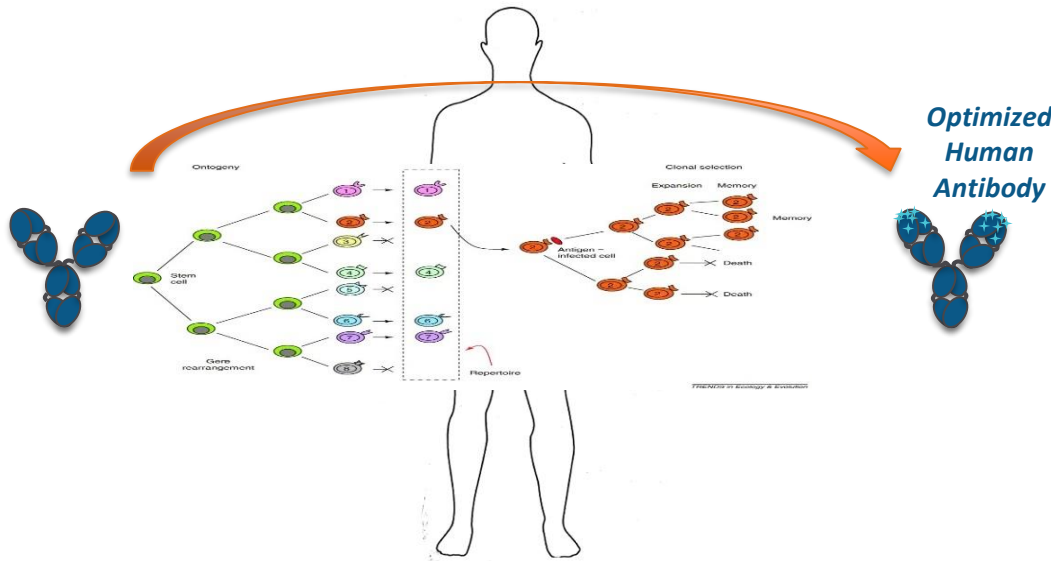
# Discovering Human Antibodies

*The Immune System is Faster than Bioengineering*



**Optimization by Bioengineering**  
*6-12 months (or longer)*

- Multi-step, iterative process
- Possible gain/loss of activity
- Labor intensive
- Costly
- Time consuming



**Optimized Naturally by Immune System**  
*7-14 days*

- No further engineering required
- Significant time efficiency

# Extreme Competition

*Partners Want Newest and Best Technologies*

***Antibody research is highly competitive***

- Multiple companies pursuing similar targets, making efficiency and speed to market **critical**
- Partners want **the best**
- Partners want **OmniAb**



# OmniAb: A Best-in-Class Technology

## *Our Animal Platforms*



*An industry-leading  
patented, validated  
human antibody rat*



*Added species yields  
additional antibodies  
and increased epitope  
coverage*



*Rat with single  
common light chain,  
designed for bispecific  
human antibodies*



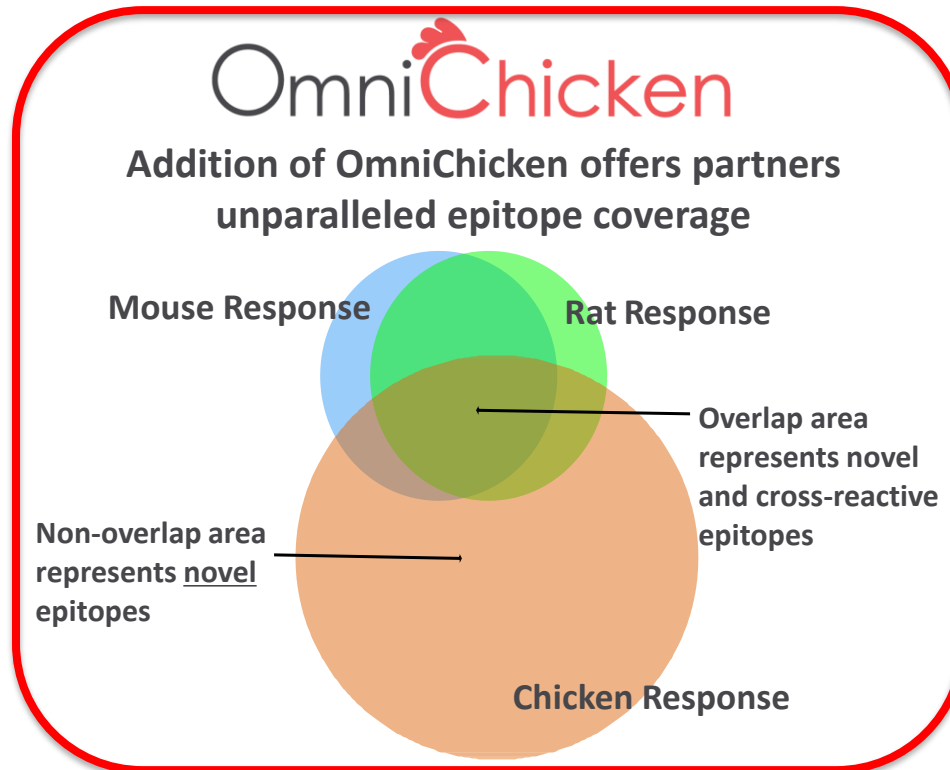
*3<sup>rd</sup> species with unique  
epitope coverage*

***Four animal platforms & three species create  
the broadest antibody repertoires available***

# OmniAb: A Best-in-Class Technology

## *Acquisition of OmniChicken™ Solidified Leadership Position*

- Because of evolutionary distance between birds and mammals, chickens enable the generation of novel antibodies against targets that are not immunogenic in rodents



# OmniAb: A Best-in-Class Technology

- OmniAb is the industry's only antibody platform with genetically engineered **rats, mice and chickens**

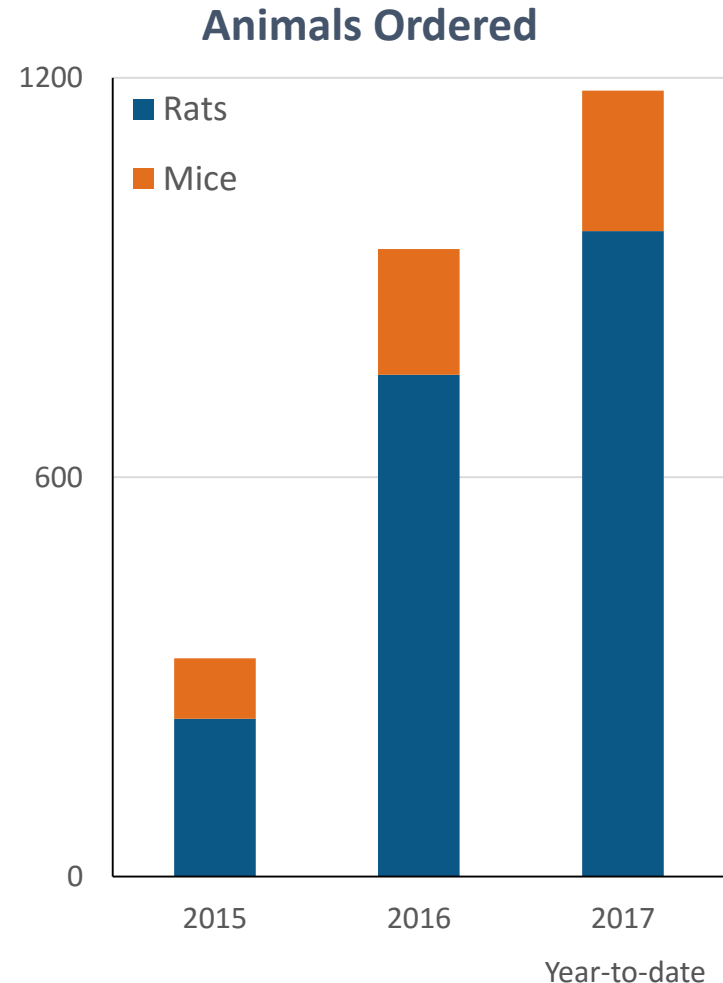


- **Combining three species results in:**
  1. *Increased antibody diversity*
  2. *Increased success of antibody lead discovery, especially for more complex targets (e.g. Ion Channels, G Protein Coupled Receptors)*

# OmniAb: A Best-in-Class Technology

## *Demand for Omni Rodents is Growing*

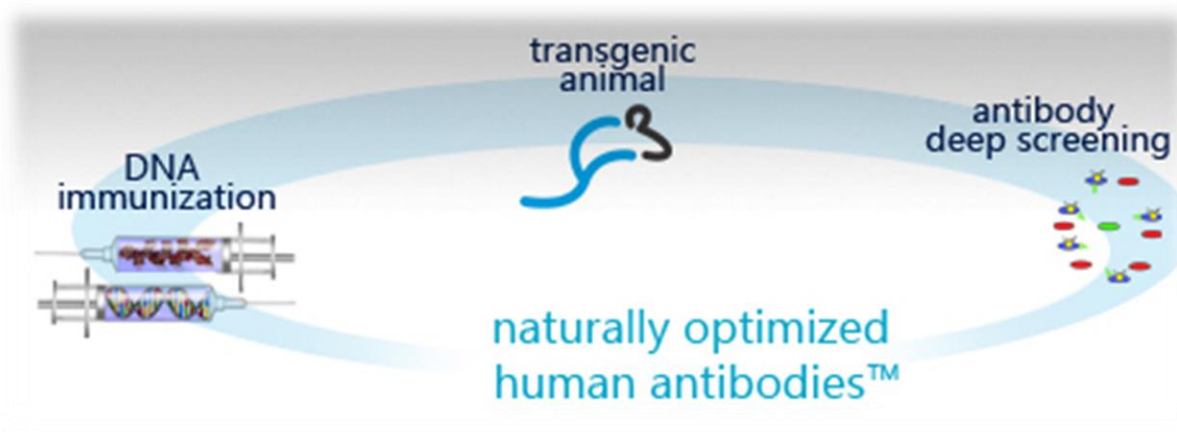
- Partners are ordering more OmniRats and OmniMice following Ligand's acquisition of OmniAb in early 2016



# OmniAb: A Best-in-Class Technology

## *Broad Use*

*We estimate that over 300 antibody targets have been or are being pursued by OmniAb partners*



*Partners report that they have obtained the highest quality antibodies for the most difficult targets when using OmniAb*



# OmniAb: A Best-in-Class Technology

## Intellectual Property

- **Broad protection** exists under issued OmniAb patents, with Freedom-to-Operate for all indications worldwide
- Key **internal know-how** further protects assets
- Other discovery technologies have been subject of significant complexity relating to Freedom-to-Operate

## Publications

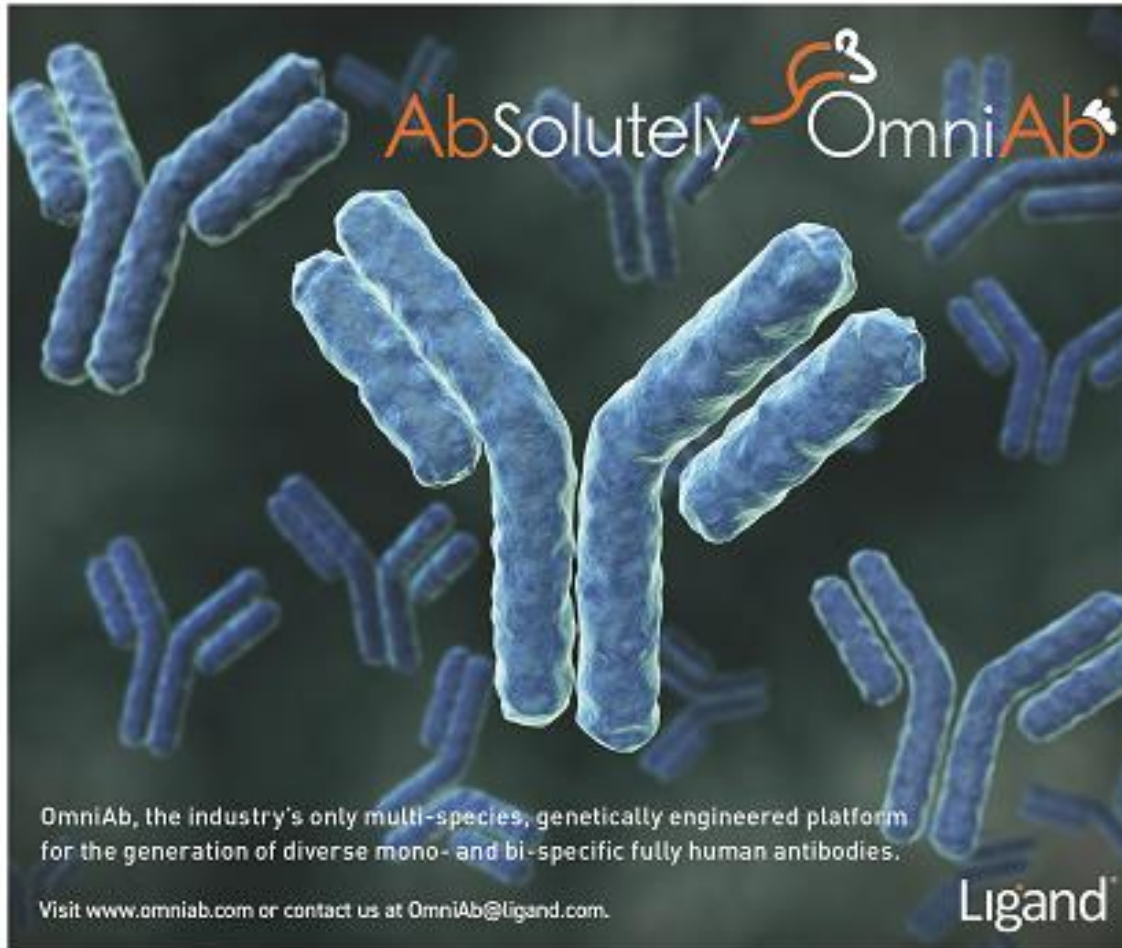
- *Science* publication of OmniRat created **global visibility** for OmniAb technology
- Partner clinical progress creates **continued visibility and clinical validation**
- **Recent publications** describing *OmniChicken* have continued visibility


## Innovation & Customer Service

- **Next generation animals**, launching in 2018, keep OmniAb on cutting edge
- Ligand's renowned customer service creates **optimal partner experience**
- Have recently added OmniChicken **collaboration services**

# OmniAb: A Best-in-Class Technology

*Active Initiatives Create Broad Awareness with Targeted Audience*



AbSolutely  OmniAb

OmniAb, the industry's only multi-species, genetically engineered platform for the generation of diverse mono- and bi-specific fully human antibodies.

Visit [www.omniab.com](http://www.omniab.com) or contact us at [OmniAb@ligand.com](mailto:OmniAb@ligand.com).

Ligand

Three Species.  
One License.

Naturally  
Optimized  
Human  
Antibodies®

 OmniRat  
naturally optimized human antibodies®

 OmniMouse  
naturally optimized human antibodies®

 OmniFlic  
naturally optimized human antibodies®

 OmniChicken  
naturally optimized human antibodies®

OmniAb, OmniRat, OmniMouse, OmniFlic, the mouse design, and NATURALLY OPTIMIZED HUMAN ANTIBODIES are trademarks of QNT Inc., registered in the United States and many other countries.

# OmniAb: Our Partners' Perspectives

## Time and Productivity Gains



### Time Savings

*"We are getting high-affinity antibodies **in a rapid period of time** ... this improves our cycle times for antibody discovery substantially"*

*"For us, this saves significant time as **we do not need to humanize**"*

### Productivity/Efficiency of Animal-based System, High Antibody Quality with OmniAb

*"There are major benefits to leveraging the in vivo selection pressure of an animal to select an antibody for you"*

*"**15 out of 15 targets** we have pursued with the technology have yielded high-quality antibodies"*

*"The animal-based approach is best for identifying quality antibodies"*

*"With the OmniAb technology, **your hit is your lead**"*

# OmniAb: Our Partners' Perspectives

## *Freedom-to-Operate and Comparison to Other Technologies*

### *Freedom-to-Operate*



*"Freedom to operate was **very clear** to us"*

*"Having a rat and a mouse available was a big selling point for us"*

### *As Compared to Competition and Other Technologies*

*"We ran OmniRat **head-to-head** versus Phage Display and OmniRat won ... the OmniRat will beat Phage Display any day"*

*"OmniRat gets us there in **half the time** as compared to another technology we've used"*

# OmniAb: A Best-in-Class Technology

*“Three Species – One License”*

 OmniRat  OmniMouse  OmniChicken

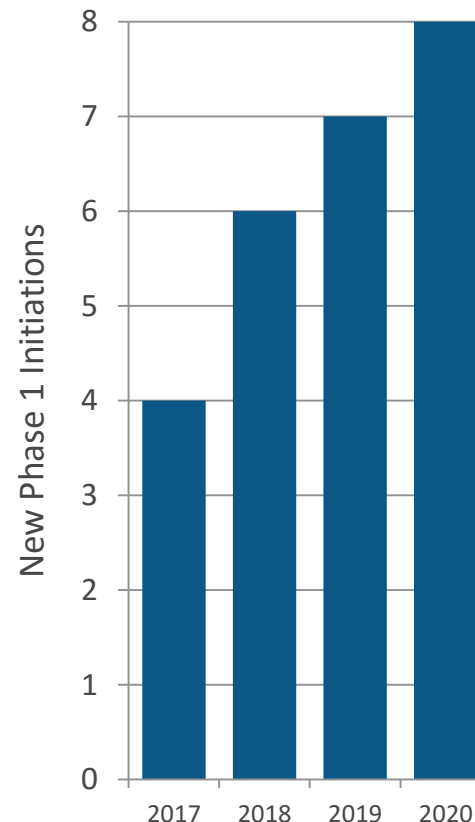
 OmniAb<sup>®</sup>

# OmniAb: Future Outlook

## *Potential New Clinical Starts by Year*

- There are **4 OmniAb-discovered antibodies** in the clinic today
  - Increased frequency and depth of interaction with our partners provides insights into potential new clinical starts
- We now estimate a total of ~25 clinical-stage programs using OmniAb-discovered antibodies by 2020

*Projected  
OmniAb-Derived  
Antibody Clinical Initiations*



# OmniAb: Future Outlook



- **Growing list** of partners following acquisition by Ligand
  - 7 new partners in 2017, 4 OmniAb antibodies in clinical phase
- **>300 antibody discovery projects** have been initiated by partners
- **OmniChicken** further established OmniAb's leadership position
  - Expanded epitope coverage



- **The global leader in antibody discovery space, estimating:**

<i>Parameter</i>	<i>2020</i>	<i>2025</i>
<i>Number of OmniAb Partners</i>	45	60
<i>Clinical-stage OmniAb Antibodies</i>	25	>40
<i>Approved Drugs</i>	-	1-3

# *Portfolio Pyramid*

*Matt Foehr*



# Portfolio Pyramid

**PROMACTA**

**Kyprolis**  
(carfilzomib) for Injection

**Evomela**  
(melphalan) for Injection  
50 mg per vial

**Baxdela IV**  
(Melinta)

**Sparsentan**  
(Retrophin)

**Brexanolone**  
(Sage Therapeutics)

**Lasofoxifene**  
(Sermonix)

**Prexasertib**  
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**BMS986231**  
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**Ganaxolone IV**  
(Marinus)

## The Top 3

*Commercial assets paying significant royalties*

## The Big 6

*Leading pipeline assets based on stage and/or potential value*

## The Next 12

*Assets emerging as next class with high revenue potential*

***Promacta<sup>®</sup>***

# Promacta®: Blockbuster Commercial Potential

- Oral medicine that boosts platelets in patients with thrombocytopenia, or low-platelets
- Partnered with Novartis worldwide
- Long patent protection with Orange Book patent expiration 2027
- Sales trending to **~\$850 million** for 2017; Consensus third-party analyst estimates project **\$1.3 billion** in 2021
- Approved for numerous indications involving low platelets, and multiple trials underway to support label expansion



HELP TAKE YOUR PATIENTS WITH  
ADULT CHRONIC IMMUNE THROMBOCYTOPENIA

FROM REPEATED RELAPSE  
TO LONG-TERM RESPONSE

☐ PROMACTA® (eltrombopag) was studied in the 3-year EXTEND clinical trial  
☐ Only oral once-daily TPO receptor agonist  
☐ Convenient dosing, so your patients can take it at home, at work, or on the go

The first time patients relapse after corticosteroids, it's time to move on to a long-term, second-line treatment. Learn more at [www.promacta.com](http://www.promacta.com).

**Indication**  
PROMACTA is indicated for the treatment of thrombocytopenia in adult and pediatric patients 1 year and older with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulin, or splenectomy.

**Limitation of Use**  
PROMACTA should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.

**Important Safety Information for PROMACTA® (eltrombopag)**

**WARNING: RISK FOR HEPATIC DECOMPENSATION IN PATIENTS WITH CHRONIC HEPATITIS C**  
In patients with chronic hepatitis C, PROMACTA in combination with interferon and ribavirin may increase the risk of hepatic decompensation. (See Section 5.1 of the full Prescribing Information for additional information).

**RISK OF SPONTANEOUS BLEEDING**  
PROMACTA may increase the risk of severe and potentially life-threatening hepatotoxicity. Monitor hepatic function and discontinue dosing as recommended. (See Section 5.2 of the full Prescribing Information for additional information).

**Hepatotoxicity**  
PROMACTA may increase the risk of severe and potentially life-threatening hepatotoxicity. Monitor serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin prior to initiation of PROMACTA, every 2 weeks during the dose adjustment phase, and monthly following establishment of a stable dose. PROMACTA (eltrombopag) and DAPPEL, which may need to be discontinued. If ALT and/or AST are elevated, perform liver tests. Exclude abnormal serum liver tests with repeat testing within 5 to 7 days. If the abnormalities are confirmed, monitor serum liver tests weekly until resolved or stabilized.

Discontinue PROMACTA if ALT levels increase to 10 times the upper limit of normal (ULN) in patients with normal liver function or 3 times the ULN in patients with preexisting elevation in transaminases and are progressively increasing, or persistent for 48 weeks or accompanied by increased direct bilirubin, or accompanied by clinical symptoms of liver injury or evidence for hepatic decompensation.

If the potential benefits for continuing treatment with PROMACTA outweighs the risk for hepatotoxicity, then consider cautiously continuing PROMACTA and monitor serum liver tests weekly during the dose adjustment phase. Hepatotoxicity may manifest as hepatomegaly, jaundice, or other signs of liver dysfunction.

If PROMACTA is discontinued, it may not be restarted. If restarted, monitor serum liver tests weekly until resolved or stabilized.

Intermittent use of PROMACTA for 14 days every 4 weeks is allowed. The duration of liver laboratory values measured approximately 3 months after initiation of PROMACTA. In all cases, the most recent laboratory results should be used.

Please see continued Important Safety Information and Brief Summary of full Prescribing Information for PROMACTA on adjacent pages.

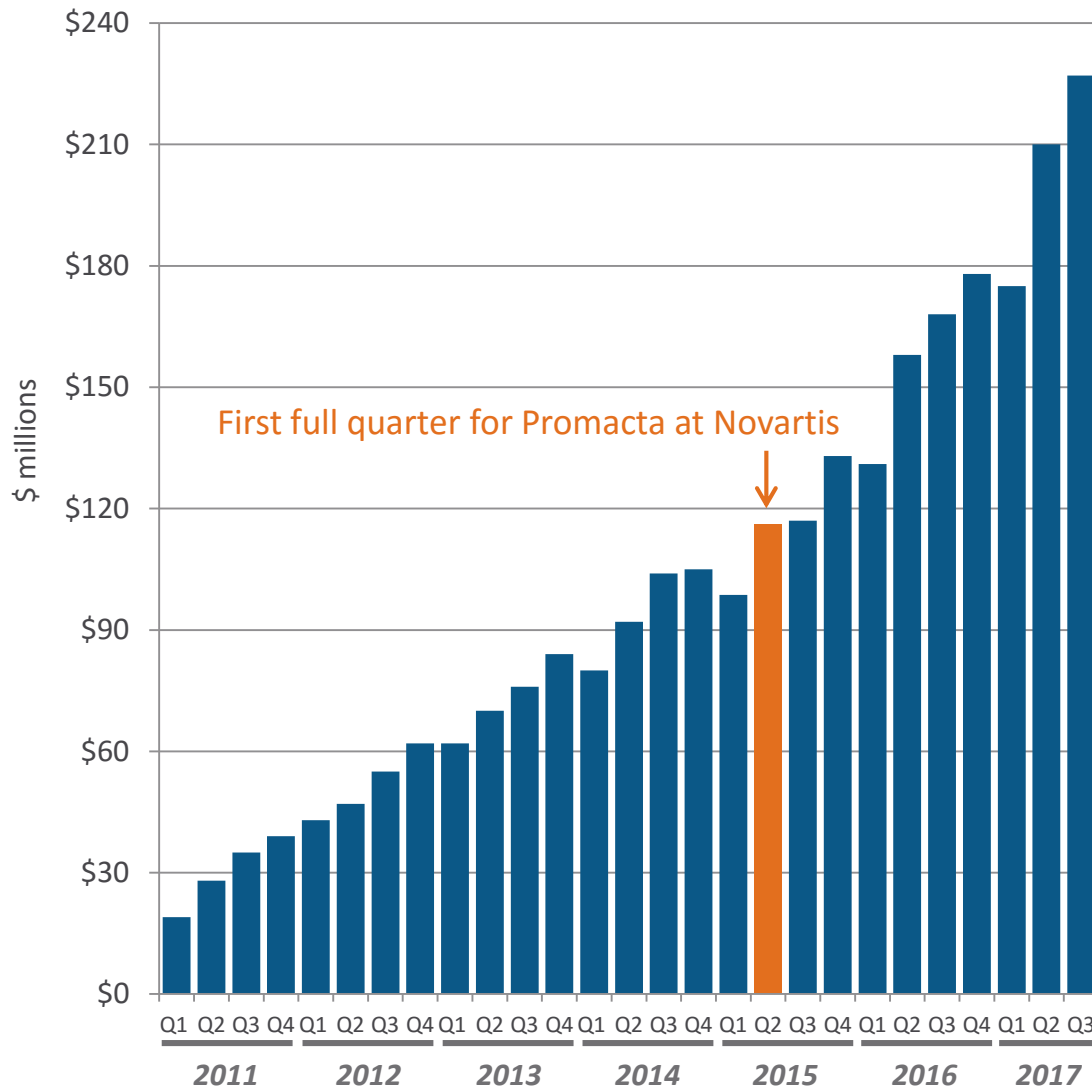
**Promacta®**  
(eltrombopag)  
25mg, 50mg, 75mg tablets

# Promacta: Label Expansion

- 36 ongoing clinical trials
- Recent data and events have continued to demonstrate the significant potential for and interest in Promacta
- Novartis conducting or supporting studies to expand label
  - First-line Severe Aplastic Anemia (SAA): Phase 2 SOAR and Phase 3 RACE studies in combination with immunosuppressive therapy (cyclosporine +/- horse ATG)**
  - Low to intermediate risk MDS: Phase 2 studies underway conducted by NIH/NHLBI (US) and Associazione Qol-one (EU)**
  - CIT: Phase 2 study of thrombocytopenia associated with tyrosine kinase therapy in CML or myelofibrosis**
- Novartis plans global regulatory filings for first-line SAA in 2018
- Low-to-intermediate risk-1 MDS data recently published in *Lancet Haematology*



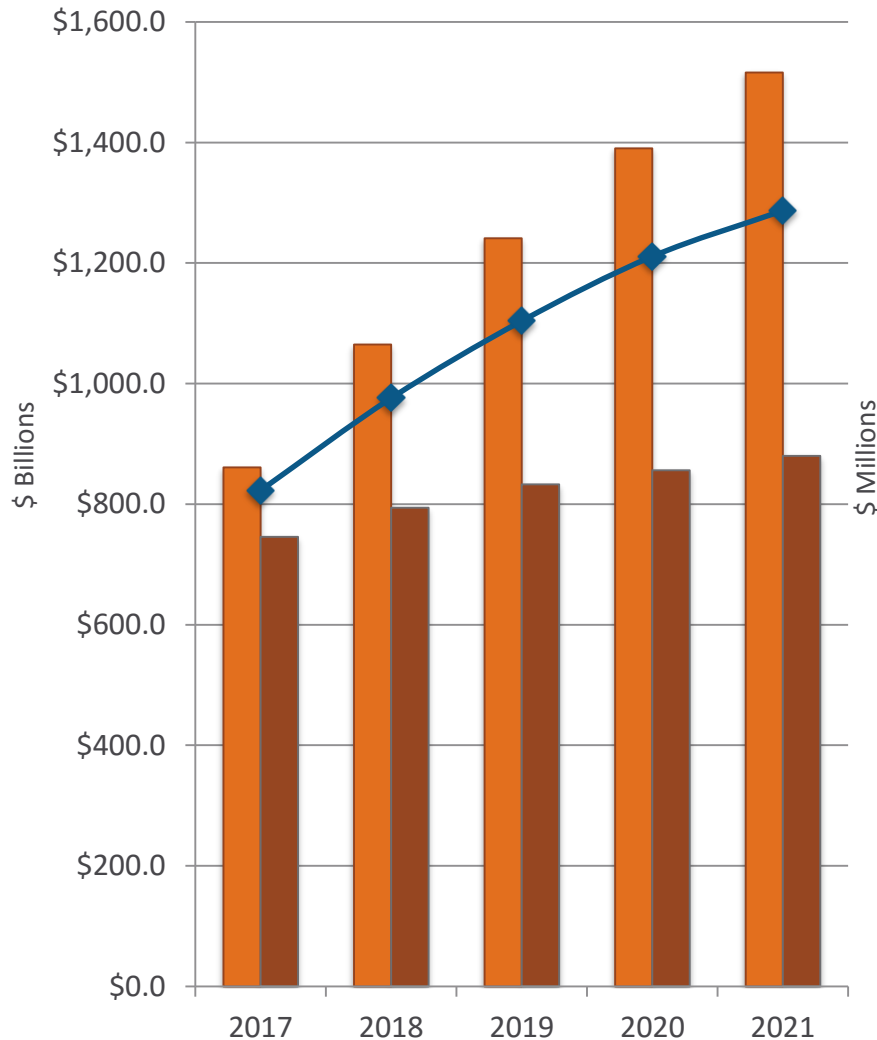
# Promacta: Quarterly Revenue



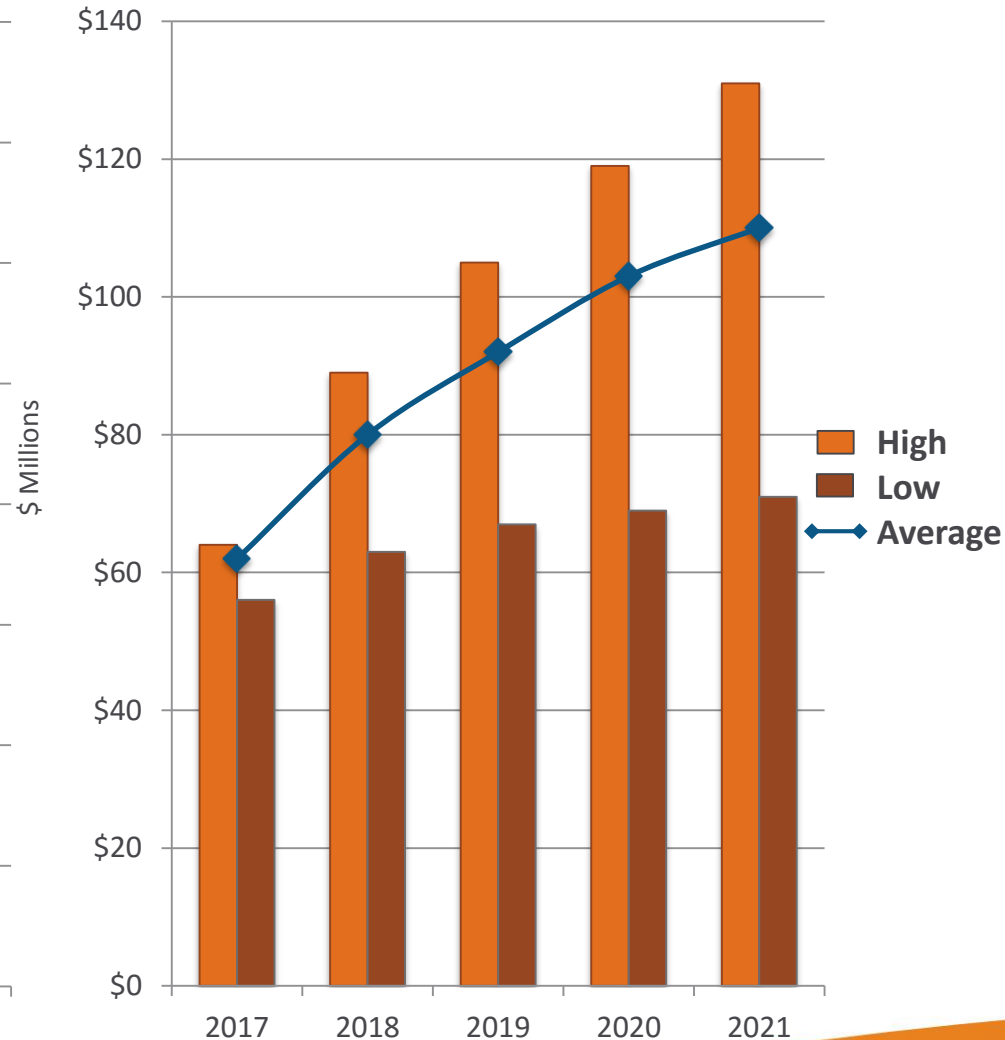
- Q3'17 revenue was \$227 million, a \$59 million increase (35%) over Q3'16
- Sales now annualize to over \$900 million
- Considered by Novartis as one of their global ***“key growth drivers”***

# Promacta Projections: NVS Sell-Side Analysts

*These Revenue Projections ...*



*...Yield these Royalty Projections*



Source: Thomson Reuters Cortellis and analyst reports - 13 Novartis covering analysts as of 11/3/17

2017 royalties calculated on a one quarter lag

Beginning Q1 2018, royalties will be recognized in the same quarter in which sales occurred

***Kyprolis®***

- Kyprolis viewed as best-in-class proteasome inhibitor for multiple myeloma (MM)
- Developed and marketed by Amgen
  - Utilizes Ligand's Captisol technology

## Approved Uses

KYPROLIS® (carfilzomib) is a prescription medication used to treat patients with relapsed or refractory multiple myeloma who have received one to three previous treatments for multiple myeloma. KYPROLIS is approved for use in combination with dexamethasone or with lenalidomide plus dexamethasone, which are other medicines used to treat multiple myeloma ... [Read More](#)

This site is intended for U.S. residents only.

[Product Information](#) | [Important Safety Information](#) | [Approved Uses](#) | [Healthcare Professionals](#)



Call 1-888-427-7478 **AMGEN ASSIST 360**  
Support, Simplified

[About Multiple Myeloma](#)

[About KYPROLIS](#)

[Starting on KYPROLIS](#)

[Getting Support](#)



- Approved for relapsed or refractory MM in the US, EU and Japan (Ono)<sup>1</sup>
  - As single agent, or in combination with dexamethasone or Revlimid and dexamethasone
- In the last 8 months, Kyprolis has demonstrated overall survival improvement in both the Phase 3 **ENDEAVOR** and Phase 3 **ASPIRE** studies, bolstering the value proposition for the drug in a competitive space

<sup>1</sup> KYPROLIS is also approved in Argentina, Australia, Bahrain, Canada, Hong Kong, Israel, Kuwait, Lebanon, Macao, Mexico, Thailand, Colombia, S. Korea, Qatar, Switzerland, Singapore, Taiwan, Jordan, Egypt, Saudi Arabia, United Arab Emirates, Turkey, Russia, Brazil, India and Oman. Additional regulatory applications for KYPROLIS are underway and have been submitted to health authorities worldwide.

Sources: Amgen public disclosures, [www.kyprolis.com](http://www.kyprolis.com)



# Kyprolis

## Amgen Public Commentary - ASPIRE and ENDEAVOR Phase 3 Data



*"In each case, KYPROLIS reduced the risk of death by 21%, and improved survival by approximately eight months, a **very meaningful clinical result that reinforces the role for KYPROLIS in driving deep and durable responses.**"*

**Sean E. Harper, MD**  
Executive Vice President, Research & Development

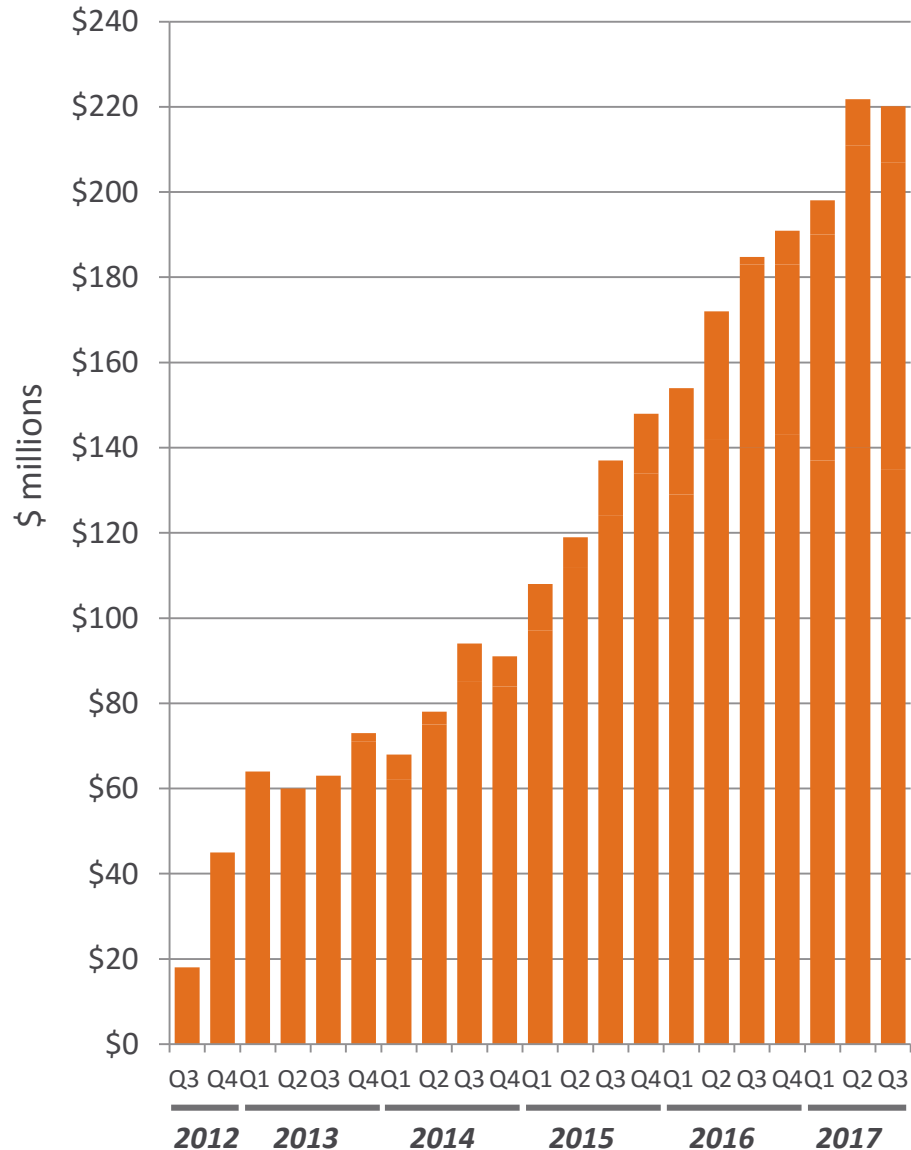
*"With these two new sets of overall survival data, our message to physicians is simple and powerful: **When multiple myeloma relapses, don't put your patient's survival at risk.**"*

**Anthony C. Hooper**  
Executive Vice President, Global Commercial Operations

*"We completed two pivotal studies showing an overall survival benefit for KYPROLIS patients with relapsed disease, **underscoring our confidence in this molecule as the new standard of care for these patients.**"*

**Robert A. Bradway**  
Chairman & Chief Executive Officer

# Kyprolis: Quarterly Revenue



- Amgen/Ono reported combined Q3 revenue of \$220 million
- Rest-of-world contribution becoming more substantial

# Kyprolis

## Status

- Third-party analysts estimate product on track to exceed **\$830 million** in global revenue in 2017
- Factors supporting potential revenue growth:
  1. *New or recently-launched territories*
  2. *Label expansion potentially supported from ongoing trials*
  3. *Use in combination with other medications*

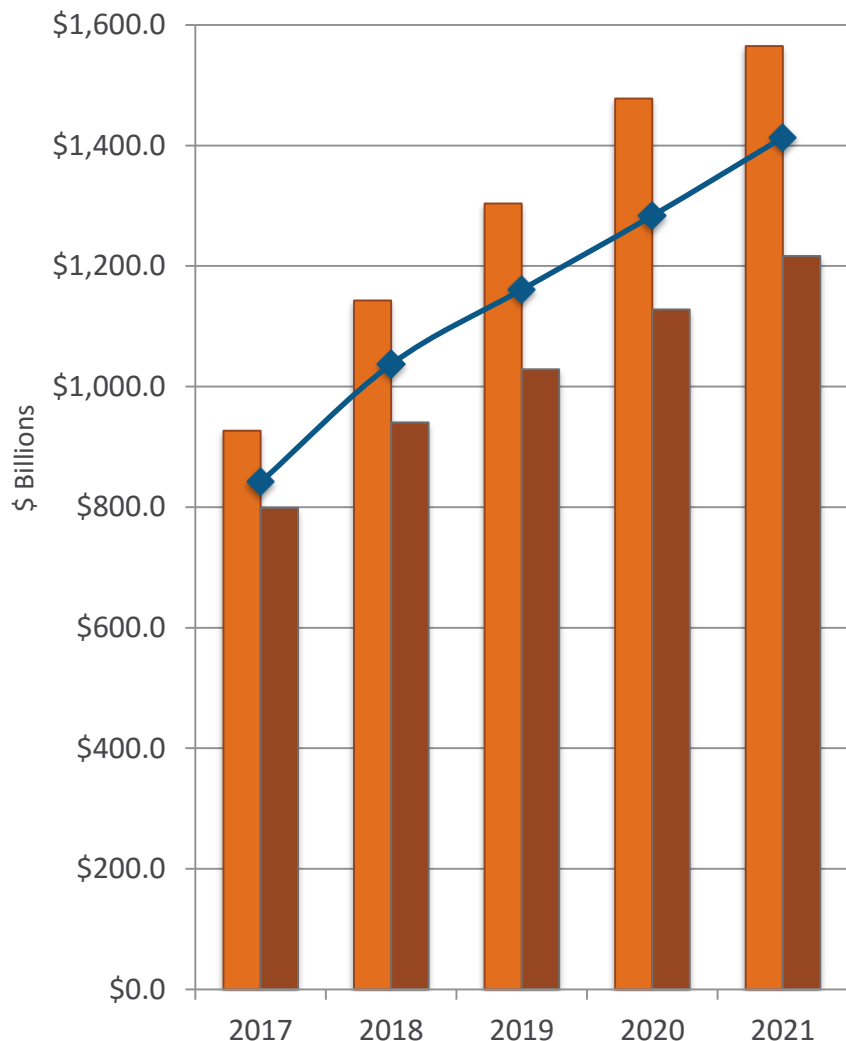
# Kyprolis

## Status and Plans

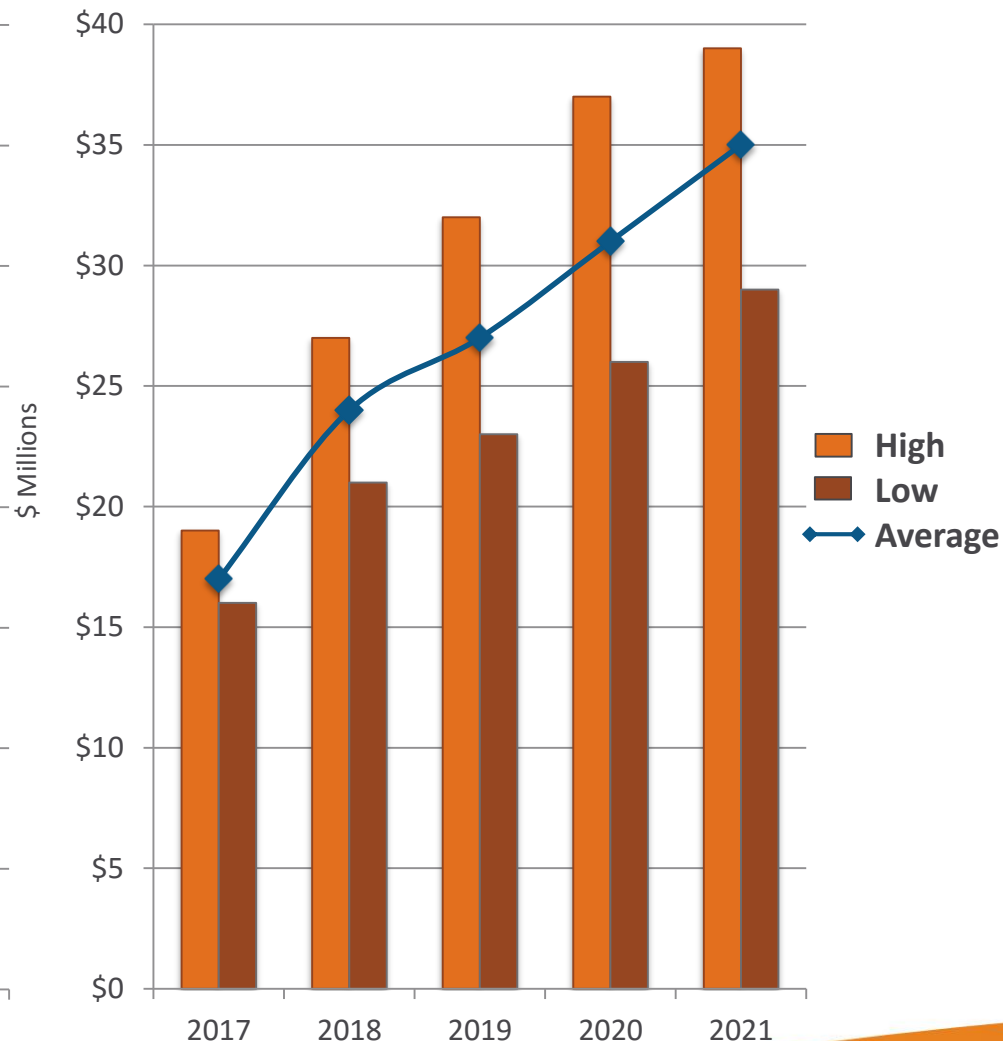
- Amgen is very active with clinical and regulatory activities for Kyprolis
  - Submitted sNDA to include Overall Survival data from **ENDEAVOR** study
    - Under review at FDA, with target action date of **April 30, 2018**
  - Regulatory submissions in preparation for **ASPIRE** Overall Survival data
  - **Once-Weekly Dosing**: Interim analysis of Phase 3 **ARROW** trial showed superior efficacy and comparable safety
  - **Relapsed/Refractory Multiple Myeloma**: Phase 3 trial in combination with Janssen's *Darzalex*® began in Q2 2017
  - **Front-Line Multiple Myeloma**: Designing Phase 3 study in combination with Revlimid and dexamethasone

# Kyprolis Projections: Sell-Side Analysts

*These Revenue Projections ...*



*...Yield these Royalty Projections*



Source: Thomson Reuters Cortellis and analyst reports, 12 Amgen and Ono Pharmaceuticals covering analysts as of 11/3/17

Excluding highest/outlier analyst

2017 royalties calculated on a one quarter lag

Beginning Q1 2018, royalties will be recognized in the same quarter in which sales occurred

***EVOMELA***®

- Captisol-enabled formulation of chemotherapy drug used for stem cell transplant conditioning in MM, approved by FDA in 2016
  - Stem cell transplant is an important course of therapy in MM, increasing in total number as patients are living longer
- Captisol improves product stability and enables the removal of propylene glycol, which is associated with renal and cardiac toxicities
- Product licensed globally to Spectrum Pharmaceuticals, who completed development and launched
  - 20% royalty on net sales to Ligand
  - Sub-licensee partner in China (CASI) recently announced priority review for approval for the product in China

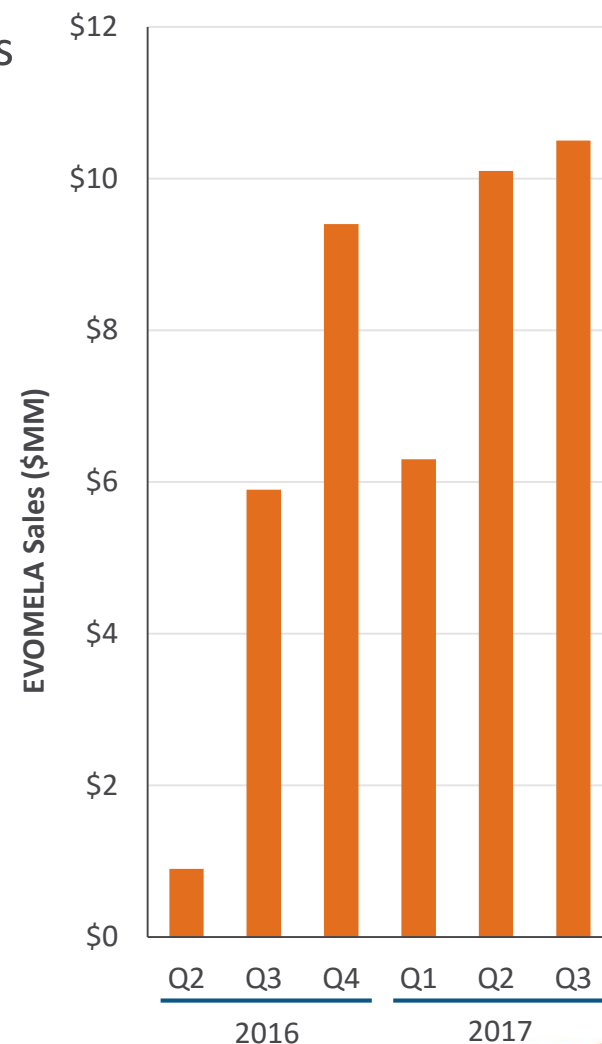


# EVOMELA: Launch Performance

- Initial adoption strong given label and clear benefits
- Product on track to do \$33 - \$38 million in 2017
- Third-party analyst outlook indicates revenue potential of \$50 - \$60 million in 2020
- Factors supporting potential revenue growth:
  1. *International sales from licensees*
  2. *Further US market expansion*
  3. *New labeled indications*

*“Regarding EVOMELA, we are thrilled with the performance. We are the **market leader** and the market has spoken on the differentiation of the product.”*







**Tom Riga**  
Chief Commercial Officer





# The Big 6: Major Pipeline Assets

*Leading pipeline assets based on stage and/or potential value*

<i>Partner</i>	<i>Program (Therapy Area)</i>	<i>Stage</i>	<i>Royalty Rate</i>	<i>Upcoming Events</i>
 <b>Melinta</b> THERAPEUTICS	<b>Baxdela-IV</b> (Infection)	Approved	2.5%	<b>Product Launch</b>
 <b>SAGE</b> THERAPEUTICS	<b>Brexanolone</b> (Neurology)	Pre-NDA	3.0%	<b>NDA Filing for PPD</b>
 <b>Retrophin</b> <sup>®</sup>	<b>Sparsentan</b> (FSGS- Kidney Disease)	Phase 2/3	9.0%	<b>Phase 3 Initiation</b>
 <b>Sermonix</b> Pharmaceuticals	<b>Lasofoxifene</b> (Oncology/Women's Health)	Phase 2/3	6.0-10.0%	<b>Phase 2 Start</b>
 <b>Bristol-Myers Squibb</b>	<b>BMS986231</b> (Cardiovascular Disease)	Phase 2/3	2.0-3.0%	<b>Phase 2b Data</b>
 <b>Lilly</b>	<b>Prexasertib</b> (Oncology)	Phase 2	1.5-3.0%	<b>Phase 2 Data in various advanced cancers</b>

# The Big 6: Neurology



*“In these studies, brexanolone provided a profound and durable effect over the study period that could be an important step in potentially changing the way health care providers think about treating this disorder.”*

– Dr. Samantha Meltzer-Brody, M.D., M.P.H., associate professor and director of UNC Perinatal Psychiatry Program of the UNC Center for Women’s Mood Disorders  
Nov. 9, 2017

## Brexanolone (Pre-NDA)

---

- Brexanolone (SAGE-547) IV is Sage’s proprietary, Captisol-enabled, formulation of allopregnanolone
  - Allosteric GABA<sub>A</sub> receptor modulator
- In development as an acute interventional treatment for post-partum depression (PPD)
- Announced positive top-line data on November 9, 2017 from two Phase 3 HUMMINGBIRD trials in severe and moderate PPD
  - Brexanolone provided rapid and durable reduction over 30 days in depressive symptoms as measured by HAM-D in both placebo-controlled multi-center trials

# The Big 6: Kidney Disease



*“These [open-label extension] findings ... underscore the potential of sparsentan to be a **durable approach to treating FSGS.**”*

*– Bill Rote, PhD, Sr. VP and Head of R&D, Retrophin, November 3, 2017*

## Sparsentan (Phase 2/3)

---

- In development for treatment of focal segmental glomerulosclerosis (FSGS), a rare kidney disorder that often leads to end-stage renal disease
  - Could be first FDA-approved therapy for FSGS
  - IgA nephropathy identified as added potential indication
- Met primary efficacy endpoint in Phase 2 DUET study, demonstrating >2-fold reduction in proteinuria compared to Irbesartan after 8-week, double-blind treatment period
  - Progressive reduction in proteinuria, combined with stable kidney function (eGFR), during 40-week open label period
- Retrophin plans to initiate pivotal Phase 3 in FSGS in 2018

# The Big 6: Cardiovascular



Bristol-Myers Squibb

*“Overall, these preliminary findings are encouraging. Therefore, further large-scale testing is **strongly encouraged** to assess the effect of this drug on outcomes in this patient population.”*

*- Editorial Comment,  
European Journal of Heart  
Failure  
October 2017*

## BMS986231 (Phase 2b)

---

- Captisol-enabled, novel, intravenous nitroxyl (HNO) donor
  - In development for acute decompensated heart failure
  - BMS acquired from Cardioxyl in late 2015 for \$2 billion, including milestone payments
- In a Phase 2a study recently published in the *European Journal of Heart Failure*, 6-hour infusion was safe with preliminary efficacy in advanced heart failure patients
  - Improved heart function and reduced pulmonary blood pressure without increasing heart rate or oxygen consumption
- Phase 2b study underway of continuous 48-hour infusion in hospitalized heart failure patients

# The Big 6: Oncology



*“Prexasertib is a first-in-class agent. ... We look forward to continued development of prexasertib in ovarian and other cancer types”*

*- Dr. Levi Garraway, SVP,  
Oncology Global Development  
& Medical Affairs  
July 25, 2017*

## Prexasertib (Phase 2)

---

- Captisol-enabled, small molecule checkpoint kinase 1 (CHK1) and CHK2 inhibitor
  - CHK inhibitors induce DNA double-strand breaks, increased replication stress and cancer cell death
- Highlighted as a “**Priority Internal Development Program**” by Lilly for focused internal R&D investment
- Demonstrated promising activity in Phase 2 trial in platinum-sensitive and resistant, high-grade ovarian cancer
  - 35% of BRCAwt+ ovarian cancer patients achieved partial response; ~2x higher than historical controls
- Ongoing trials in small cell lung cancer, head and neck cancer, and advanced metastatic cancer

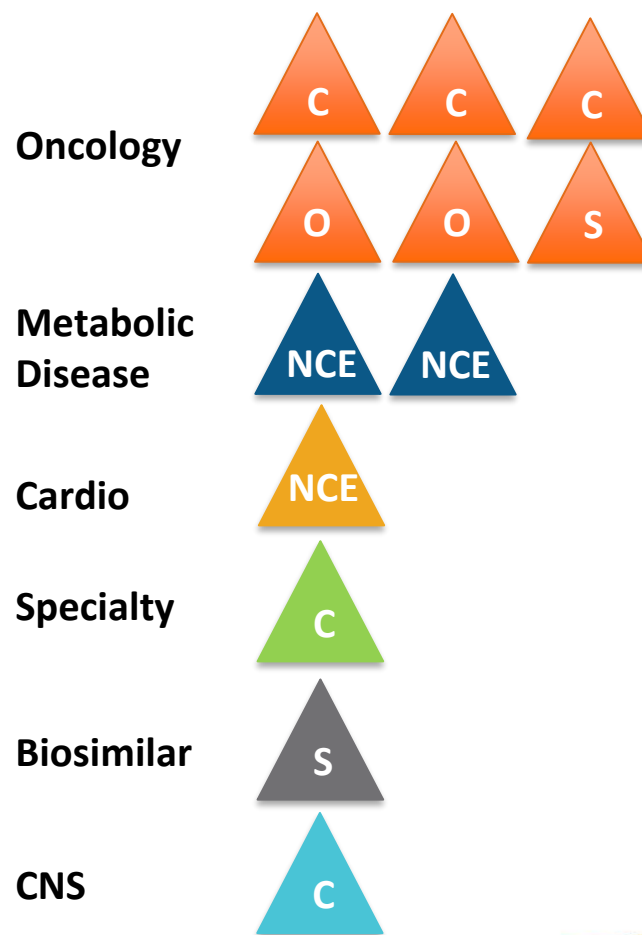
# ***The Next 12***

# The Next 12: Composition

*Assets emerging as next class with high revenue potential*

- 12 additional pipeline programs continue to expand the breadth and diversity of Ligand's growing portfolio
- Diverse partners and indications
- Diversity of underlying technology/IP
  - 5 Captisol-enabled programs (C)
  - 3 New Chemical Entity programs (NCE)
  - 2 Selexis program (S)
  - 2 OmniAb programs (O)
- Increasing number are large molecules
- All are well-resourced programs with highly-committed partners
  - Emerging data and progress
  - Potential to contribute meaningfully to Ligand's future growth

## Composition of The Next 12



# The Next 12: Oncology



## Merestinib (Phase 2)

---

- Captisol-enabled, small molecule MET kinase inhibitor
  - Reversible type II ATP-competitive inhibitor of MET
- Phase 1 and Phase 2 trials underway in advanced cancer and biliary tract cancer
  - Trials expected to complete in 1H and 2H 2018, respectively

## Pevonedistat (MLN4924, Phase 2)

---

- Captisol-enabled, novel NEDD8 activating enzyme inhibitor
- Previous studies have indicated effectiveness in melanoma patients who were resistant to other therapies
- Currently being investigated in high-risk MDS
  - Phase 2 in advanced MDS estimated completion Dec. 2017
  - Phase 3 PANTHER study in high-risk MDS to begin Nov. 2017





# The Next 12: Oncology



## AMG-330 (Phase 1)

---

- Captisol-enabled, anti-CD33 x anti-CD3 bispecific T-cell engager (BiTE®) antibody, for treatment of acute myeloid leukemia (AML)
- Phase 1 study in relapsed/refractory AML underway
  - Data read-out estimated 2018 ([clinicaltrials.gov](http://clinicaltrials.gov))

## Seribantumab (MM-121, Phase 2)

---

- First-in-class, HER3 mAb targeting heregulin (HRG) positive cancers; a Selexis technology program
  - Granted orphan drug designation for HRG-positive NSCLC in October 2017 and Fast Track designation in July 2016
- Two Phase 2 studies in NSCLC and breast cancer in-progress
  - Phase 2 NSCLC study data expected 2H 2018
  - Phase 2 breast cancer trial started August 2017



# The Next 12: Antibodies

## APVO436 (Preclinical)

- Bispecific anti-CD123 and anti-CD3 OmniAb-derived mAb
  - CD123 is highly expressed in several hematological malignancies (e.g. AML, ALL and MDS)
- Designed to simultaneously target CD123 and CD3 and redirect T-cell cytotoxicity against CD123-expressing tumors
  - Preclinical data presented at AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics annual meeting in October

## JNJ-64007957 (Phase 1)

- Novel, bispecific anti-BCMA x CD3 OmniAb-derived mAb being developed for multiple myeloma (MM)
  - Binds validated target B Cell Maturation Antigen (BCMA) and CD3, with potent activity demonstrated in MM models
- Phase 1 underway in patients with multiple myeloma
  - Estimated primary completion Nov. 2018 ([clinicaltrials.gov](https://clinicaltrials.gov))



# The Next 12: CNS and Biosimilar



## Ganaxolone IV (Phase 2)

---

- Captisol-enabled, positive allosteric modulator of GABA<sub>A</sub>
- Completed Phase 1 study in status epilepticus (SE), and plan to initiate Phase 2 SE study in 2017
  - Received FDA orphan drug designation for the treatment of SE
- Initiated Phase 2 MAGNOLIA trial in June 2017 in women with severe PPD

## CHS-0214 (Phase 3)

---



- Biosimilar etanercept (Enbrel); Selexis technology program
  - Successfully completed five clinical studies, including:
    - Three comparative PK studies
    - Two Pivotal Phase 3 studies (psoriasis and rheumatoid arthritis)
- Guidance on EU filing expected 1H 2018

# The Next 12: Ophthalmology and Hypertension



## Reproxalap (ADX-102, Phase 3)

---

- Captisol-enabled eye-drop formulation of ADX-102
  - Novel, small-molecule aldehyde trap for ocular diseases
- In 2017, positive Phase 2 results announced in allergic conjunctivitis and in dry eye
- Multiple Phase 3 studies to begin in 1H 2018
  - Allergic conjunctivitis, noninfectious anterior uveitis, and Sjogren-Larsson Syndrome















## Esaxerenone (CS-3150, Phase 3)

---

- Oral, non-steroidal, selective mineralocorticoid receptor antagonist for hypertension and congestive heart failure
- In September 2017, positive Phase 3 top-line results announced from pivotal ESAX-HTN trial in Japanese patients with essential hypertension
  - Filing planned in Japan in 1Q 2018

# The Next 12: Emerging Assets

Partner	Program (Therapy Area)	Technology	Stage	Royalty Rate	Upcoming Events
	Merestinib (Oncology)	Captisol	Phase 2	1.5-3.0%	Phase 2 Data (Advanced Cancer)
	Pevonedistat (Oncology)	Captisol	Phase 2	**	Phase 2 Data (High Risk MDS)
	AMG-330 (Oncology)	Captisol	Phase 1	**	Phase 1 Data (AML)
	Seribantumab (Oncology)	Selexis	Phase 2	<1%	Phase 2 Data (NSCLC)
	APVO436 (Oncology)	OmniAb	Preclinical	**	IND Filing
	JNJ-64007957 (Oncology)	OmniAb	Phase 1	**	Phase 1 Data (Multiple Myeloma)
	Ganaxolone IV (CNS)	Captisol	Phase 2	**	Phase 2 Data (PPD)
	CHS-0214 (Etanercept Biosimilar)	Selexis	Phase 3	**	EU Filing
	Reproxalap (Ophthalmology)	Captisol	Phase 3	Low single digit	Phase 3 Data (Allergic Conjunctivitis)
	Esaxerenone (Hypertension)	NCE	Phase 3	**	Japan NDA Filing
	VK5211 (Metabolic)	NCE	Phase 2	7.25-9.25%	Phase 2 Data (Hip Fracture)
	VK2809 (Metabolic)	NCE	Phase 2	7.25-9.25%	Phase 2 Data (Hyperlipidemia)

\*\* Royalty rate currently undisclosed

77 Note: Janssen OmniAb license includes all payments in form of development and commercial milestones.



**CAPTISOL<sup>®</sup>**

*Matt Foehr*

## *The leading cyclodextrin technology*

- Captisol is a patented cyclodextrin designed to:
  - Maximize safety
  - Improve solubility, stability and bioavailability
  - Lessen the volatility, irritation, smell or taste of drugs
- Supported with highly reliable supply and world-class technical service
  - Multisite and multi-metric-ton cGMP supply chain using highest-quality partner
    - *2.5 metric ton batch size, validated to pharmaceutical standards*
  - Globally-recognized solubility experts on Ligand team

## A Successful Platform - Five Initiatives Building for the Future

### 1. Recently extended manufacturing agreement with Hovione **through 2024**

- Captisol partners value high product quality and stability of supply

### 2. Adding new European distribution center, further supporting global nature of our partners' manufacturing plans and driving business efficiencies

### 3. Continuing to discover new use settings for Captisol to expand and diversify our customer base

- Recent peer-reviewed publications

**Hovione** 



Received: 16 November 2016 | Revised: 14 March 2017 | Accepted: 23 April 2017  
DOI: 10.1002/ij.3395

WILEY

#### SPECIAL ISSUE: RESEARCH ARTICLE

### Captisol®: an efficient carrier and solubilizing agent for essential oils and their components

Miriana Kfoury<sup>1</sup> | J.D. Pipkin<sup>2</sup> | Vince Antle<sup>2</sup> | Sophie Fourmentin<sup>1</sup> 

<sup>1</sup>Unité de Chimie Environnementale et Interactions sur le Vivant (UCEIV, EA 4492), SFR Condorcet FR CNRS 3417, ULCO, F-59140 Dunkerque, France

<sup>2</sup>Ligand Pharmaceuticals Inc., San Diego, California, USA

Correspondence  
Sophie Fourmentin, Unité de Chimie Environnementale et Interactions sur le Vivant (UCEIV, EA 4492), SFR Condorcet FR CNRS 3417, ULCO, F-59140 Dunkerque, France.  
Email: lamotte@univ-littoral.fr

#### Abstract

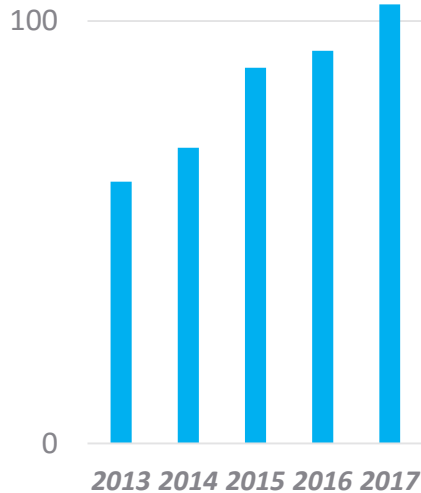
Essential oils (EOs) and their individual components have several biological properties and are used in cosmetics, food and pharmaceutical industries. However, their application still presents a challenge owing mainly to their volatility and their poor aqueous solubility and stability. The aim of this study was to evaluate, for the first time, the ability of Captisol® (sulfobutylether- $\beta$ -cyclodextrin, SBE- $\beta$ -CD) and Captisol-G® (sulfobutylether- $\gamma$ -cyclodextrin, SBE- $\gamma$ -CD) to encapsulate the main volatile components of six essential oils (EOs), to enhance the aqueous solubility of these EOs and to generate controlled release systems. The performance of these CDs was compared to hydroxypropyl- $\beta$ -cyclodextrin (HP- $\beta$ -CD) and  $\gamma$ -cyclodextrin ( $\gamma$ -CD), respectively. Formation constants ( $K_a$ ) of the 40 inclusion complexes were determined by Static Headspace-Gas Chromatography (SH-GC). Then, Total Organic Carbon (TOC) was used to explore and quantify the efficiency of Captisol® and HP- $\beta$ -CD to enhance the solubility of the six EOs. Finally,



## *A Successful Platform - Five Initiatives Building for the Future*

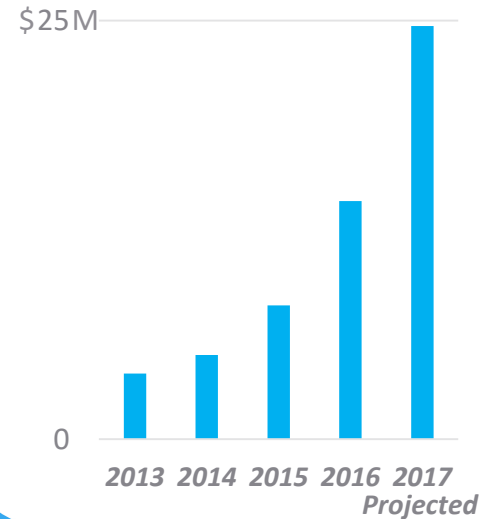
4. Investing in a global intellectual property estate with composition, process and product-specific patent families
  - Issued patents in over 60 countries
  - Patent coverage through 2033 in major markets
  
5. Our expanding Drug Master File (DMF) safety package is a key value-driver, BOTH strengthening and accelerating regulatory filings for our partners
  - Vast safety and clinical database with >200 clinical and safety studies maintained with FDA
  - Key toxicology studies expanding dose and use in specific patient populations added recently

**Number of  
New Research Agreements**



- The number of new Research Agreements continues to grow
  - Indicative of interest and use
  - Not included in Shots-on-Goal count

**Captisol-derived Royalties**



- With an increasing number of commercial assets, Captisol-related royalties have also grown substantially
  - Captisol royalties have increased more than 6x in the last four years

- The AAPS annual meeting is the world's top gathering of pharmaceutical scientists
  - AAPS includes >10,000 of the top formulators and pharmaceutical scientists
- 2017 Captisol partner event on November 13<sup>th</sup> had largest turnout ever
  - Recognized major partner achievements at evening awards ceremony



American Association of  
Pharmaceutical Scientists

## 2017 AAPS Annual Meeting

November 12-15, 2017

San Diego Convention Center



# *Glucagon Receptor Antagonist Program*

*Eric Vajda, Ph.D.  
VP, Preclinical R&D*

# Diabetes

*A serious and growing epidemic*



**30 million** Americans have diabetes

**84 million** Americans have prediabetes

**\$407 billion** spent on diabetes care annually

***Diabetes also significantly increases risks of other serious health problems:***

Heart Disease

Stroke

Kidney Failure

Neuropathy










Lower-Limb Amputations

Blindness

Centers for Disease Control and Prevention, National Diabetes Statistics Report, 2017;  
Rowley, et al., Diabetes 2030: Insights from Yesterday, Today, and Future Trends.  
Population Health Management. 2017 Feb 1; 20(1)6-12.  
American Diabetes Association "Fast Facts" 2017

# Existing Diabetes Therapies are Blockbusters

*But many patients still not meeting glycemic goals*

	Marketer	Drug	Reduction in HbA1c (%) <sup>1</sup>	Global Sales <sup>2</sup>
DPP-IV	 <b>MERCK</b>	Januvia® (sitagliptin)	0.7	\$6.1 B
	 <b>Lilly</b> <b>Boehringer Ingelheim</b>	Tradjenta® (linagliptin)	0.6	\$1.5 B
	 <b>AstraZeneca</b>	Onglyza® (saxagliptin)	0.7 - 0.8	\$720 M
SGLT-2	 <b>Lilly</b> <b>Boehringer Ingelheim</b>	Jardiance® (empagliflozin)	0.3 - 0.8	\$600 M <sup>3</sup>
	 <b>Johnson &amp; Johnson</b>	Invokana® (canagliflozin)	0.6 - 0.8	\$1.4 B
	 <b>AstraZeneca</b>	Farxiga® (dapagliflozin)	0.4-0.5	\$835 M
GLP-1	 <b>novo nordisk</b>	Victoza® (liraglutide)	1.1	\$3.0 B
	 <b>Lilly</b>	Trulicity® (dulaglutide)	0.9 - 1.1	\$926 M
	 <b>AstraZeneca</b>	Byetta/Bydureon® (exenatide)	0.5 - 0.9	\$254 M/\$578 M

<sup>1</sup>Placebo corrected. Source: Prescribing information. Clinical trials with novel drug as add-on therapy to metformin

<sup>2</sup>Global sales according to company full year 2016 financial reports unless otherwise noted

<sup>3</sup>Global sales are estimated from Eli Lilly 2016 report and Boehringer Ingelheim 2015 report








# Need for Novel Therapies

## Advantages of a Potent GRA

- Product profile and recent clinical data suggest significant market advantages for a safe, highly potent, oral GRA

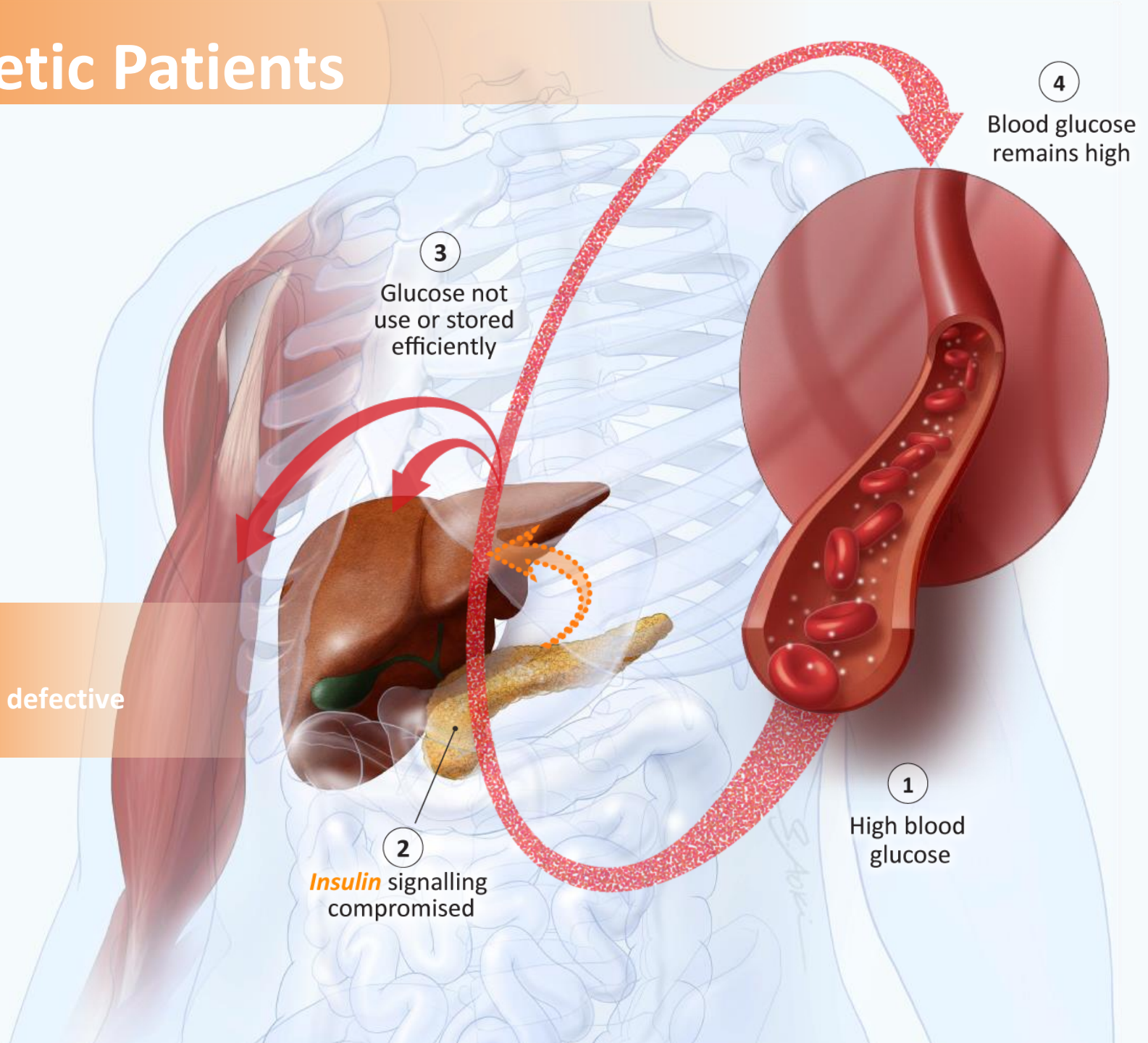
<i>Existing Class</i>	<i>Product Profile</i>	<i>GRA Advantage</i>	<i>GRA Potentially Competitive with Class</i>	<i>Potential GRA Combo with Class</i>
<b>DPP-IV</b>	<i>Modest reduction of plasma glucose</i>	 <b>Higher glucose reduction</b>	✓	✓
<b>SGLT-2</b>	<i>Contraindicated for renally impaired patients, safety considerations</i>	 <b>Potentially effective in renally impaired</b>	✓	✓
<b>GLP-1</b>	<i>Only available as injectables</i>	 <b>Oral</b>	✓	✓



# Diabetic Patients

## Insulin

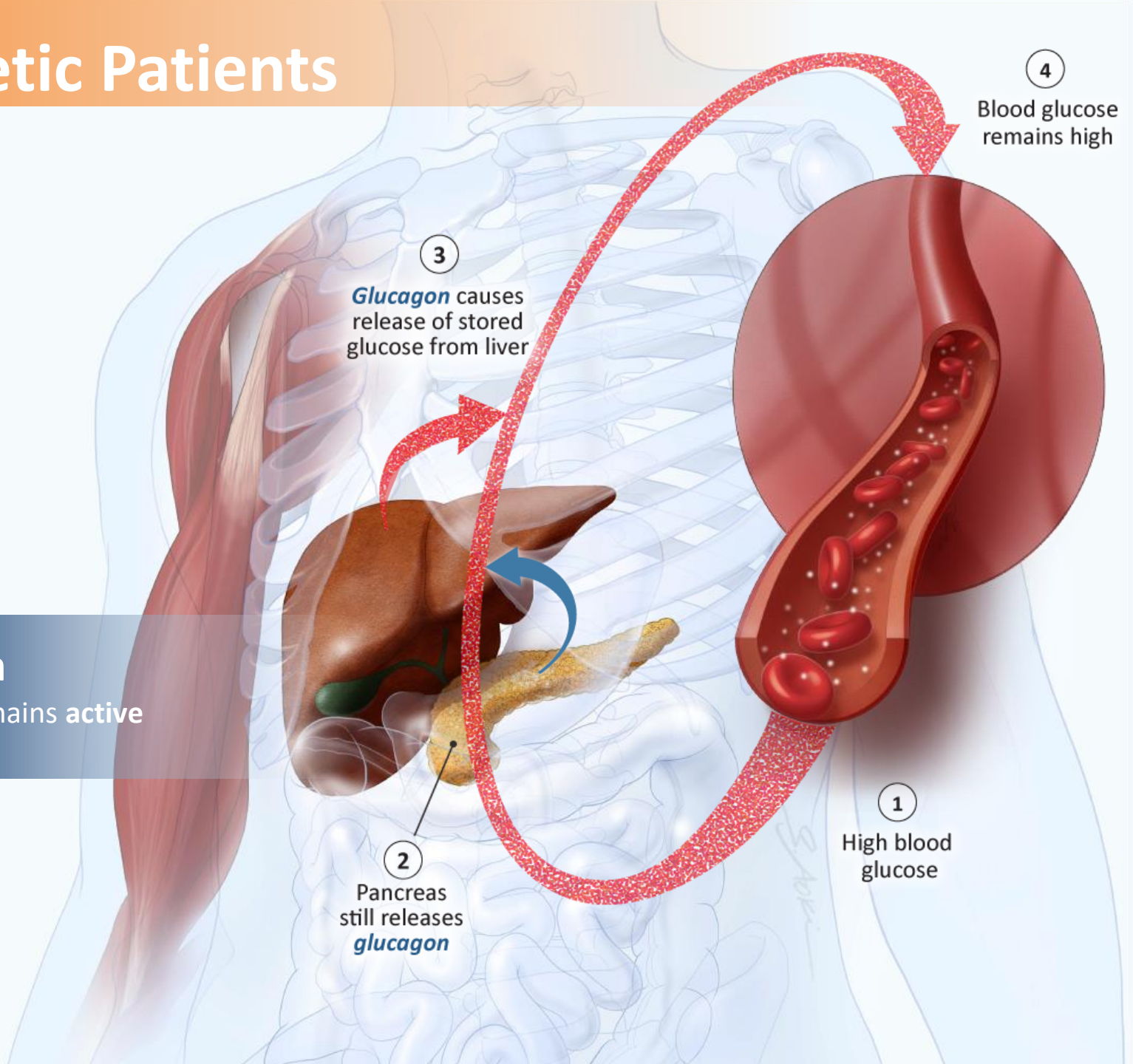
Signalling is defective



# Diabetic Patients

## Glucagon

Signalling remains active





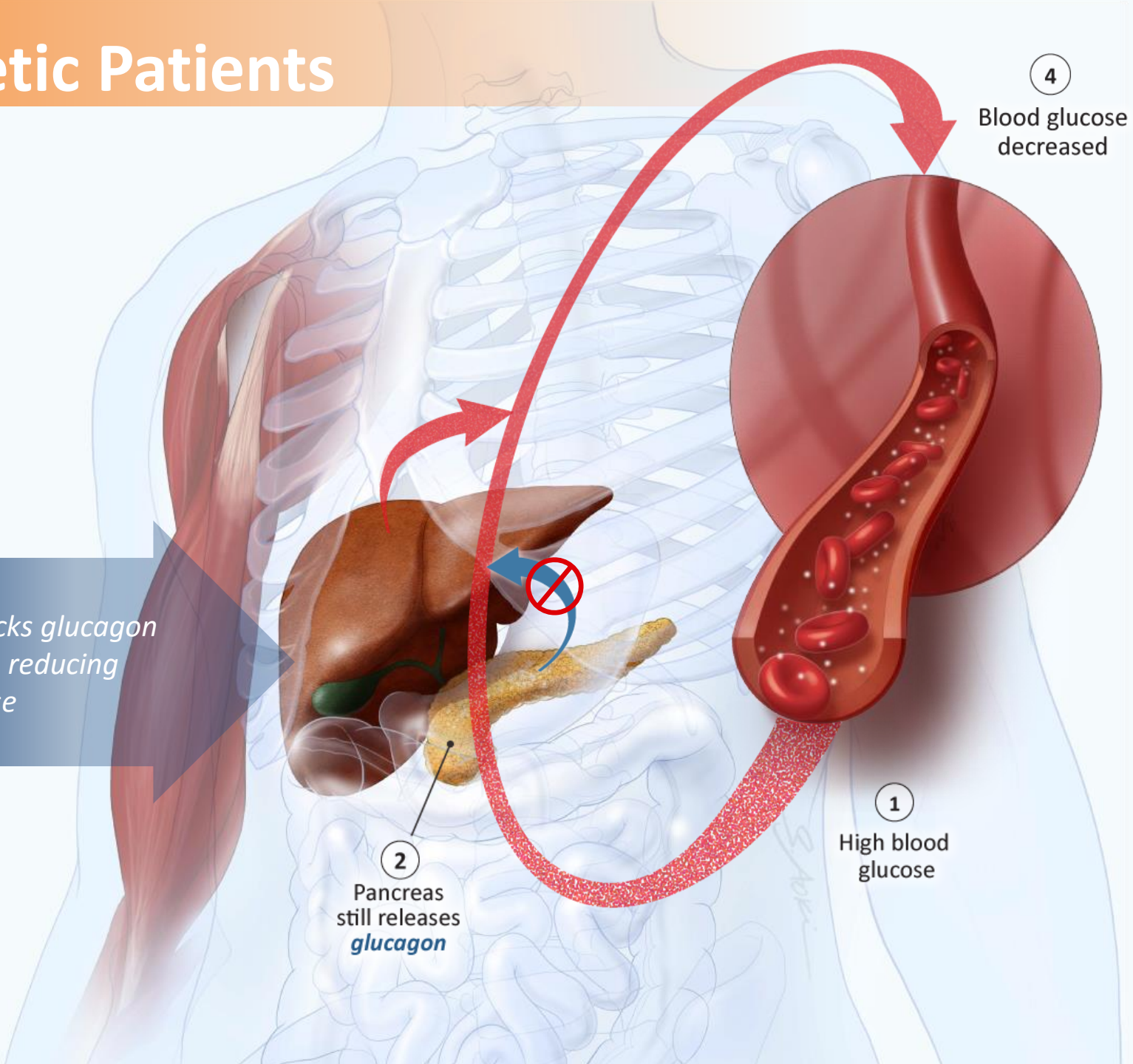
# Diabetic Patients

***LGD-6972** blocks glucagon action in liver, reducing glucose release*

2  
Pancreas  
still releases  
**glucagon**

1  
High blood  
glucose

4  
Blood glucose  
decreased



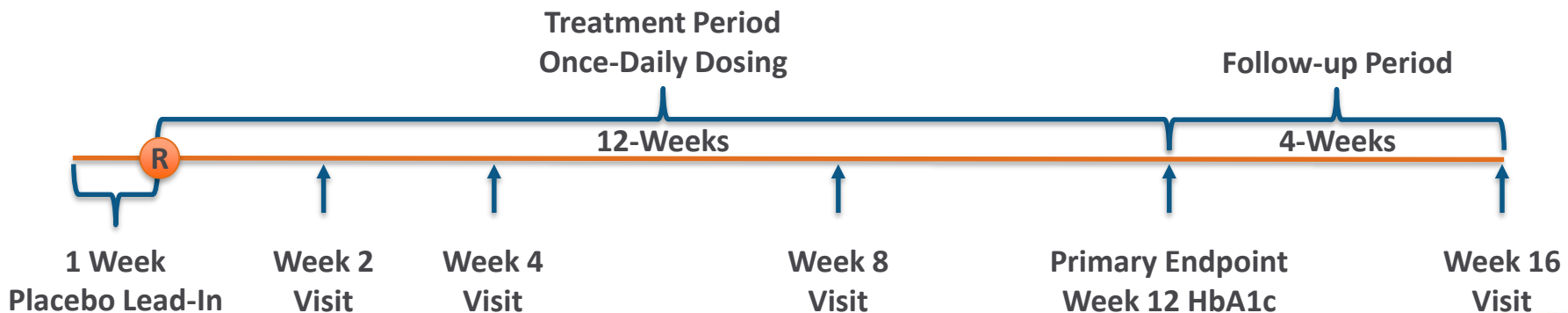
# Ligand's GRA: LGD-6972

- LGD-6972 is an oral small molecule that potently binds to the glucagon receptor *in vitro* and competitively antagonizes the actions of glucagon
  - Glucose reduction has been demonstrated in animal models of both type 1 and type 2 diabetes
- Clinical trials have demonstrated favorable efficacy and safety profiles
- LGD-6972 has **novel chemistry and strong drug-like properties**
- Global patents, if granted, would not be expected to expire **until 2035**

# GRA Phase 2 Study

## Summary of Study Design

- Subjects with type 2 diabetes on a stable dose of metformin treated with one of three doses of LGD-6972 (5 mg, 10 mg or 15 mg) or placebo once daily for 12 weeks
  - Primary endpoint was change from baseline in hemoglobin A1c (HbA1c) after 12 weeks of treatment compared to placebo
  - A total of 166 subjects were randomized among 29 clinical sites



# GRA Phase 2 Study

## Top-Line Results - Announced in Q3

- LGD-6972 treatment for 12 weeks achieved high statistical significance ( $p < 0.0001$ ) at all doses tested in the primary endpoint of change from baseline in HbA1c compared to placebo
  - Demonstrated a robust, dose-dependent reduction in HbA1c

<i>ITT Population</i>	<i>Placebo (n = 41)</i>	<i>5 mg (n = 43)</i>	<i>10 mg (n = 39)</i>	<i>15 mg (n = 40)</i>
<b>Baseline HbA1c % (SD)</b>	8.16 (0.99)	8.23 (1.06)	8.27 (0.93)	8.19 (0.89)
<b>Change from Baseline<sup>1</sup></b>	<b>-0.15 (0.11)</b>	<b>-0.90 (0.11)</b>	<b>-0.92 (0.12)</b>	<b>-1.20 (0.11)</b>
<b>p-value vs. Placebo</b>	-	<0.0001	<0.0001	<0.0001

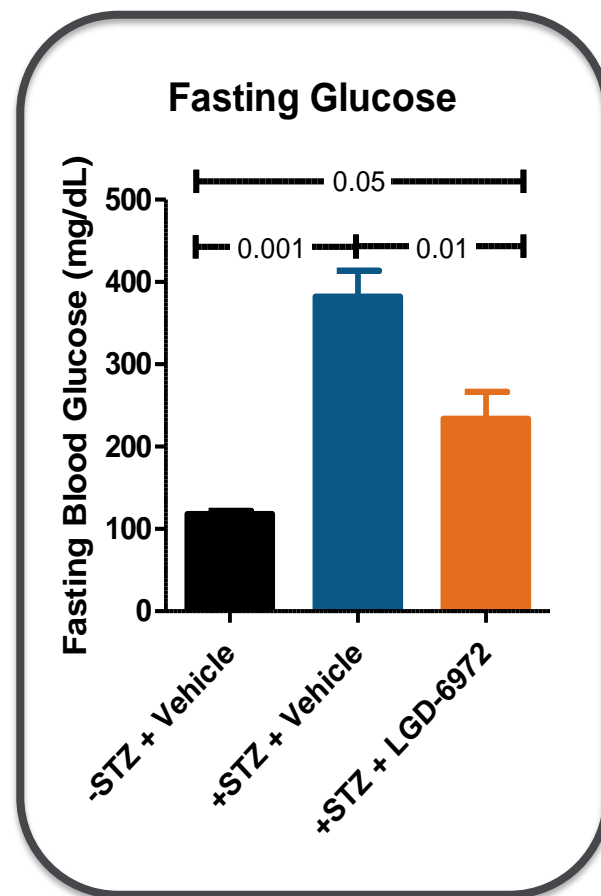
<sup>1</sup>LS-mean (SE) Change from Baseline to Week 12 with LOCF

- LGD-6972 was safe and well-tolerated with **no drug-related SAEs** and **no dose-dependent changes in lipids, body weight or blood pressure**

# GRA

## Additional Potential Oral Application in Type 1 Diabetes

- Type 1 diabetes represents another potential indication for LGD-6972
  - Approximately 1.25 million American adults and children have type 1 diabetes
- Recent research suggests that a GRA could **reduce daily insulin requirements and glucose volatility** in patients with type 1 diabetes
- LGD-6972 reduced fasting glucose and glucose volatility in mouse type 1 diabetes model



# *Financial Overview and Outlook*

*Matt Korenberg*



# Strong Financial Performance and Outlook

- 2017 continues Ligand's track record of annual growth in revenues, cash flow and profits
- Financial outlook for 2018 and beyond expected to show continued growth and the leverage in our model
- Substantial long-term growth potential from existing commercial assets and robust pipeline
- Certainty and longevity of growth profile provides attractive opportunity for investors

# Q3 Revenue Review



- Overall revenue increase of 54% over Q3 2016
- Royalty revenue grew 40% year-over-year, driven by Promacta, Kyprolis and EVOMELA

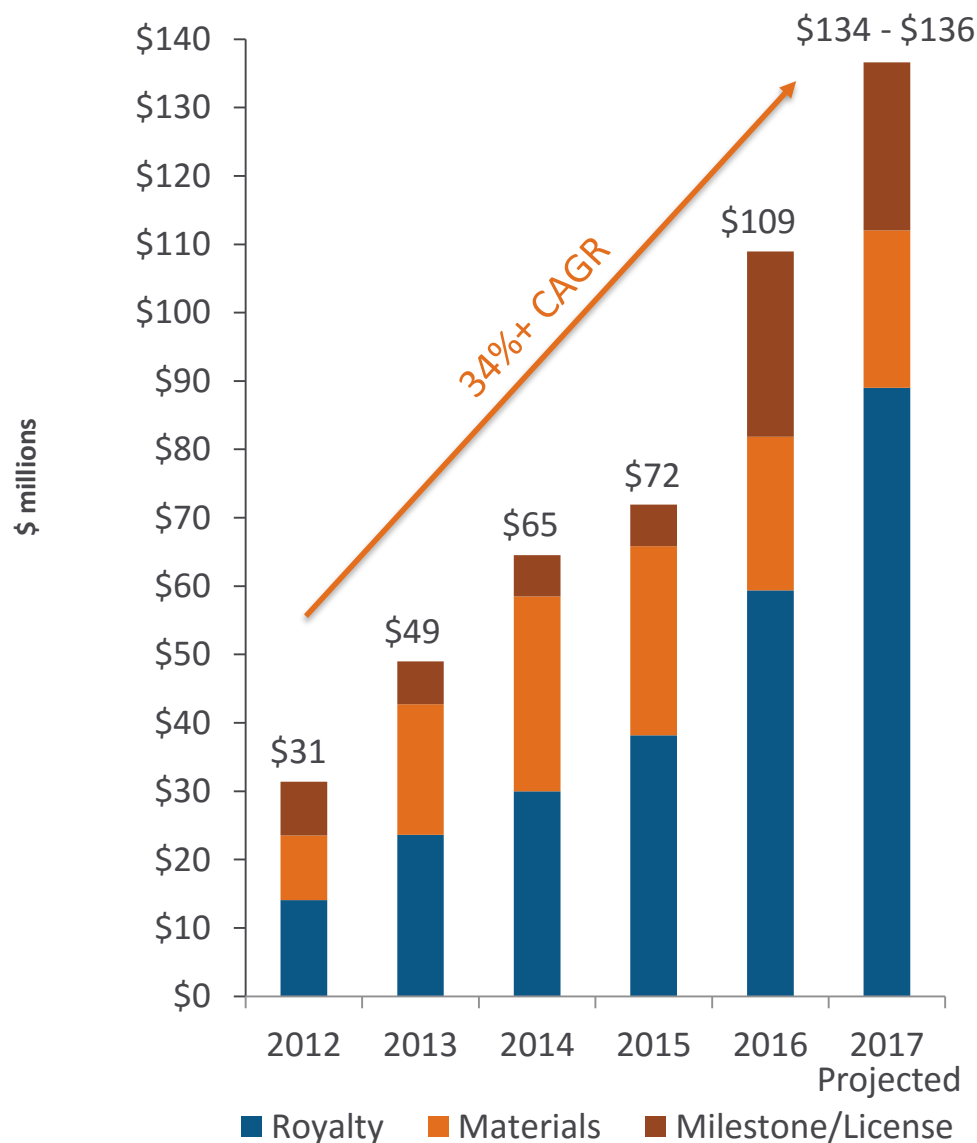
# Q3 Results Review

- Corporate gross margin at 93% for Q3 2017 reflecting mix of revenue
- Cash operating expenses ~\$6.5M with full year on track for \$30M to \$31M – up slightly due to expected Q4 Crystal integration and operating expenses
- Income tax expense for GAAP of \$3.6M, effective tax rate 30%; cash tax rate to remain <1%
- GAAP Net Income of \$8.4M or \$0.36 per share compared to \$1.1M or \$0.05 per share a year ago. Adjusted Net Income of \$15.3M or \$0.69 per share compared to \$9.6M or \$0.44 per share a year ago
- Finished the quarter with cash and equivalents of \$202M, and now have \$175M net of Crystal acquisition, as of November 14, 2017

# Reconciliation of GAAP EPS to Adjusted EPS

<b>Q3'17 GAAP Earnings Per Share</b>	<b>\$0.36</b>
Stock-based compensation expense	0.22
Non-cash interest expense	0.12
Amortization related to acquisitions	0.08
Increase in contingent liabilities	0.06
Loss from Viking	0.04
Other	(0.02)
Income tax effect of adjusted reconciling items	(0.18)
Excess tax benefit from stock-based compensation	(0.04)
2019 Senior Convertible Notes share count adjustment	0.04
<b>Q3'17 Adjusted Earnings Per Share</b>	<b>\$0.69</b>
<b>GAAP Shares</b>	<b>23.55</b>
Dilutive potential common shares issuable of redeemable convertible notes	(1.33)
<b>Adjusted Shares*</b>	<b>22.22</b>

# Sustained Revenue Growth



- Consistent, strong annual revenue growth driven by:
  - High royalty growth
  - Increasing contribution from milestones
  - Consistent contribution from material sales
- 2017 Adjusted EPS guidance recently increased to \$2.95 to \$3.00

# Commentary on 2018 Revenue Outlook

- Formal guidance will be given in early 2018
- Royalty:
  - Partner revenue reports of Q4 product sales will impact outlook
- Materials:
  - Timing of orders at year end may shift revenue between 2017 and 2018
- Milestone/License:
  - Timing of milestones at year end may shift revenue between 2017 and 2018

# 2018 Royalty Commentary

*\$ in millions*

*Underlying revenue expected to surpass \$2 billion in 2018 with royalty tiering pushing average royalty rate above 5% for the first time in Ligand's history*

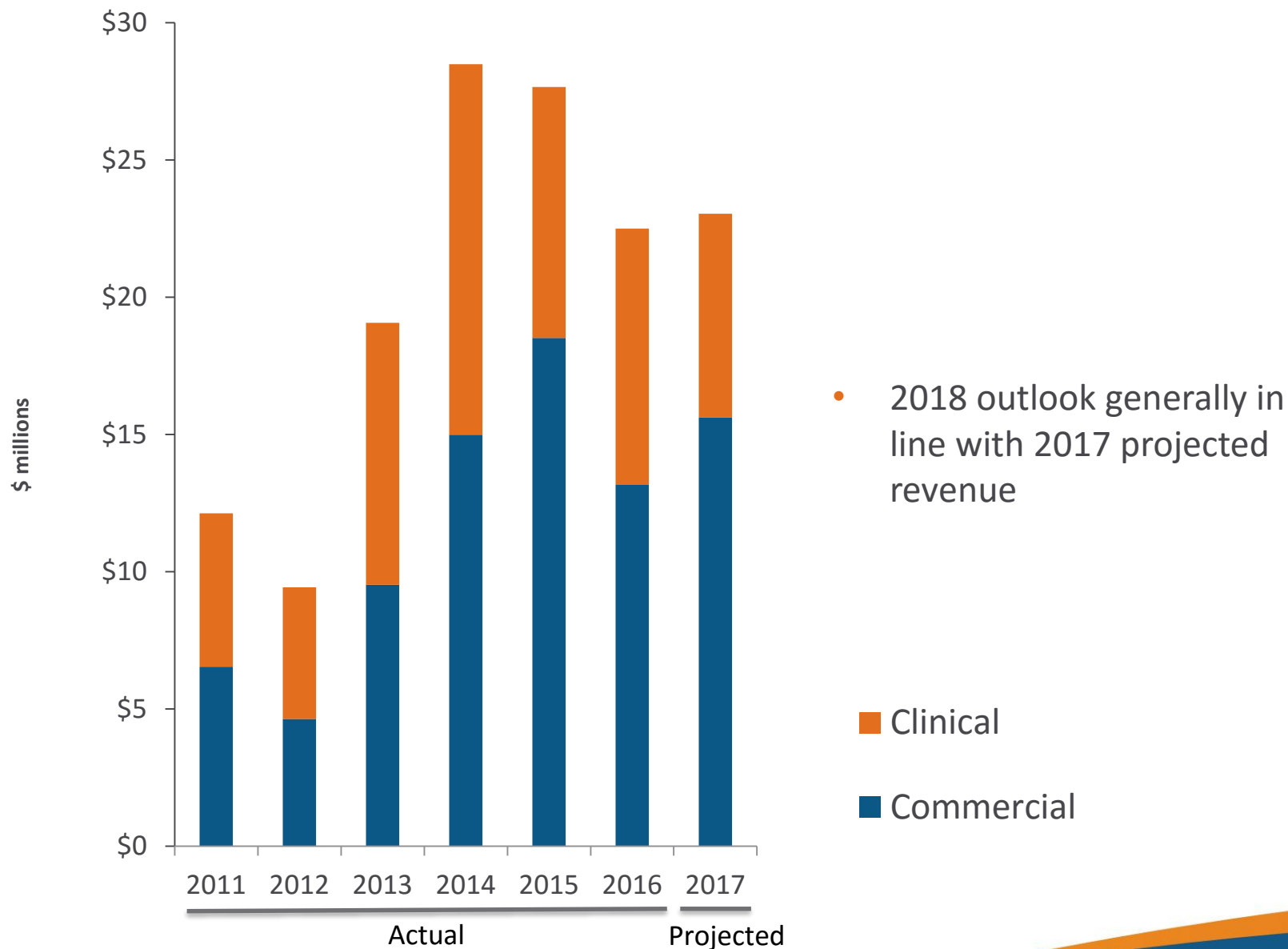
Illustrative 2018 Royalty Table Based on Sell-side Analyst Projections

Product	Q3 Sales	Q3'17	Sell-side Estimates			Implied Royalties	
		Annualized	Low	High		Low	High
Promacta	\$227	\$908	\$794	\$1,065	➔	\$64	\$89
Kyprolis	\$221	\$883	\$892	\$1,078	➔	\$19	\$25
Evomela	\$11	\$42	\$30	\$40	➔	\$6	\$8
Other (13 marketed products that generate royalty for Ligand)						\$1	\$2
					Total	\$90 - \$124	

- Management will continue to refine our 2018 estimate based on Q4 results from partners, but based on the table above, we see 2018 royalty growth of 15% to 25%

Note: Evomela low and high projections based on approximately 15% decrease/increase from last 4 quarters

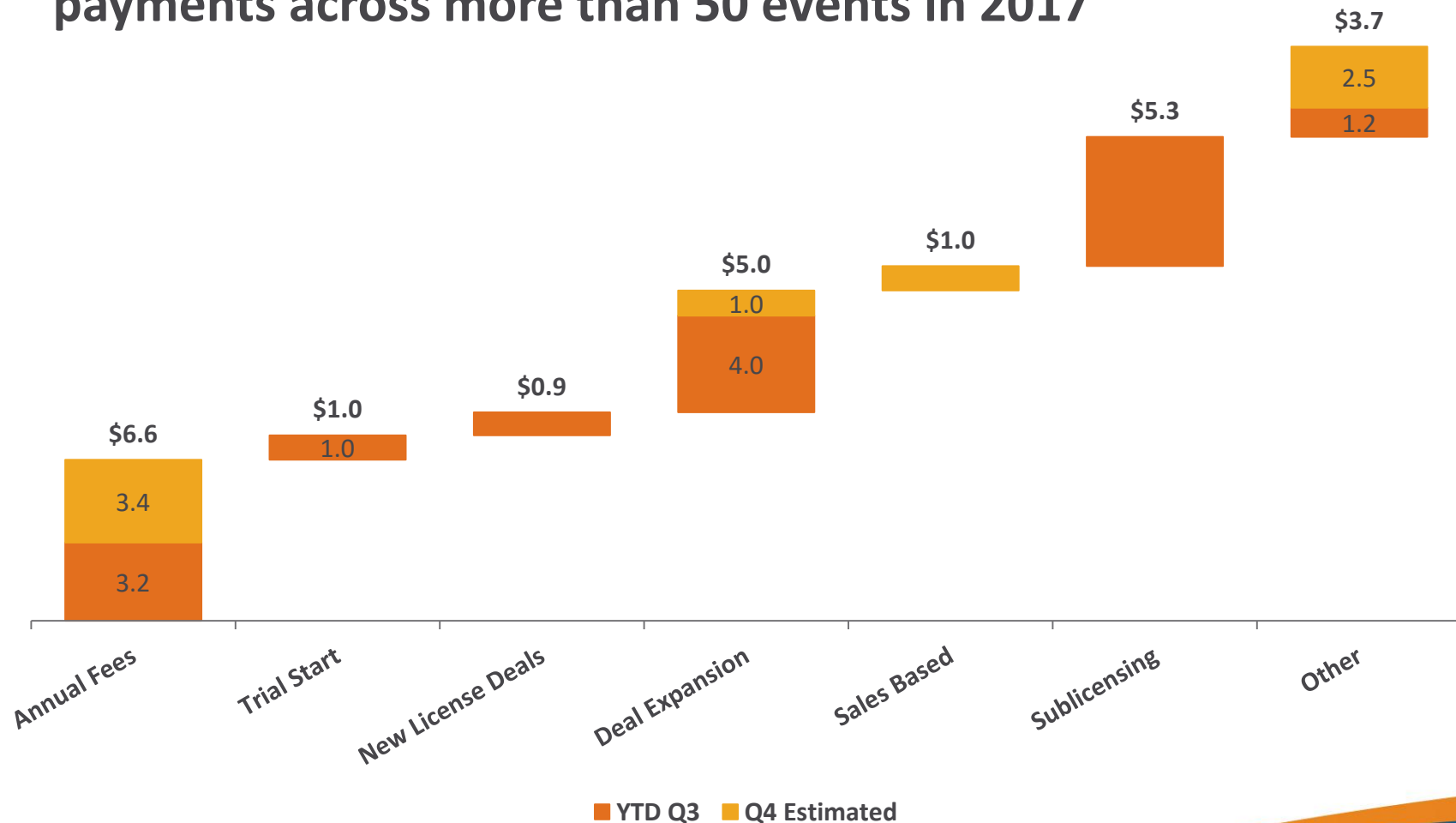
# 2018 Materials Revenue Commentary





# Summary of 2017 Milestone/License

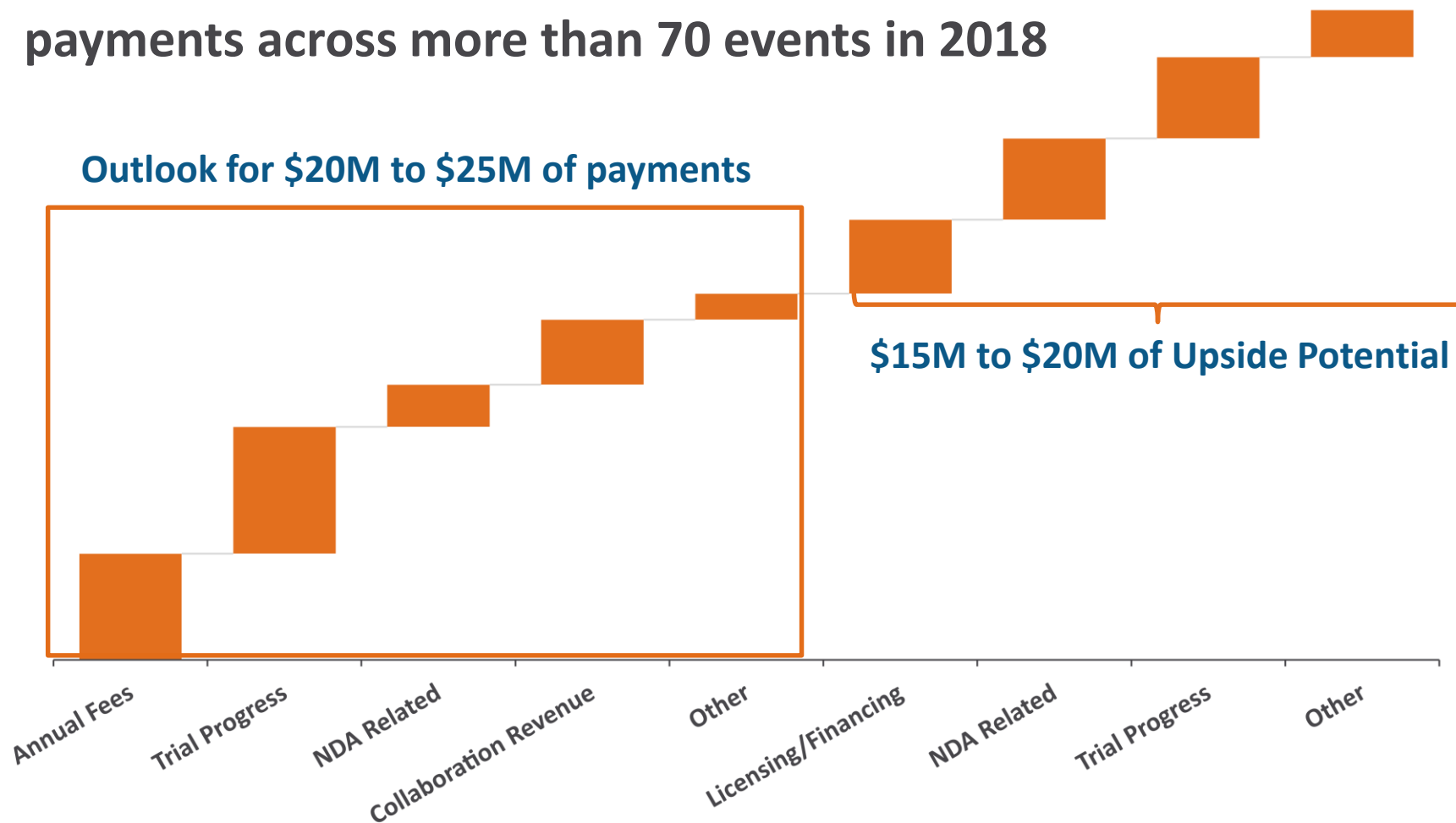
Expecting \$23 - \$24 million in milestone/license payments across more than 50 events in 2017



# 2018 Milestone Commentary

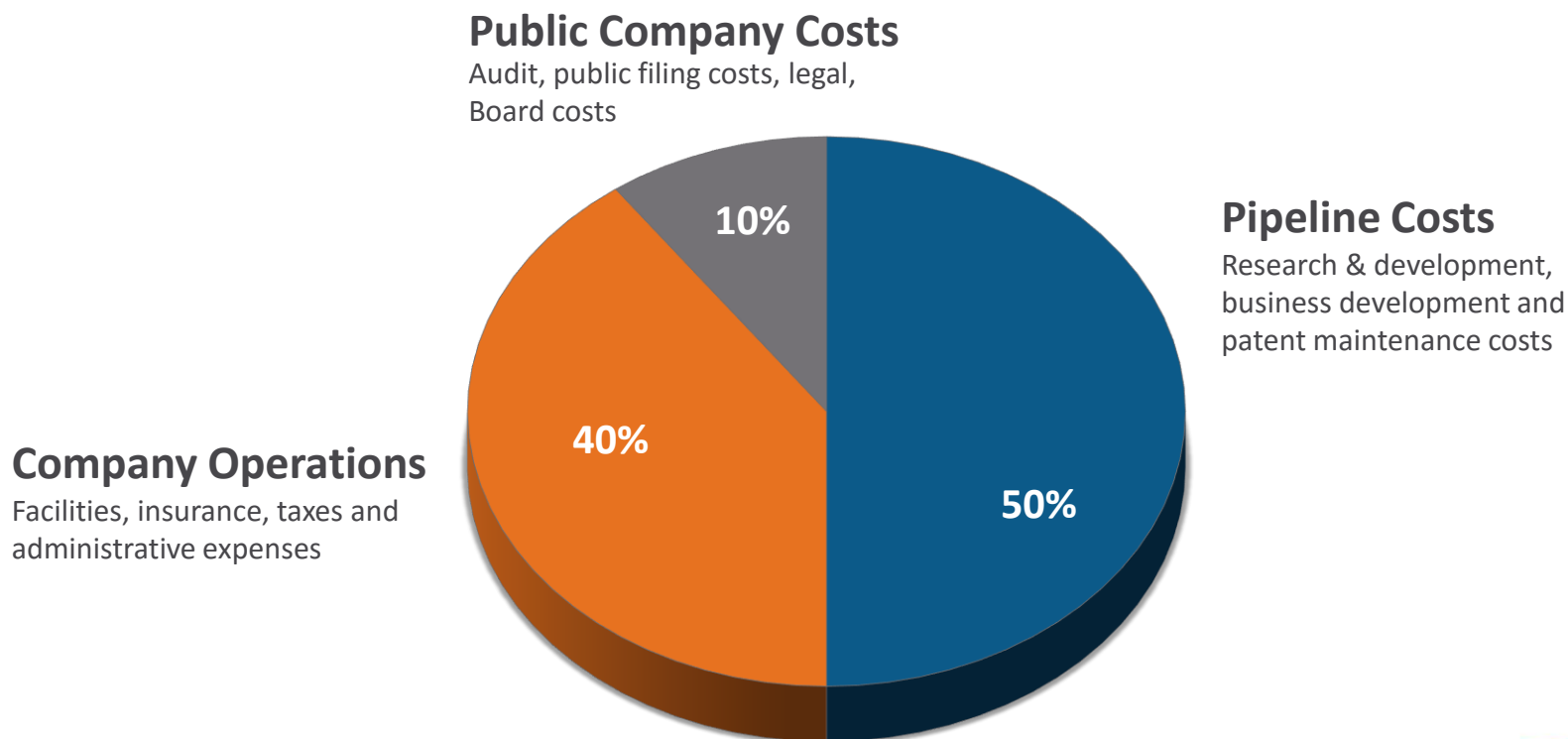
Potential for \$40+ million in milestone/license payments across more than 70 events in 2018

Outlook for \$20M to \$25M of payments



# 2018 Projected Cost Structure

- Cash expenses of \$30 to \$32 million, similar to expected 2017 expenses
- Efficient cost structure that supports activities to further expand the “Shots-on-Goal” portfolio



# 2018 Preliminary Outlook

	2018 Outlook
Revenue	<ul style="list-style-type: none"> <li>• <b><u>Royalty</u></b> Q4 will inform; sell-side analyst research shows \$90M to \$124M centering around 15% to 25% growth</li> <li>• <b><u>Materials</u></b> 2018 demand expected to be in line with 2017 demand of ~\$23M</li> <li>• <b><u>Milestone/License</u></b> initial analysis shows \$20M to \$25M with \$15M to \$20M potential upside</li> </ul>
Corporate gross margins	<ul style="list-style-type: none"> <li>• 94% - 96%</li> </ul>
Cash operating expense	<ul style="list-style-type: none"> <li>• Expected to be relatively flat to 2017 at \$31M</li> </ul>
Fully-diluted share count	<ul style="list-style-type: none"> <li>• Approximately 22.3M at year end with no 2018 issuance expected beyond stock based compensation</li> </ul>
Adjusted EPS tax rate	<ul style="list-style-type: none"> <li>• Expected range of 36% to 39%</li> </ul>
Cash tax rate	<ul style="list-style-type: none"> <li>• &lt;1%</li> </ul>

# 2018 Revenue Impact from ASC 606

## Royalties

- Previously recognized our royalties one quarter after the underlying product revenue was realized by partners
- Under ASC 606, we expect to recognize our royalties in the same quarter as the underlying product revenue is realized

## Materials

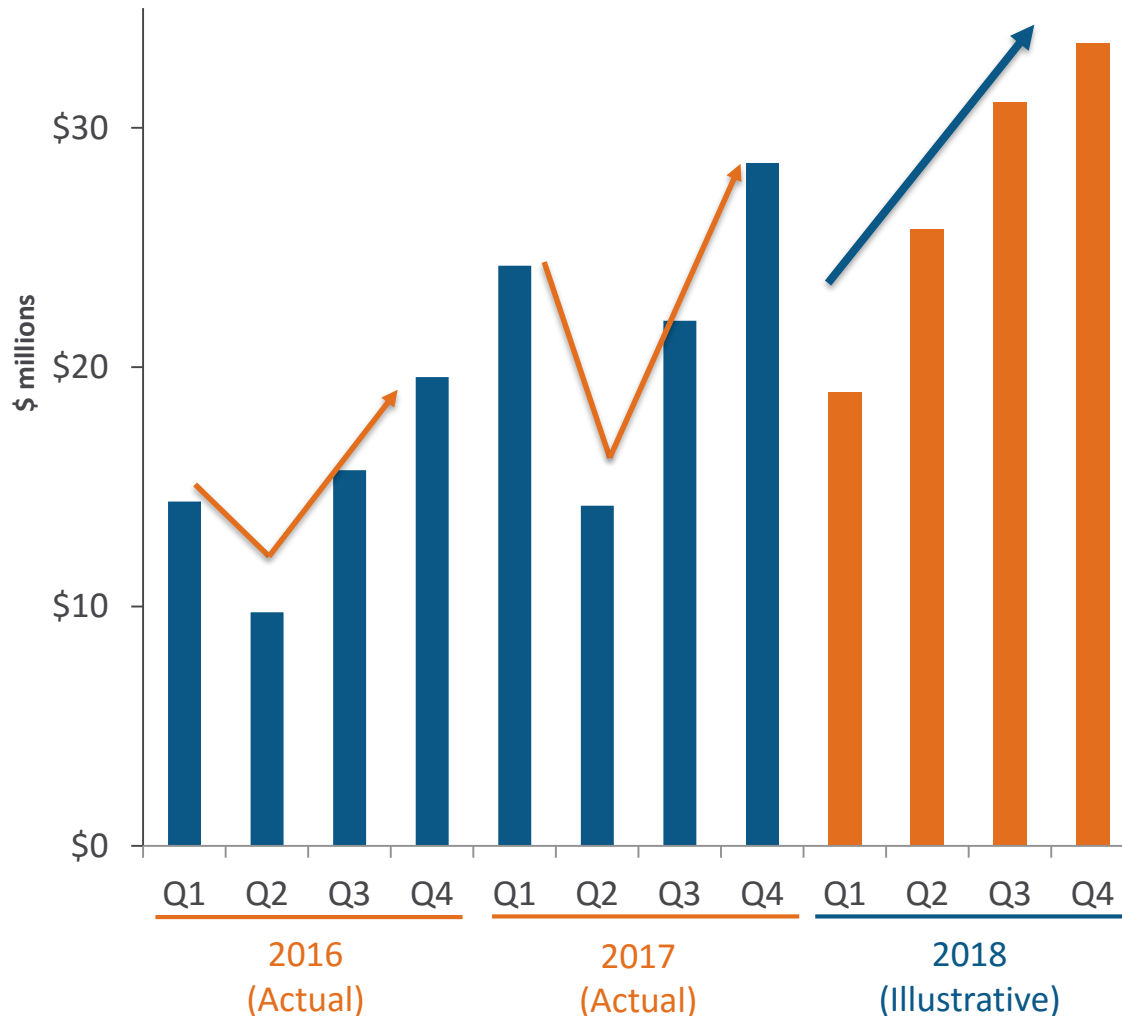
- No expected impact

## Milestone/License

- Previously recorded revenue primarily upon occurrence of an event (trial start, IND filing, FDA approval, etc.)
- Under ASC 606, required to assess the probability of each event occurring and book revenue when deemed probable
- Based on Ligand experience, significant majority of our milestones, if not all, are not probable until event occurs

# Quarterly Royalty Revenue Pattern

*Quarterly revenue patterns starting in 2018 will differ from historical trends, due to ASC 606*



- Prior to 2018, royalties were reported on a lag and Q2 saw a dip due to the annual resetting of royalty tiers
- Royalties will now be reported in the quarter they are earned, moving annual reset one quarter earlier

# Mergers and Acquisitions Philosophy

- Ligand is interested in a wide variety of assets that add to the diversity of our portfolio
- In evaluating potential company and asset acquisitions, there are several key characteristics we look for:
  - Minimal operational requirement, low associated spend and cash flow positive
  - Technology that can be out-licensed to generate additional fully-funded Shots on Goal
  - Assets with long patent life that will contribute peak revenue to Ligand in 10+ years
- Most assets will not share all of these characteristics, but we focus on finding assets that can be made to fit our model

# Upcoming Potential Partner/Licensee Events

## *Potential milestones for Ligand and partners in coming quarters*

<u>Company</u>	<u>Program</u>	<u>Milestone</u>
<i>Lundbeck</i>	Carnexiv	US Launch
<i>Melinta Therapeutics</i>	BAXDELA	US Launch
<i>Novartis</i>	Promacta	FDA Filing (1 <sup>st</sup> line SAA)
<i>Coherus Biosciences</i>	CHS-0214	MAA Filing
<i>Daiichi Sankyo</i>	Esaxerenone/CS-3150	Japanese regulatory filing (Hypertension)
<i>Sage Therapeutics</i>	SAGE-547	NDA submission (Postpartum Depression)
<i>Retrophin</i>	Sparsentan	Phase 3 start
<i>Amgen</i>	Kyprolis	PDUFA for ENDEAVOR Overall Survival data addition to label
<i>Amgen</i>	Kyprolis	Phase 3 start (NDMM in combo with REVLIMID <sup>®</sup> /Dex)
<i>Takeda</i>	Pevonedostat	Phase 3 start (High-risk MDS)
<i>Takeda</i>	Pevonedostat	Phase 2 completion (Advanced MDS)
<i>Marinus</i>	Ganaxolone IV	Phase 2 completion
<i>Internal Program</i>	GRA	Phase 2 full dataset presentation (Type 2 Diabetes)
<i>VentiRx</i>	VTX-2337	Phase 2 completion (Ovarian cancer; Head & Neck cancer)



# Upcoming Potential Partner/Licensee Events

*Potential milestones for Ligand and partners in coming quarters*

<u>Company</u>	<u>Program</u>	<u>Milestone</u>
<i>Lilly</i>	Merestinib	Phase 2 completion (Biliary Tract Cancer)
<i>Lilly</i>	Prexasertib	Phase 2 completion (Small Cell Lung Cancer)
<i>Viking Therapeutics</i>	VK5211	Phase 2 completion (Hip Fracture)
<i>Viking Therapeutics</i>	VK2809	Phase 2 completion (Hypercholesterolemia/NASH)
<i>Aldeyra Therapeutics</i>	Reproxalap (ADX-102)	Phase 2 completion (Allergic Conjunctivitis)
<i>GSK</i>	GSK2894512	Phase 2 completion (Atopic Dermatitis)
<i>CURx Pharma</i>	IV-Topiramate	Phase 2 start (Epilepsy)
<i>Sermonix</i>	Lasofoxifene	Phase 2 start (Breast Cancer)
<i>Bristol Meyers Squibb</i>	CXL-1427/BMS-986231	Phase 2 completion (Heart Failure)
<i>Precision Biologics</i>	NPC-1C	Phase 1/2 completion (Pancreatic Cancer)
<i>GSK</i>	GSK2816126	Phase 1 completion (DLBCL)
<i>Aptevo Therapeutics</i>	APVO436	IND filing (AML)
<i>Vireo Health</i>	Cannabinoids	IND for Captisol-enabled Formulations

Ligand<sup>®</sup>