



# Stephens NY Investment Conference

*November, 2018*

*NASDAQ: LGND*

# Safe Harbor Statement

*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 2018 or thereafter or that third party research summarized herein is correct or complete.*

*The forward-looking statements made in the presentation are subject to several risk factors, including, statements regarding intent, belief, or current expectations of the Ligand, its internal and partnered programs, including Promacta™, Kyprolis® and EVOMELA®, Ligand's reliance on collaborative partners for milestone and royalty payments, royalty and other revenue projections based on third party research, regulatory hurdles facing Ligand's and partners' product candidates, uncertainty regarding Ligand's and partners' product development costs, the possibility that Ligand's and partners' drug candidates might not be proved to be safe and efficacious and commercial performance of Ligand's and/or its partners' products, risks related to Ligand's internal controls, its compliance with regulations, accounting principles and public disclosure, and other risks and uncertainties described in its public filings with the Securities and Exchange Commission, available at [www.sec.gov](http://www.sec.gov). Additional risks may apply to forward-looking statements made in this presentation. Information regarding partnered products and programs comes from information publicly released by our partners. This presentation describes the typical roles and responsibilities of Ligand and our partners, and is not intended to be a complete description in all cases. Our trademarks, trade names and service marks referenced herein include Ligand and Captisol. Each other trademark, trade name or service mark appearing in this presentation belongs to its owner. The process for reconciliation between adjusted financial numbers presented on slide 37, and the corresponding GAAP figures is shown on slide 39.*

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# 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:*

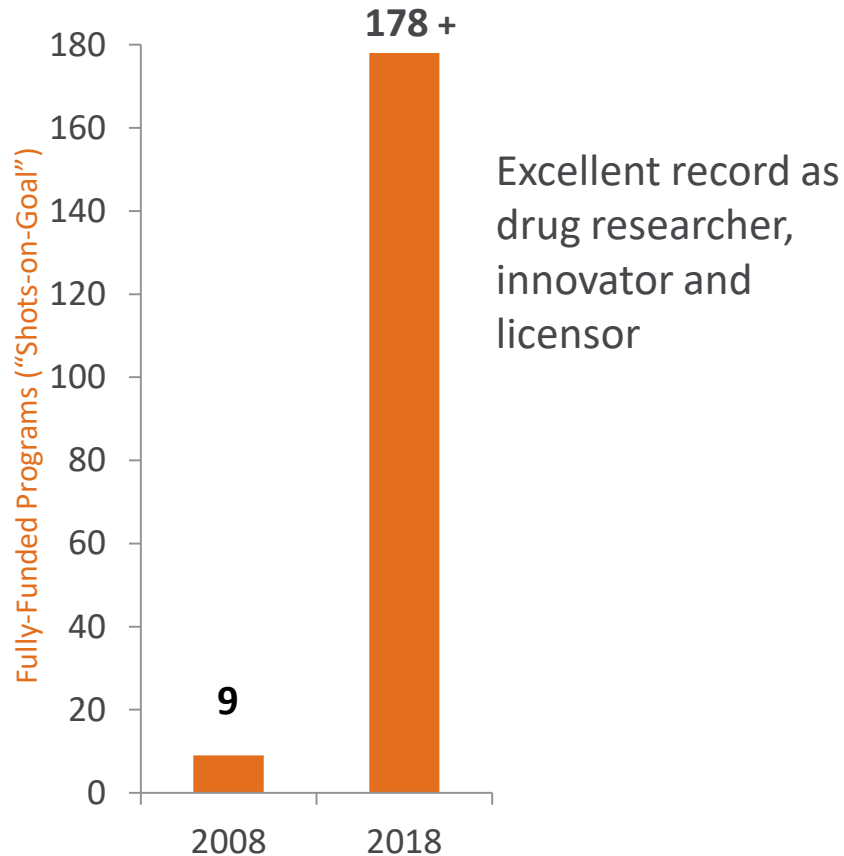
- Conduct early research, discover drugs
- Provide tools that make drugs possible
- License data and patents
- Acquire new technologies and assets
- Operate with low costs and maintain lean sharecount

### *What Our Partners Do:*

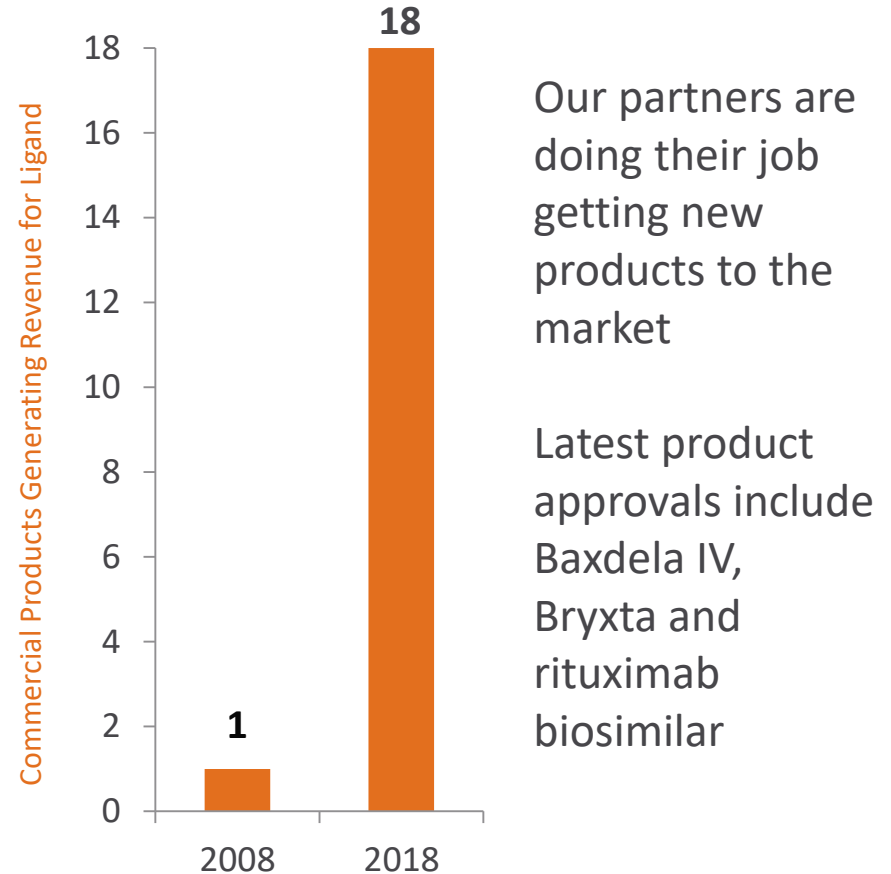
- Decide which indications to pursue
- Design studies; manage regulatory work
- Price drugs and secure reimbursement
- Market drugs
- Fund all development and commercialization

# 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*



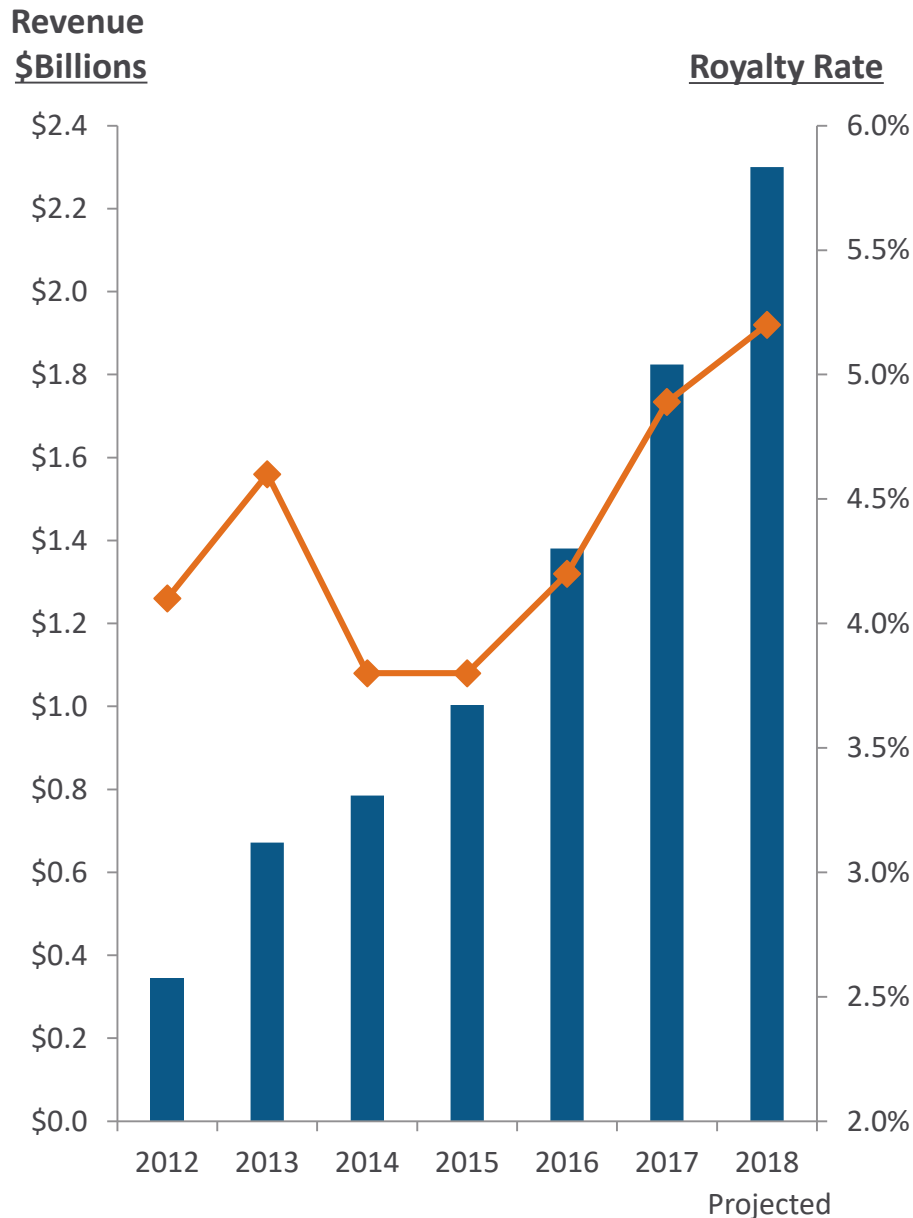
*Large and Growing*  
*High Quality*  
*Many Late Stage*

*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
- 2018 Corporate gross margins projected to be 96%

Current 2018 outlook, underlying revenue will exceed \$2.3 billion and average royalty will exceed 5%



# RPT – Ligand's Foundation of Value

*Revenue*



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

*Pipeline*



*Large and Growing*  
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*Many Late Stage*

*Technology*



*Best-in-Class*  
*Leverageable*  
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# Pipeline

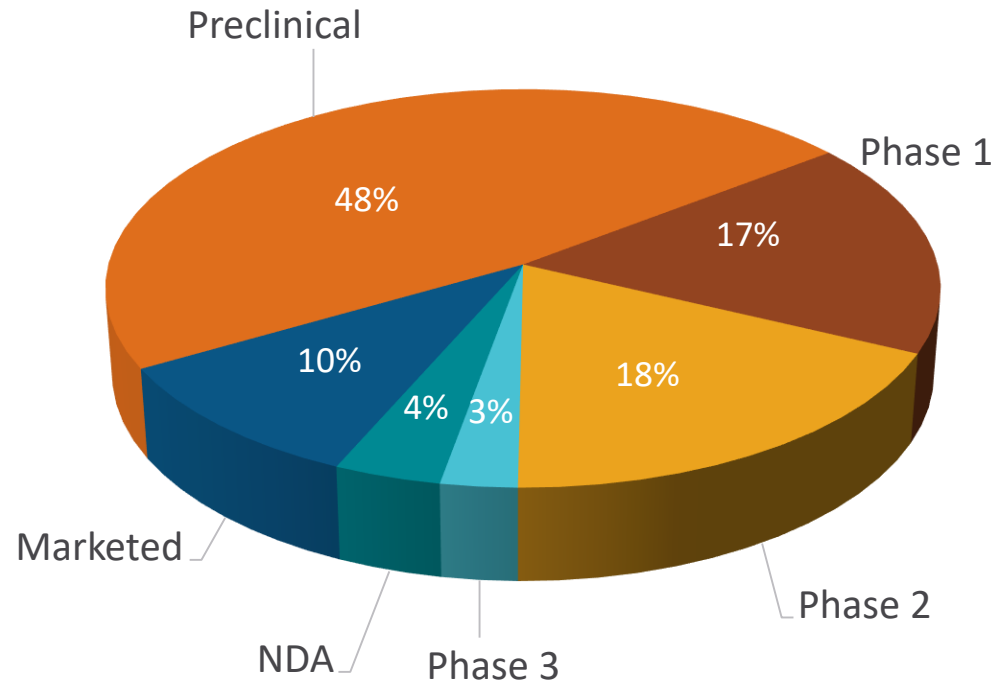
## *Why is Ligand's Pipeline Valuable?*

- 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

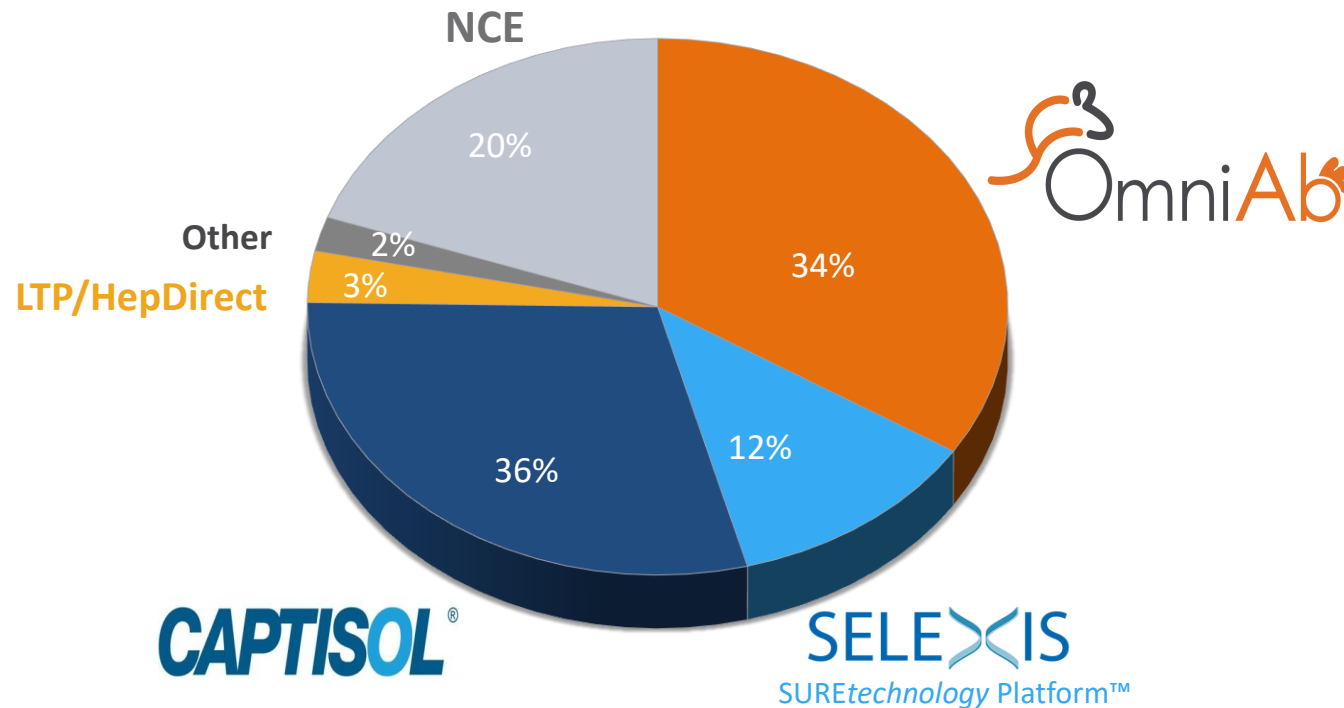
## *Over 178 Partnered Programs*

- Portfolio remains diversified across development stages
- Over 100 different partners
- Nearly 52% of programs in clinical development or later
- 14% marketed or NDA stage



# Diversified Underlying Intellectual Property

*Partnered programs are spread across multiple IP families*



- The underlying IP of Ligand's portfolio of 178+ partnered programs is spread across multiple, global families of intellectual property
- Between OmniAb and Selexis assets, antibodies/large molecules now make up **46% of the portfolio**

# Broad Array of Partners Use Our Technologies

*Over 100 Partners Spread Throughout the Pharmaceutical Industry*

## Specialty

### Pharma

Pfizer  
Novartis  
J&J  
GSK  
Merck  
Baxter  
BMS  
Eli Lilly  
Takeda  
Otsuka  
Daiichi-Sankyo

### Biotech

Amgen  
Exelixis  
SAGE  
Viking  
MEI  
Chiva  
Retrophin  
Merrimack  
Glenmark  
VentiRx  
Symphogen  
WuXi

Celgene  
Melinta  
Gilead  
Aldeyra  
Roivant  
Genmab  
Millennium  
Meridian  
C-Stone  
Marinus  
TG Therapeutics  
Five Prime  
Seattle Genetics

### Pharma

Eisai  
Spectrum  
Sermonix  
Upsher-Smith  
Glenmark  
Ono  
Sedor  
CURx

### Generics

Alvogen  
Par  
Zydus Cadila  
Coherus  
OncoBiologics  
BioCad  
Beloteca

*Over 40 additional companies*

# 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 178 partnerships **exceed \$2.5 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, Seelos, others

# 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*



*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*

**CAPTISOL<sup>®</sup>**

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

*Broad, global patent protection*

*Large Drug Master Files*

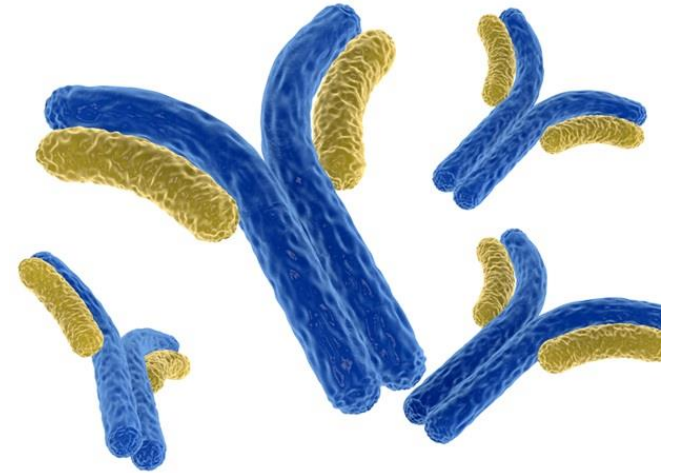
*Now with most pharma partners,  
most approved products*



# The Potential of Antibody Therapy

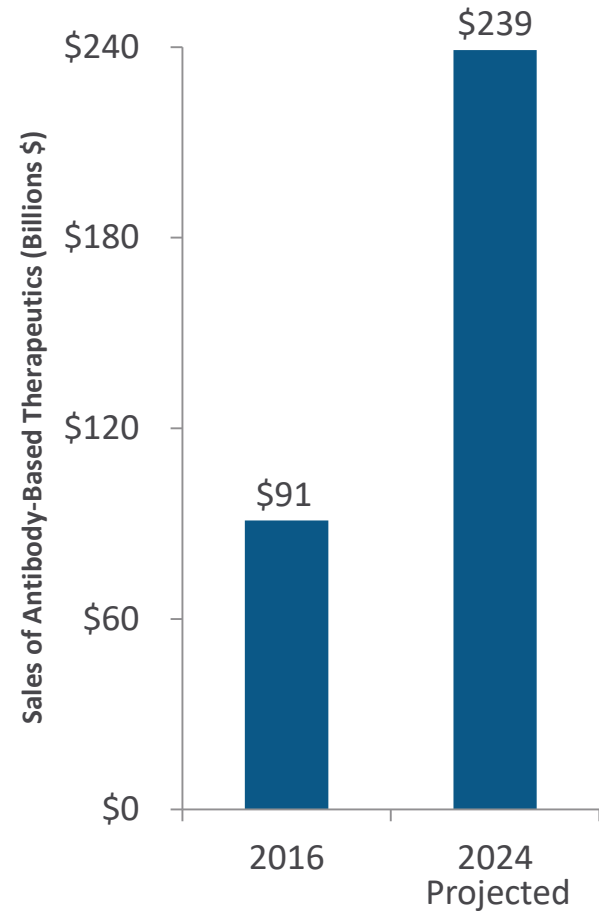
## *Harnessing the Power of the Immune System*

- Antibody therapy leverages an animal's ability to make proteins that bind to specific molecules on cells in response to toxic or foreign substances
- Antibodies can kill targeted cells (ie cancer) or impact the way cells function
- Antibodies are a major, fast growing class of medicines. Ligand has valuable technology serving the space
- R&D is underway to develop antibodies for a broad array of indications, including cancer, inflammation, auto-immune, neurological, viral diseases and many others



# Antibodies: Major Opportunity for Ligand

- In 2016, Ligand made a major strategic investment into antibody discovery by acquiring OMT, Inc. for ~\$178 million
- In 2017, Ligand expanded its antibody discovery program by acquiring Crystal Bioscience for ~\$25 million
- Global sales of antibodies estimated to approach \$240 billion in 2024
- 520 industry-wide programs in development, more than tripled since 2008



# OmniAb: A Best-in-Class Technology

*“Three Species, One License”*



- Ligand’s OmniAb technology is a drug discovery platform that enables drug companies to discovery antibodies
- Ligand has entered license agreements with over 30 companies
- Under the license agreements, Ligand is entitled to financial payments including:
  - License fees
  - Milestones
  - Royalties

***Promacta***<sup>®</sup>

# Promacta®: Blockbuster Commercial Potential

- Oral medicine that boosts platelets in patients with thrombocytopenia, or low-platelets
- Partnered with Novartis worldwide
- Sales trending to exceed \$1 billion in 2018; Consensus third-party analyst estimates project \$1.4 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

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 require the use of therapy.

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 ADVERTISING**  
PROMACTA may increase the risk of severe and potentially life-threatening hepatotoxicity. Monitor hepatic function and discontinue therapy 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 DDPPI, which may lead to increased hepatotoxicity. If ALT and/or AST are elevated, perform liver tests. Evaluate abnormal serum liver tests with repeat testing within 5 to 6 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.

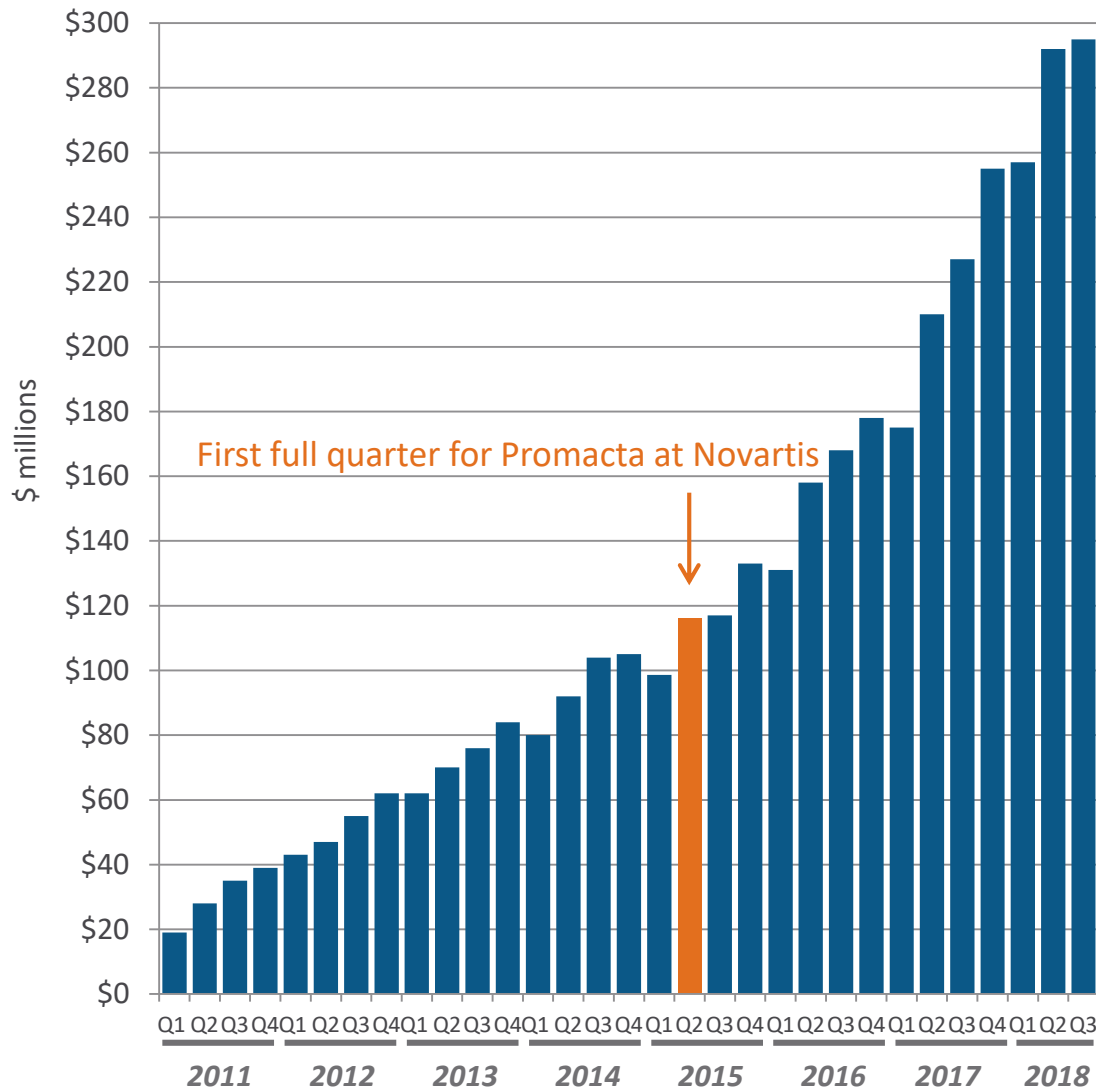
If the potential benefit for continuing treatment with PROMACTA outweighs the risk for hepatotoxicity, then consider cautiously continuing PROMACTA and monitor serum liver tests weekly during the dose adjustment phase. Exposure to may increase if PROMACTA is restarted. If not resolved, discontinue PROMACTA.

For treatment of patients for ITP who are already on therapy, the absence of liver laboratory values measured approximately 3 months after initiation of PROMACTA, in all cases, the most recent laboratory PROMACTA discontinuation.

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

Once-daily oral  
**PROMACTA®**  
(eltrombopag)  
25mg, 50mg, 75mg tablets

# Promacta: Quarterly Revenue



- Q3'18 revenue was \$295 million, an \$68 million increase (30%) over Q3'17
- Acquisition of product by Novartis from GSK significantly increased sales and growth trends
- Sales now annualize to over \$1 billion
- Ligand earns tiered royalties between 4.7% and 9.3%

GSK/NOVN (post Q1'14) reported quarterly sales.

GSK figures converted from GBP to USD at then current exchange rates

***Kyprolis®***

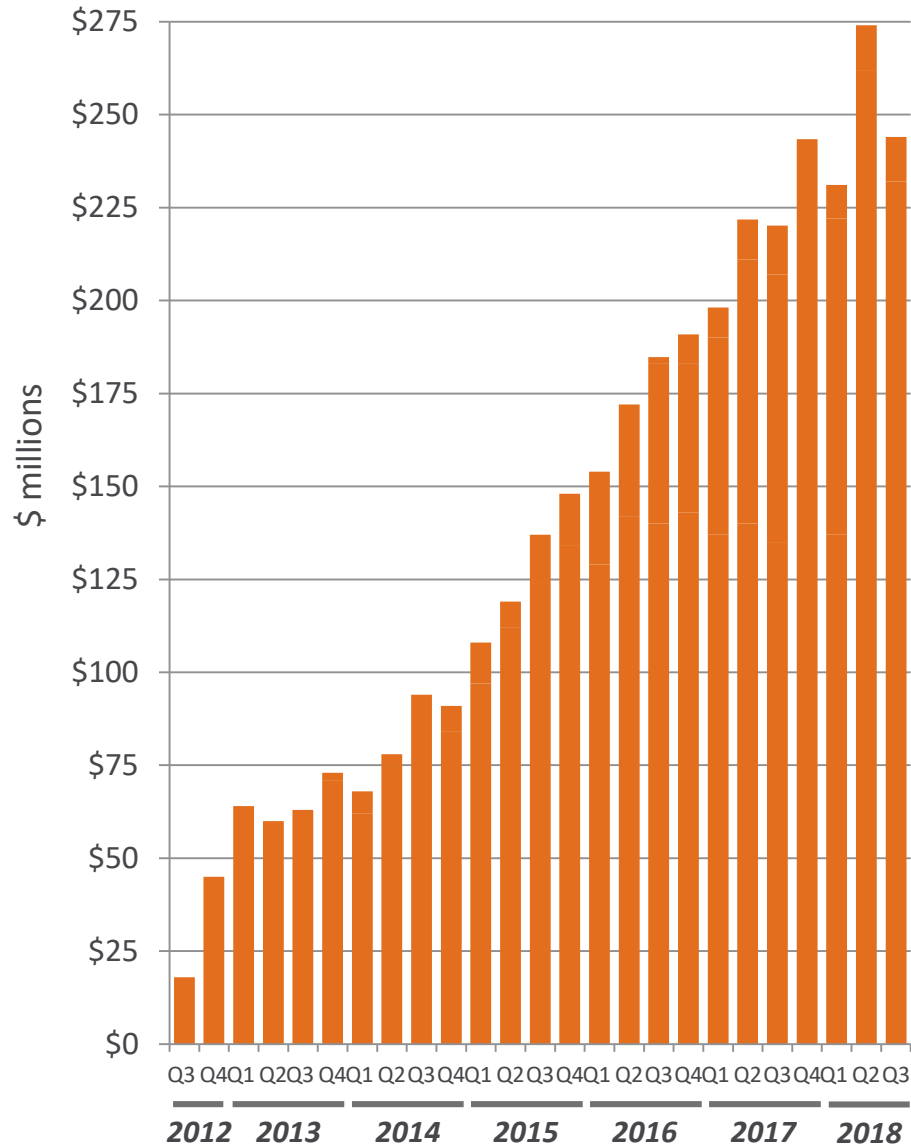
- Kyprolis viewed as best-in-class proteasome inhibitor for multiple myeloma (MM)
- Developed and marketed by Amgen
  - Utilizes Ligand's Captisol technology
- Approved for relapsed or refractory MM in the US, EU and Japan (Ono)<sup>1</sup>
  - As single agent, or in combination with dexamethasone or Revlimid and dexamethasone
- Kyprolis has demonstrated overall survival improvement in Phase 3 trials, bolstering the potential for the drug in a competitive space
- Amgen actively investing in more studies with potential to expand the label and use of the drug

<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









# Kyprolis: Quarterly Revenue



- Amgen/Ono reported combined Q3 revenue of \$244 million
- Rest-of-world contribution becoming more substantial
- Ligand earns 1.5% to 3% royalties

# 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>Zulresso</b> (Neurology)	NDA	3.0%	<b>December 19, 2018 PDUFA Date</b>
	<b>Sparsentan</b> (FSGS- Kidney Disease)	Phase 3	9.0%	<b>Phase 3 Interim Data</b>
	<b>Lasofloxifene</b> (Oncology/Women's Health)	Phase 2/3	6.0-10.0%	<b>Phase 2 Data</b>
	<b>BMS986231</b> (Cardiovascular Disease)	Phase 2/3	2.0-3.0%	<b>Phase 2b Data</b>
	<b>Prexasertib</b> (Oncology)	Phase 2	1.5-3.0%	<b>Phase 2 Data in various advanced cancers</b>
	<b>RVT-1502</b> (Diabetes)	Phase 2	Low double digit to mid teens %	<b>Clinical Progression</b>

# Glucagon Receptor Antagonist (GRA)

## *Roivant/Metavant Partnership – RVT-1502*

- Glucagon is a hormone that stimulates the liver to produce glucose
  - GRAs are designed to lower glucose levels for treatment of diabetes
- Ligand discovered and initially developed a novel molecule that potently binds the glucagon receptor and antagonizes the actions of glucagon
  - Ligand completed successful Phase 1 and Phase 2 clinical trials
  - Global patents covering various forms of the molecule, if granted, would not be expected to expire until 2039
- Ligand entered a major deal with Roivant for GRA in March 2018
- Ligand received \$20 m at signing, and is eligible to receive \$528 m in milestone payments, and royalties ranging from low double digits to mid-teens



# Seelos Therapeutics

## *Focused on Novel Products to Treat CNS Diseases*

- Seelos Therapeutics recently announced plan to merge with Apricus Biosciences
  - If completed, merger will result in *Nasdaq*-listed company with a continued focus on novel products for CNS diseases with significant unmet medical needs
- Four Ligand-partnered programs are in the Seelos pipeline
  - **SLS-006**: *First-in-class* small molecule **partial dopamine agonist** for Parkinson's Disease that has successfully completed Phase 2, plans for pivotal registration studies to commence in 2019
  - **SLS-008**: Once-daily oral **CRTH2** program for undisclosed pediatric orphan indication
  - **SLS-010**: **Histamine 3 receptor** inverse agonist for narcolepsy and related disorders
  - **SLS-012**: **Captisol-enabled™ acetaminophen** for post-operative pain
- Ligand eligible to receive milestones of \$144 m and royalties ranging from 4% to 10%



Seelos Therapeutics, Inc.

# Highlighted Program

## VK2809

NCE Program



- VK2809 is a selective thyroid hormone receptor beta (TR- $\beta$ ) agonist
  - Partnered with Viking Therapeutics in 2014
- Potential applicability in broad range of indications, including:
  - Non-alcoholic fatty liver disease (NAFLD)
  - Hypercholesterolemia
  - GSD-1a
- Phase 2 trial in NAFLD and hypercholesterolemia top-line data released in September 2018 with positive results
  - Full data expected to be released at AASLD
- Preparation for Phase 1 clinical study of VK2809 in GSD-1a is ongoing
- Ligand eligible to receive \$75 m in development milestones (per indication), up to \$150 m in commercial milestones, and 3.5% to 7.5% royalty

# Acquisition of Vernalis plc

- In October 2018, Ligand acquired Vernalis plc for \$43 million in cash
  - Vernalis is a structure-based drug discovery biotech based in United Kingdom
- The acquisition of Vernalis provides Ligand with the following:
  - Portfolio of more than 8 shots on goal in the respiratory, oncology and CNS sectors
  - 70-person R&D team based in Cambridge, England with an active portfolio of collaborations that have the potential to generate additional shots on goal
  - Compound library and early-stage, unpartnered programs providing BD opportunities
  - Net cash on hand after deal expenses of approximately \$32 million
  - Partners include; Corvus, Verona, Celgene, Servier, Daiichi Sankyo and others

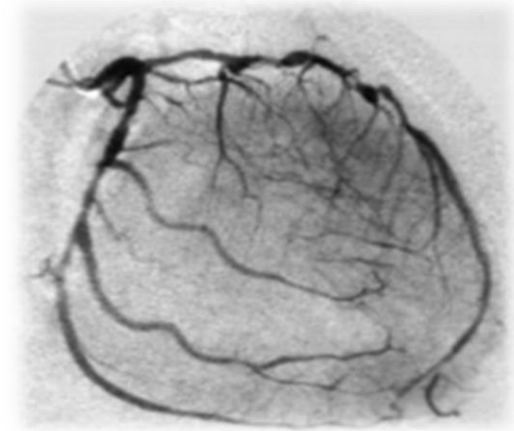


# *Internal R&D*

# Captisol-enabled Iohexol

## *Leveraging Captisol® Technology to Make Drugs Safer*

- Recently established new program to develop Captisol-enabled, next generation contrast agents for diagnostic imaging
- Patented uses of Captisol to reduce acute kidney injury (AKI) during medical interventions, including:
  - **Iodinated contrast agents:** *iohexol, iopamidol, iodixanol*
  - **Anticancer agents:** *cisplatin, doxorubicin, methotrexate*
  - **Aminoglycosides:** *gentamicin*
- Captisol-enabled Iohexol has successfully completed preclinical studies and Ligand plans to progress into clinical development





# Iodinated Contrast Agents

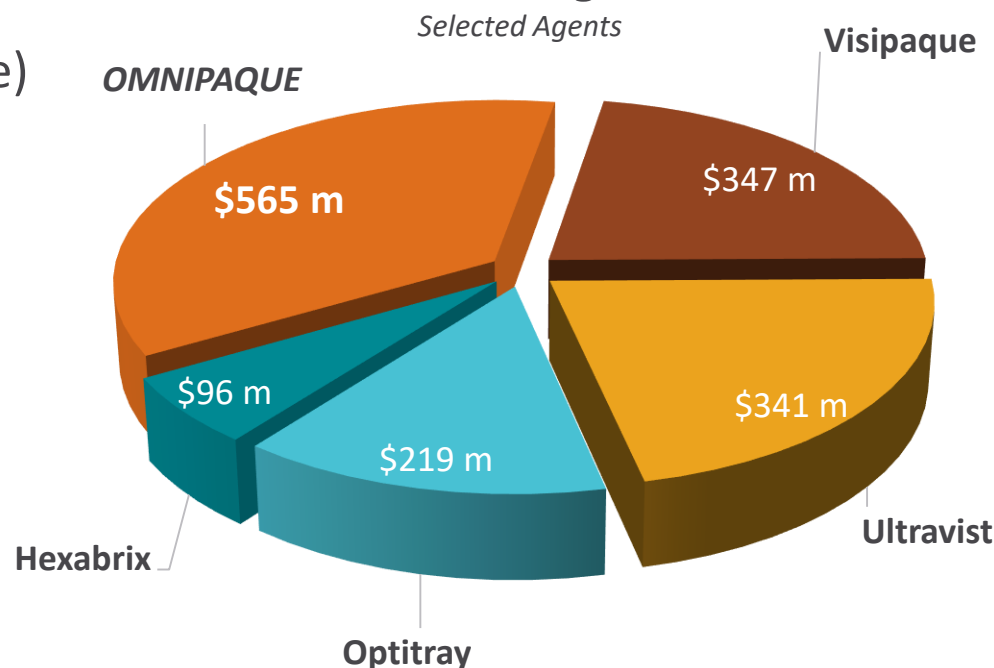
## Market and Needs

- 30 million imaging procedures/yr in the US
  - Iodinated contrast agents represent >60% of all X-ray imaging agents sold (~\$1.5 B market)
- Iohexol (OMNIPAQUE™, GE Healthcare) is the most widely-used injectable diagnostic contrast agent for X-ray imaging procedures
  - Global sales >\$500 M
  - \$250 M+ in US, ~30% market share
  - No generic competition
  - Reported incidence of contrast-medium induced nephropathy reported at 26% for Iohexol<sup>1</sup>

*“Acute Kidney Injury remains a concern for patients undergoing cardiac interventional procedures utilizing intravascular iodinated contrast”*

McCullough, J Am College of Cardiology 2016;68:1465-73

## Iodinated Contrast Agents - US Sales

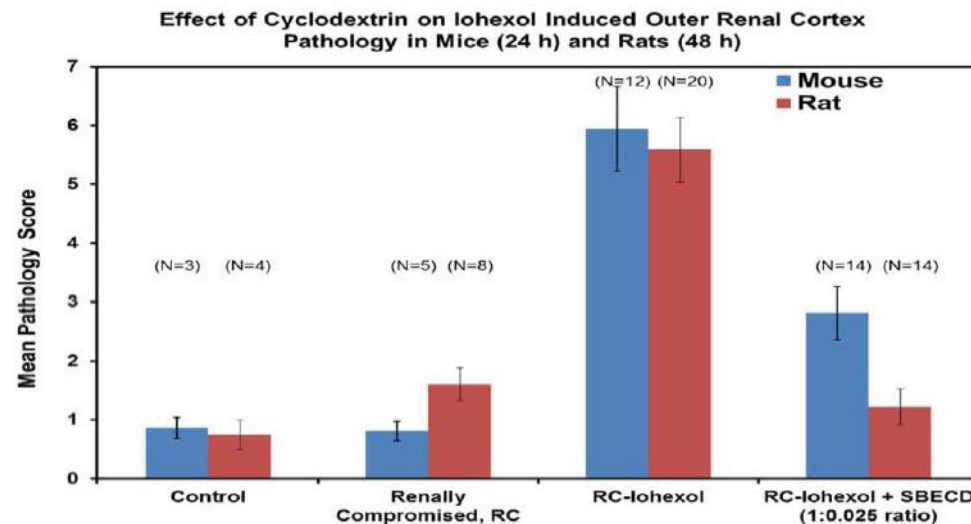


The Global Imaging Agents Market (Report MCP-3336)  
Global Industry Analysts, Inc., September 2016

# Captisol-enabled Iohexol

## Leveraging Captisol Technology to Make Drugs Safer

- Captisol-enabled Iohexol reduces renal pathologies in animal models
  - Mean scores show **>50% prevention** of Iohexol-induced pathologies
- Selected as next product for internal development, based on:
  1. *Large number of patients affected globally*
  2. *Lack of alternatives*
  3. *Established IP portfolio*
  4. *Potential for abbreviated development and approval process*
- Potential for high Captisol use
  - Estimated up to 10-15 metric tons annually



Rowe ES, et al. *Journal of Neuroimaging* 2016; 26(5):511-8

# Captisol-enabled Iohexol

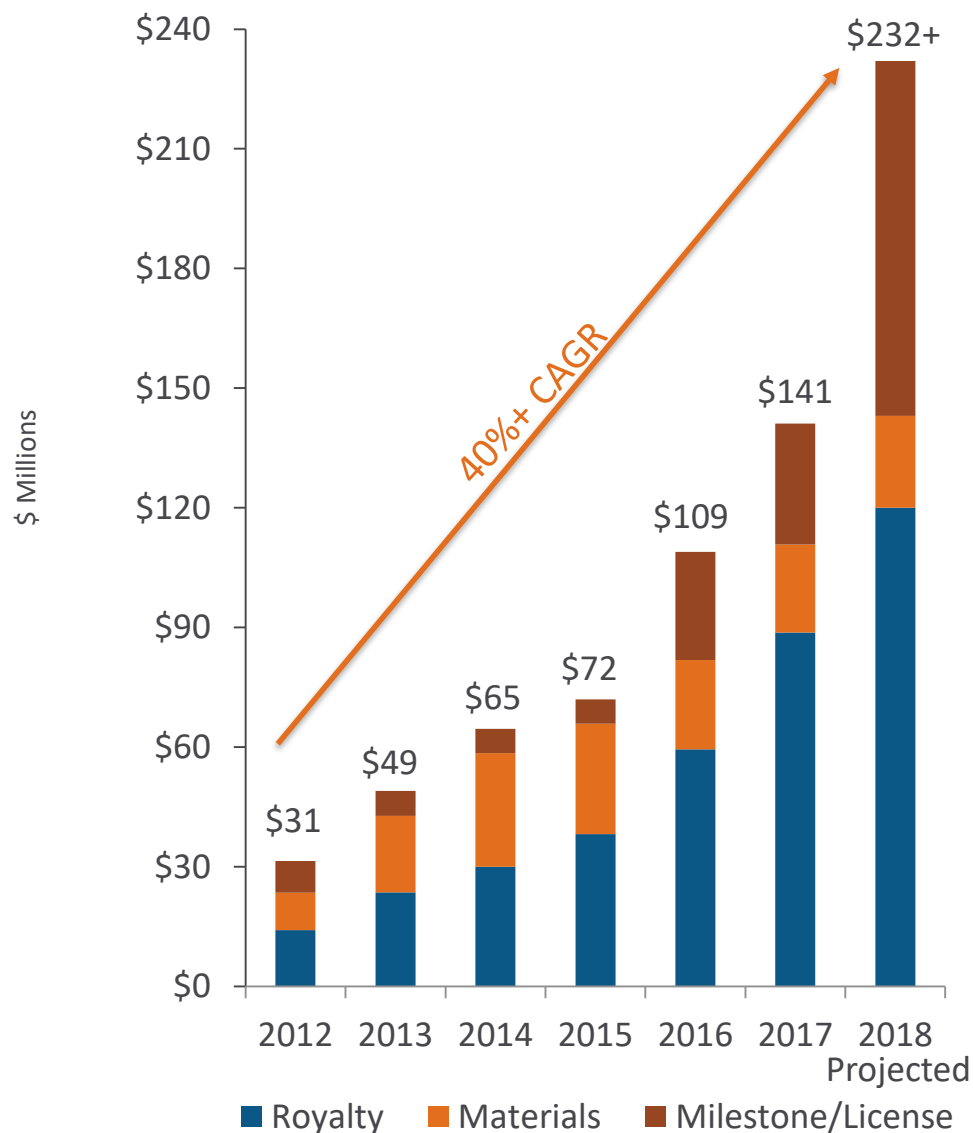
## Commercial Landscape

- Cardiovascular (CV) imaging is a large, growing segment of the market
- More than 50% of CV imaging procedures are performed in patients  $\geq 65$  years old, and substantial portion have risk factors for acute kidney injury
  - A continuing issue with recent and broad medical visibility<sup>1</sup>
  - No products are approved to prevent or treat acute kidney injury
- CE-Iohexol to potentially establish a new safety standard
  - Differentiation in labeled safety, competitive strategy for potential partner(s) to gain sizeable market share
  - Plan to pursue partnering opportunities following clinical work



# *Financial Overview and Outlook*

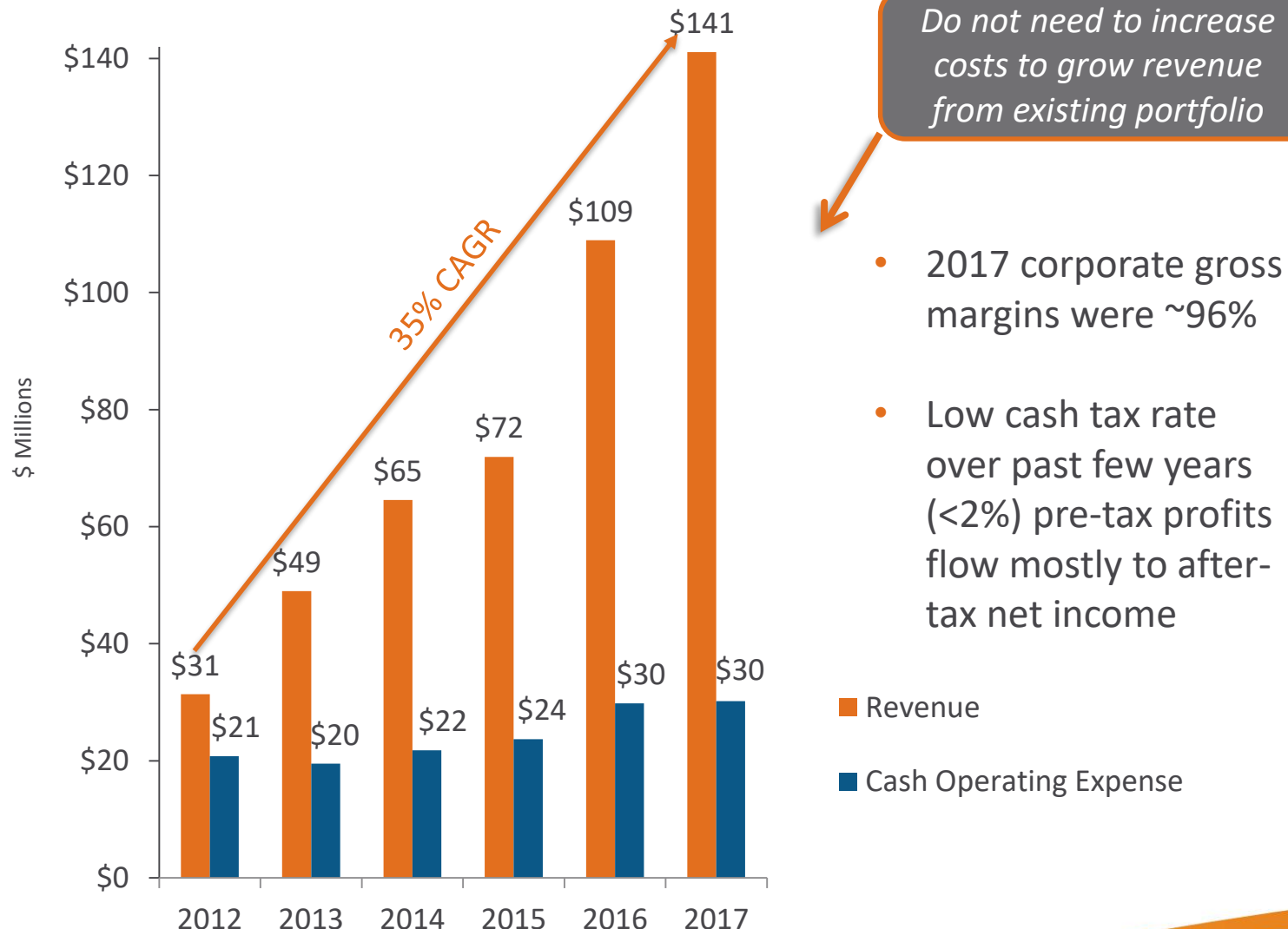
# Sustained Revenue Growth



- Consistent, strong annual revenue growth driven by:
  - High royalty growth
  - Increasing contribution from milestones
  - Consistent contribution from material sales
- 2018 adjusted EPS would be approximately \$6.30 with total revenue of \$232 million
- Potential for additional \$8 million of 2018 milestones

# Revenue Growth Paired with Modest Costs

*Resulting in Increasing Operating Margins*



Note: Cash operating expense calculated as GAAP R&D/G&A expense, adding back stock based compensation and depreciation and amortization

Sources: Ligand 10K's found on sec.gov

# Reconciliation of GAAP EPS to Adjusted EPS

<b>2017 GAAP Earnings Per Share</b>	<b>\$0.53</b>
Stock-based compensation expense	1.06
Non-cash interest expense	0.49
Amortization related to acquisitions	0.78
Increase in contingent liabilities	0.11
Loss from Viking	0.09
Other	(0.16)
Income tax effect of adjusted reconciling items	(0.83)
Deferred tax asset adjustment	1.40
Excess tax benefit from stock-based compensation	(0.20)
Valuation allowance release	(0.18)
2019 Senior Convertible Notes share count adjustment	0.17
<b>2017 Adjusted Earnings Per Share</b>	<b><u>\$3.26</u></b>
<b>GAAP Shares</b>	<b>23.48</b>
Dilutive potential common shares issuable of redeemable convertible not	(1.21)
<b>Adjusted Shares</b>	<b>22.27</b>

*Adjusted EPS guidance excludes stock-based compensation expense, non-cash debt-related costs, changes in contingent liabilities, transaction-related amortization, pro-rata net losses of Viking Therapeutics as well as fair value adjustments to our holdings in their common stock, convertible note receivable and warrants, mark-to-market adjustments for amounts owed to licensors, changes in contingent liabilities related to our CVRs, the excess convert shares covered by bond hedge and certain one-time non-recurring items*

# Calendar of Potential Events

*Potential Milestones for Ligand and Partners over next ~12 months*

## Clinical Data

*VK2809 Phase 2 full data presentation at AASLD*

*Viking*

*BMS-986231 Phase 2 data in Heart Failure*

*Bristol Myers Squibb*

*Baxdela full Phase 3 data in community-acquired bacterial pneumonia*

*Melinta*

*Prexasertib Phase 2 in Cancer*

*Lilly*

## Progression

*Sparsentan Phase 3 Start in IgA Nephropathy*

*Retrophin*

*VK2809 Phase 1 Start in rare glycogen storage disease*

*Viking*

*Lasofoxifene Phase 2 data in metastatic breast cancer*

*Sermonix*

*RVT-1502 Clinical Progression in diabetes*

*Metavant*

## Approvals

*Zulresso FDA Action*  
*Sage Therapeutics*

*Evomela China FDA Action*

*CASI (Spectrum)*

*Baxdela Ex-US action*  
*Menarini/Eurofarma (Melinta)*

*Promacta FDA Priority review of sNDA*  
*Novartis*





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*November, 2018*

*NASDAQ: LGND*

