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REMARKABLE IMPACT ON PATIENTS' LIVES

AbbVie R&D Day

Chicago, IL | June 3, 2016

REMARKABLE IMPACT ON PATIENTS' LIVES RIGHT STRATEGY STRONG TALENT TANGIBLE RES
STRONG EXECUTION IMMUNOLOGY ONCOLOGY VIROLOGY NEUROLOGY REMARKABLE IMPACT
ON PATIENTS' LIVES RIGHT STRATEGY STRONG TALENT TANGIBLE RESULTS STRONG EXECUT

Forward-Looking Statements and Non-GAAP Financial Information

Some statements in this presentation may be forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995. The words "believe," "expect," "anticipate," "project" and similar expressions, among others, generally identify forward-looking statements. AbbVie cautions that these forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those indicated in the forward-looking statements. Such risks and uncertainties include, but are not limited to, challenges to intellectual property, competition from other products, difficulties inherent in the research and development process, adverse litigation or government action, and changes to laws and regulations applicable to our industry. Additional information about the economic, competitive, governmental, technological and other factors that may affect AbbVie's operations is set forth in Item 1A, "Risk Factors," of AbbVie's 2015 Annual Report on Form 10-K, which has been filed with the Securities and Exchange Commission. AbbVie undertakes no obligation to release publicly any revisions to forward-looking statements as a result of subsequent events or developments, except as required by law.

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During the course of this meeting, AbbVie will be presenting information about the uses of AbbVie products and AbbVie compounds in clinical development that have not been approved by the U.S. FDA. AbbVie, in no way, intends to recommend or imply that any AbbVie product or compound in development should be used for unapproved uses, or is safe or effective for uses not approved by the FDA.

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R&D Day: Opening Remarks

Richard Gonzalez

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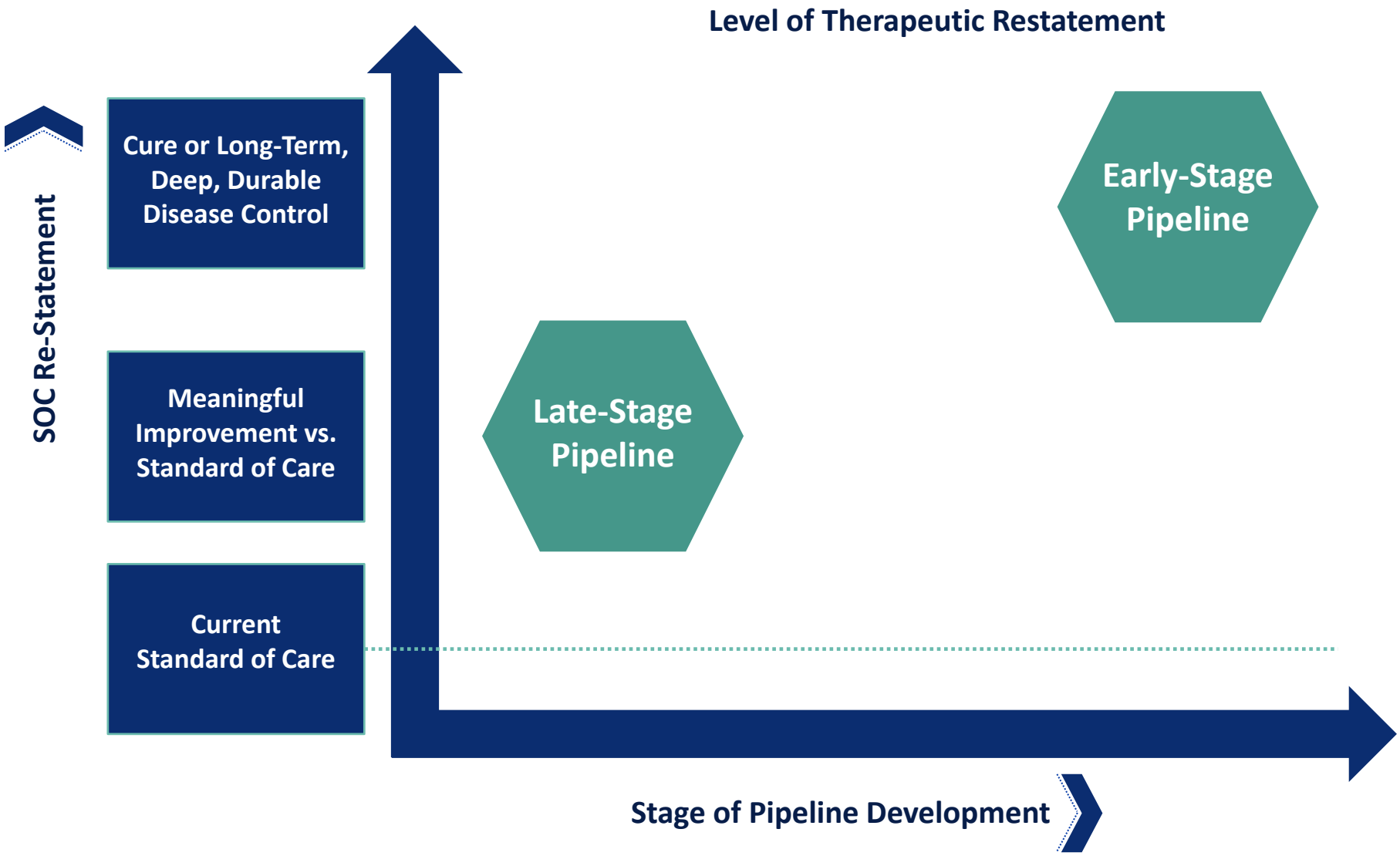
AbbVie's R&D Strategy: Re-Stating Standard of Care



Science and Innovation are the Lifeblood of Our Company

AbbVie Mission

Create an innovation-driven, patient-focused, specialty biopharmaceutical company capable of achieving top-tier performance through outstanding execution and a consistent stream of innovative new medicines

Innovative Medicines

- Compelling Patient Benefit
- Differentiated Clinical Performance
- Economic Value

Elevate standard of care and address significant unmet need

Areas of Focus

Core Therapeutic Focus	**Oncology**	Uniquely positioned with growing leadership position in Hematologic Oncology; Rova-T provides strong foundation for Solid Tumors
	Immunology	Leveraging deep scientific expertise to develop next-generation biologics and small molecules that elevate standard of care
	Virology	Highly competitive next-generation HCV combination that addresses remaining unmet medical need
Emerging Focus	**Neuroscience**	Developing disease-modifying therapies for Alzheimer's disease, multiple sclerosis and other neurodegenerative conditions
Targeted Investment	**Other**	Focused investments in areas that fit our core strengths (i.e., Elagolix, cystic fibrosis collaboration, atrasentan, etc.)

Tremendous Progress in R&D Since Our Launch as an Independent Biopharmaceutical Company

1. **Heightened our level of R&D spend** to reflect the meaningful opportunities in our pipeline
2. Built upon already strong capabilities with the **addition of new talent** to our R&D organization
3. **Strengthened discovery efforts** through collaborations with leading academic and other institutions
4. **Augmented our pipeline** through concerted focus on strategic licensing, acquisition and partner activity
5. **De-risked key late-stage programs** through numerous positive data readouts

Robust Pipeline Supports Long-Term Growth

Near-Term Growth Assets

- Eight key, late-stage de-risked assets
- High probability of regulatory and commercial success
- Differentiated profiles
- On market today or poised to launch over the next 2-3 years

- **Imbruvica**
- **Rova-T**
- **Risankizumab**
- **Venclexta**
- **ABT-494**
- **Next-Gen HCV**
- **Elagolix**
- **Zinbryta**

50+ Additional Development Programs

- Robust portfolio of promising programs
- Have already established strong proof-of-concept for numerous assets

- **Anticipate key data readouts from several programs over next 12-24 months to determine next steps**
  - **Veliparib**
  - **ABT-414**
  - **Atrasentan**
  - **Several DVD-Ig programs**
  - **Partnered assets (dual PI3K, IL-6 nanobody, etc.)**

Innovative Early-Stage Opportunities

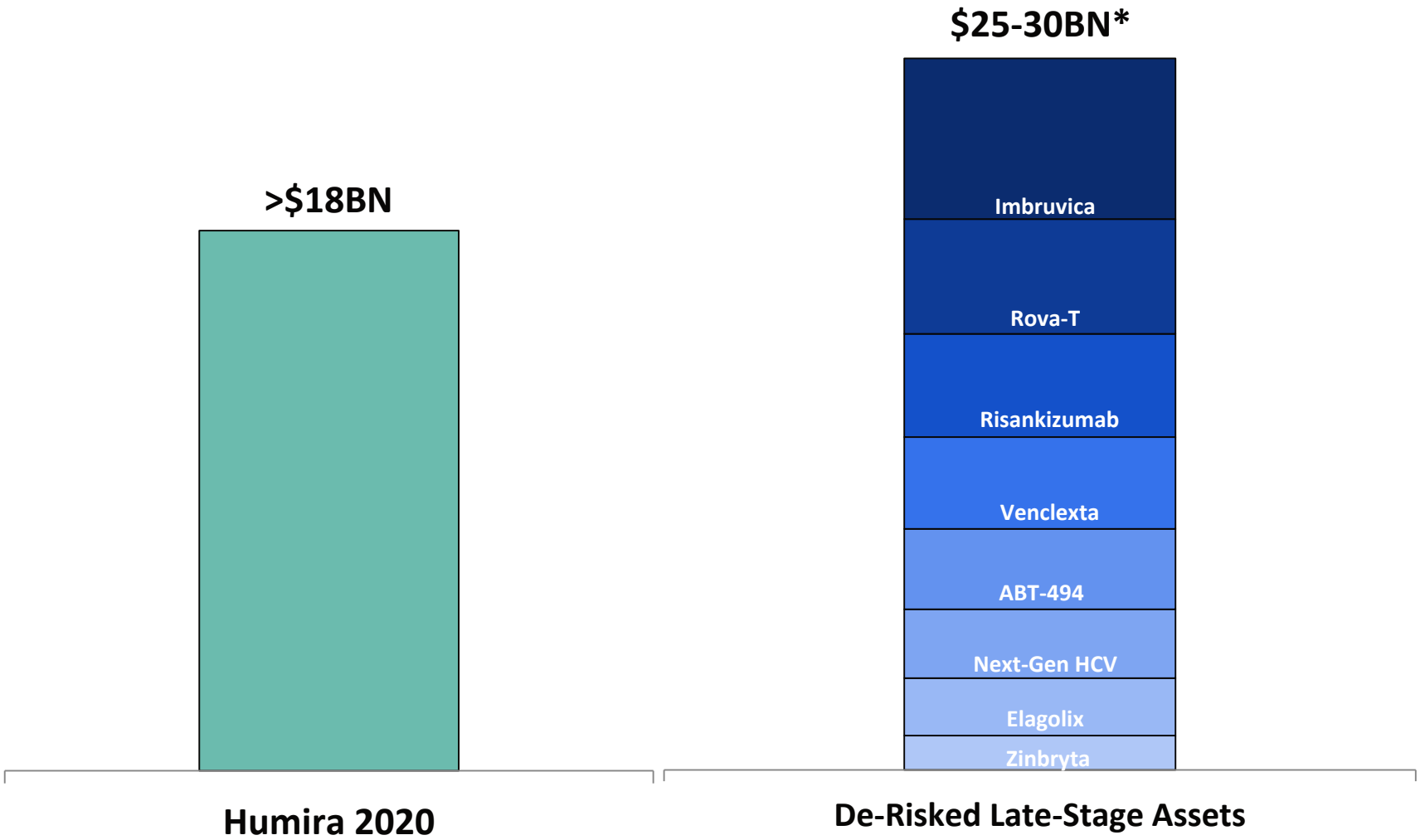
- Early-stage development programs in areas of high unmet need
- Enhanced discovery platforms have high potential for continued asset generation to drive development efforts going forward

- **Entering clinic with novel immuno-oncology and neuroscience assets**
- **New discovery platforms, including Calico and Stemcentrx, augment existing discovery/early development efforts, have potential to accelerate asset generation**
- **Early-stage programs to begin driving growth in mid-2020s and beyond**

Near-Term Growth Assets are Significantly De-risked

Asset	Details
Imbruvica *On-market with five approved indications, additional indications expected over next several years*	Currently approved for five indications, including recent label update to include 1L CLL; numerous mid- and late-stage studies underway for range of blood cancers
Venclexta *On-market with initial indication, additional indications expected over next several years*	First-in-class BCL-2 inhibitor recently approved for first indication; mid-to-late-stage development ongoing for numerous hematologic malignancies
Zinbryta *2016 Launch*	Pivotal data demonstrated significant benefit vs. active comparator; regulatory submissions under review, decisions expected mid-2016
Next-Gen HCV *2017 Launch*	Mid-stage data indicate combination can deliver cure rates approaching 100% across genotypes; pivotal data expected 2H16
Rova-T *2018 Launch*	Compelling Phase 1/2 data in relapsed SCLC; Phase 3 underway; potential in a variety of solid tumors with DLL 3 expression
Elagolix *2018 Launch*	Compelling profile illustrated in two registrational trials; on track for regulatory submission in 2017
ABT-494 *2019 Launch*	Phase 2 RA trials demonstrated potential for best-in-class profile in TNF-IR and MTX-IR; comprehensive Phase 3 program now underway
Risankizumab *2019 Launch*	Phase 2 Ps study illustrated potential for best overall profile; Phase 3 currently underway, with potential to advance in several other immune-mediated conditions

Magnitude of Near-Term Growth Assets Alone Ensures Substantial Growth Beyond 2020



*Represents nominal peak-year revenue opportunity for eight key near-term growth assets

AbbVie: A Unique Investment Opportunity

AbbVie offers top-tier revenue and EPS growth, significant cash flow and strong return of capital to shareholders

- **Compelling, de-risked late-stage pipeline poised to fuel long-term growth**
- **Early-stage pipeline includes programs with the potential to dramatically re-state standard of care**
- **Strong track record of execution**
- **Attractive return of capital philosophy, balanced between supporting growth and returning cash to shareholders**
- **Remain committed to delivering on our long-term objectives**
- **Double-digit EPS growth on average expected through 2020**

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Introduction and Overview of R&D Strategy

Michael Severino, M.D.

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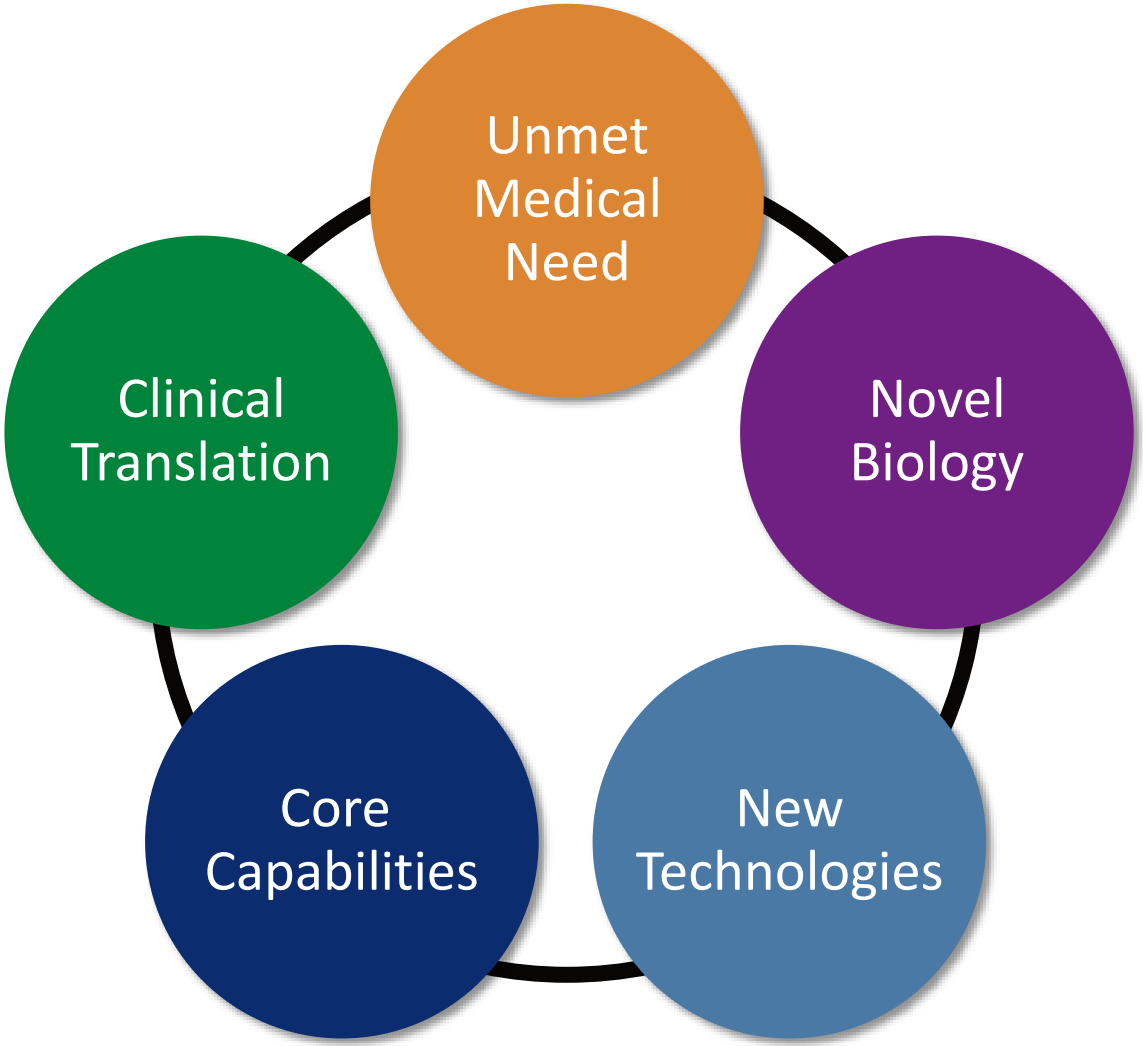
A Number of Important Considerations Guide Our R&D Strategy



Our Discovery Efforts Are Focused on Three Main Areas

Oncology	• Grow our strong position in hematologic malignancies • Establish a foundation in solid tumors • Leverage our experience in immunology to develop next-generation immuno-oncology therapies
Immunology	• Use core skills in immunology to develop next-generation therapies that raise the standard in Rheumatology, Dermatology and Gastroenterology
Neuroscience	• Capitalize on emerging biology and new technologies to expand into Alzheimer's disease and the neurodegenerative components of multiple sclerosis

In Addition, We Intend to Pursue Areas That Are a Strong Fit for Our Core Strengths

HCV	• Pursue next-generation regimens that address remaining unmet need
Elagolix	• Bring an important new therapeutic option to women with endometriosis and uterine fibroids
Cystic Fibrosis	• Explore whether new insights in biology and medicinal chemistry can lead to a transformational therapy

Strong Talent Is an Essential Part of This Strategy

We Are Proud of Our Talent at AbbVie

Recent hires or new to role

Tom Hudson, M.D.
VP, Oncology Discovery/Early Development

Eric Karran, Ph.D.
VP, Foundational Neuroscience Center

Rob Scott, M.D.
CMO and VP, Development

Shao-Lee Lin, M.D., Ph.D.
VP, Global Therapeutic Areas
and International Development

Laura Gault, M.D., Ph.D.
Neuroscience, Clinical Development

Chris Miller, Ph.D.
Director, Genetics & Genomics Research

Anthony Slavin, Ph.D.
Director, Immunology Biology

Susie Jun, M.D., Ph.D.
VP, Oncology Translational Medicine

Therese Podrebarac, M.D.
VP, Immunology Development

Brad Shotwell, Ph.D.
Senior Group Leader, Hit to Lead Chemistry

Laura Gasparini, Ph.D.
Project Director, Neuroscience

Albert Lai, Ph.D.
Project Director, Oncology

Guowei Fang, M.D.
Head of Discovery, Pharmacyclics

Patrick John Marroum, Ph.D.
Director, Biopharmaceutics, Clinical Pharmacology
and Pharmacometrics

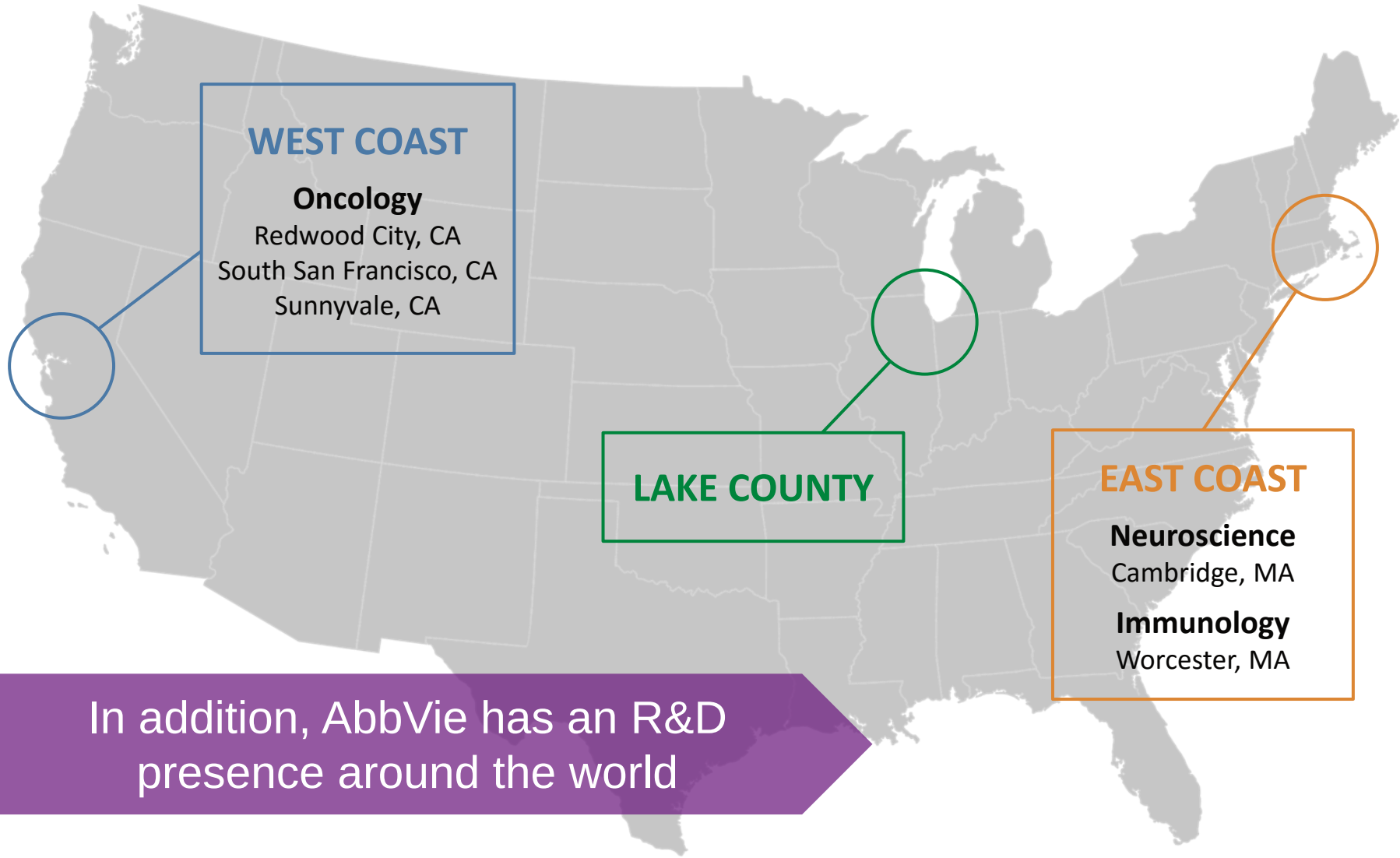
Phil Hajduk, Ph.D.
VP, Research Informatics

Paul Peloso , M.D.
Group Medical Director, Elagolix, General Medicine TA

Maureen Kelly, M.D.
Group Medical Director, Risankizumab, Immunology TA

Adam Petrich, M.D.
Associate Medical Director, Oncology

We Are Increasing our Presence in Hubs of Biotechnology and External Innovation



In addition, AbbVie has an R&D presence around the world

Our Internal Efforts Are Complemented by Our Access to External Innovation

Academic Collaborations

Yale

BROAD INSTITUTE

MD Anderson Cancer Center

Washington University in St. Louis

The University of Chicago

DEMENTIA Consortium

UCSF

The Walter and Eliza Hall Institute of Medical Research

Industry Partnerships

Calico

CytomX Therapeutics

argenx

Infinity Pharmaceuticals

Genentech
A Member of the Roche Group

Roche

Boehringer Ingelheim

Bristol-Myers Squibb

janssen
Pharmaceutical Companies of Johnson & Johnson

apogenix

SeattleGenetics

Galápagos

F-star

Acquisitions

Stemcentrx

pharmacyclics
An AbbVie Company

immuVen

Facet Biotech

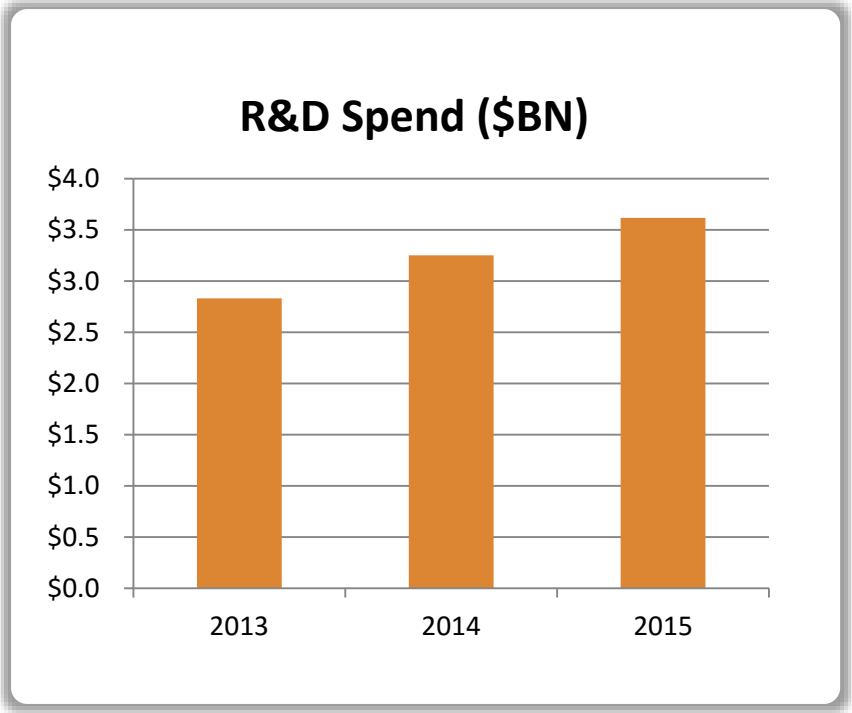
Not a comprehensive list

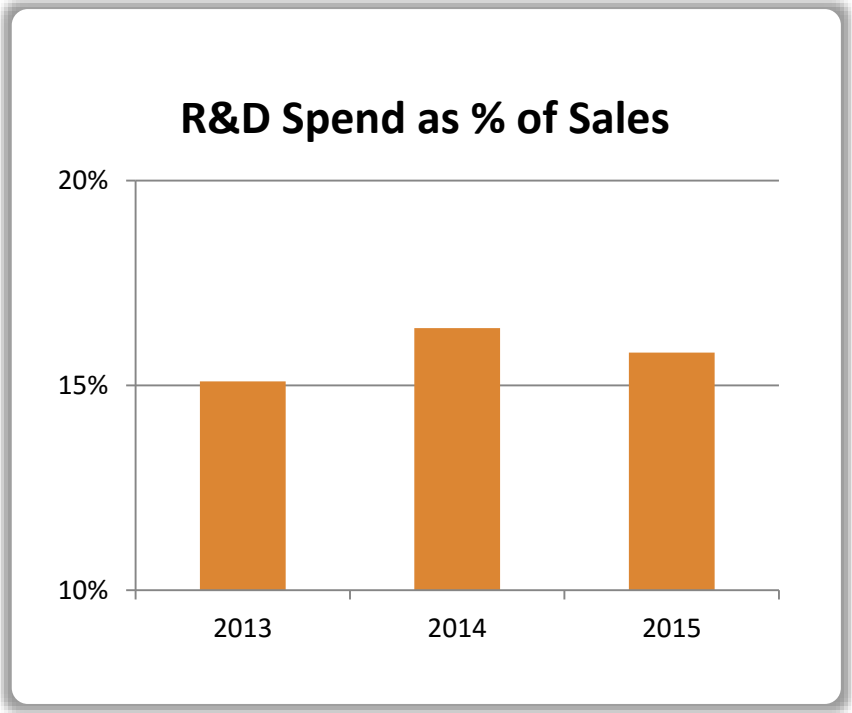
Our Calico Collaboration Offers an Additional Opportunity to Explore Novel Biology

Portfolio of ~20 programs targeting fundamental biological mechanisms that underlie neurodegeneration, cancer and other diseases of aging

Adapted from *Cell* 153, June 6, 2013

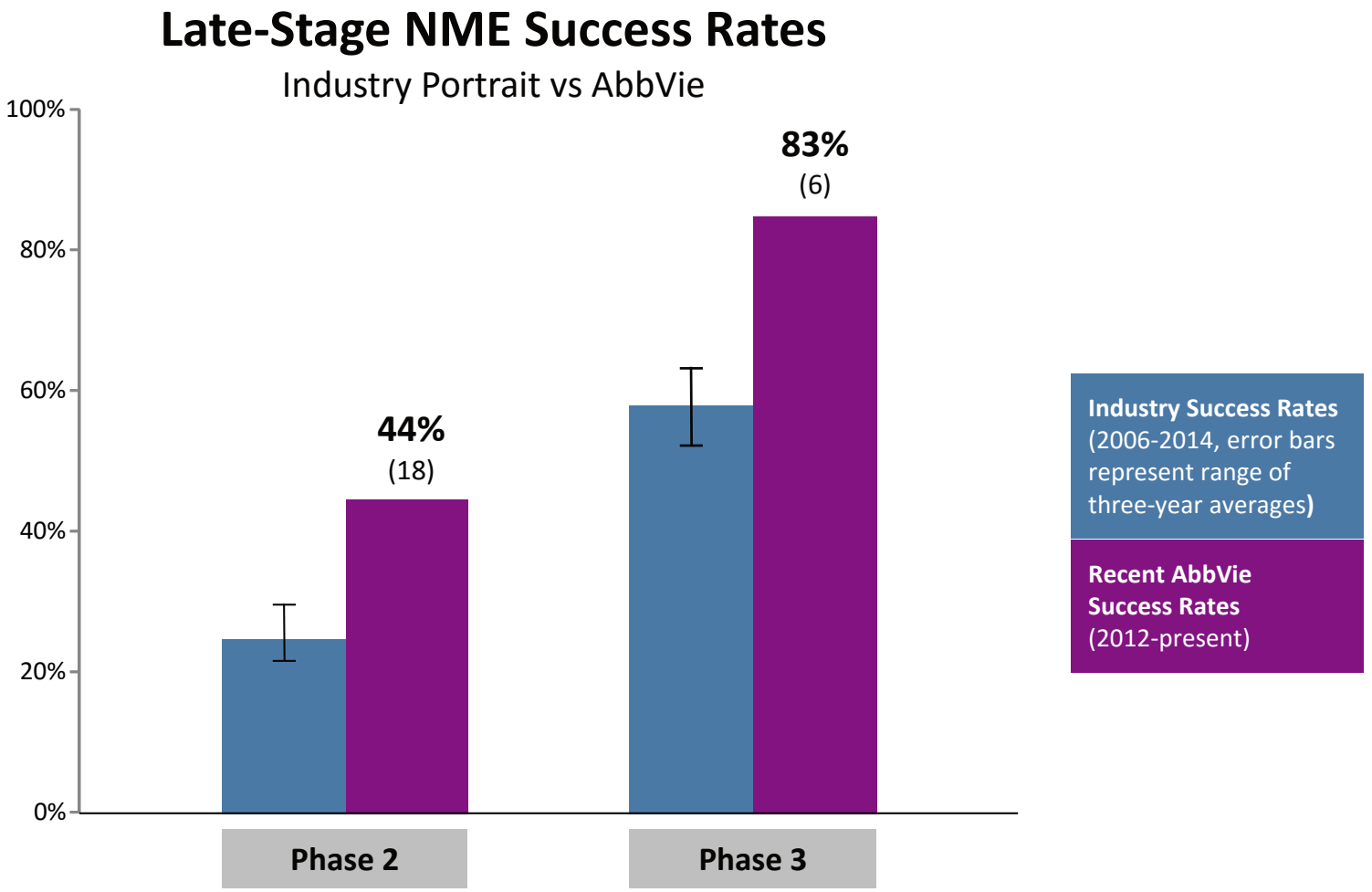
Our Strategy Is Supported by Strong Financial Commitment





Note: Non-GAAP; excluding specified items

AbbVie's Phase 2 and Phase 3 Success Rates Compare Favorably to Industry Benchmarks



Source: Pharmaceutical Benchmarking Forum/KMR 2015; industry Portrait defined as combined data from all pharma companies participating in PBF/KMR Benchmarking Forum

(xx) Numbers in parenthesis indicate number of phase events (Go/no-go decisions) for ABBV

Pipeline Supports Our Future Growth

Select Pipeline Assets

Phase I	Phase II	Registrational/Phase III	Submitted	Recent Approvals
Rova-T: Neuroendocrine Tumors **SC002:** Solid Tumors **SC003:** Solid Tumors **PTK7*:** Solid Tumors **EFNA4*:** Solid Tumors **ABBV-838:** Multiple Myeloma **ABBV-399:** Solid Tumors **ABT-165:** Solid Tumors **ABT-RTA 408:** Solid Tumors **ABBV-075:** Solid Tumors and Hem Onc **ABBV-085:** Solid Tumors **ABBV-221:** Solid Tumors **Imbruvica:** Solid Tumors	**Venclexta:** AML **Venclexta:** iNHL/DLBCL **Venclexta:** Multiple Myeloma **Duvelisib:** iNHL (R/R) **Imbruvica:** Multiple Myeloma **Imbruvica:** AML **Imbruvica:** FL (TN) **Imbruvica:** MZL (R/R) **Imbruvica:** Graft V Host	**Rova-T:** SCLC **Venclexta:** CLL (Relapsed/Refractory) **Venclexta:** CLL (Front-line; Unfit) **Imbruvica:** Pancreatic Cancer **Imbruvica:** DLBCL (TN) **Imbruvica:** FL (R/R) **Imbruvica:** MCL (TN) **Duvelisib:** CLL (R/R) **Elotuzumab:** Multiple Myeloma (TN) **Veliparib:** NSCLC (Squamous) **Veliparib:** NSCLC (Non-squamous) **Veliparib:** Breast Cancer (Neoadjuvant) **Veliparib:** Breast Cancer (BRCA) **Veliparib:** Ovarian Cancer **ABT-414:** GBM	**Imbruvica:** CLL (TN, 65+; EU) **Venclexta:** CLL (R/R, 17P del; EU)	**Humira:** HS (U.S. and EU) **Humira:** New Formulation **Humira:** New Pen Device
	Risankizumab: Crohn's Disease **Risankizumab:** PsA **Risankizumab:** Asthma **ABT-122:** RA **ABT-122:** PsA **ABT-494:** Crohn's Disease **ABT-981:** Osteoarthritis **ALX-0061:** RA	**Risankizumab:** Psoriasis **ABT-494:** RA	**Humira:** Uveitis (U.S. and EU)	**Duopa:** Advanced Parkinson's **Zinbryta:** Multiple Sclerosis (U.S. and EU)
ABT-957: Alzheimer's **ABBV-8E12:** PSP & AD **ABT-555:** MS and SCI	**ABT-RTA 408:** FA &MM	**ABT-493/ABT-530:** HCV	**Viekira 3QD:** HCV (U.S. and EU)	**Viekira Pak:** HCV **Viekira Pak:** RBV-free (GT1b cirrhotic) **Technivie:** HCV (GT4) **2-DAA Japan:** HCV (GT1b)
ABBV-974: Cystic Fibrosis **ABBV-2222:** Cystic Fibrosis **ABBV-2451:** Cystic Fibrosis		**Elagolix:** Endometriosis **Elagolix:** Uterine Fibroids **Atrasentan:** Diabetic Nephropathy		**Imbruvica:** CLL (TN, U.S.) **Imbruvica:** CLL (R/R combo with B/R) **Empliciti:** Multiple Myeloma (Relapsed/Refractory; U.S. EU) **Venclexta:** CLL (R/R 17P del; US)

- Oncology
- Immunology
- Neuroscience
- HCV/Liver Disease
- Other

*Stemcentrx partnered asset

Our Near-Term Growth Assets Are Significantly De-risked

- **8 products** currently in pivotal development or recently launched
- Potential for **>20 new drug** or new indication approvals by the end of 2020, including **seven approvals** expected to contribute in 2016 and beyond
- Recent data readouts continue to de-risk key assets, increasing our level of confidence in **high likelihood** of clinical, regulatory and commercial success

Venclexta

Imbruvica

Rova-T

Elagolix
(Endometriosis, Uterine Fibroids)

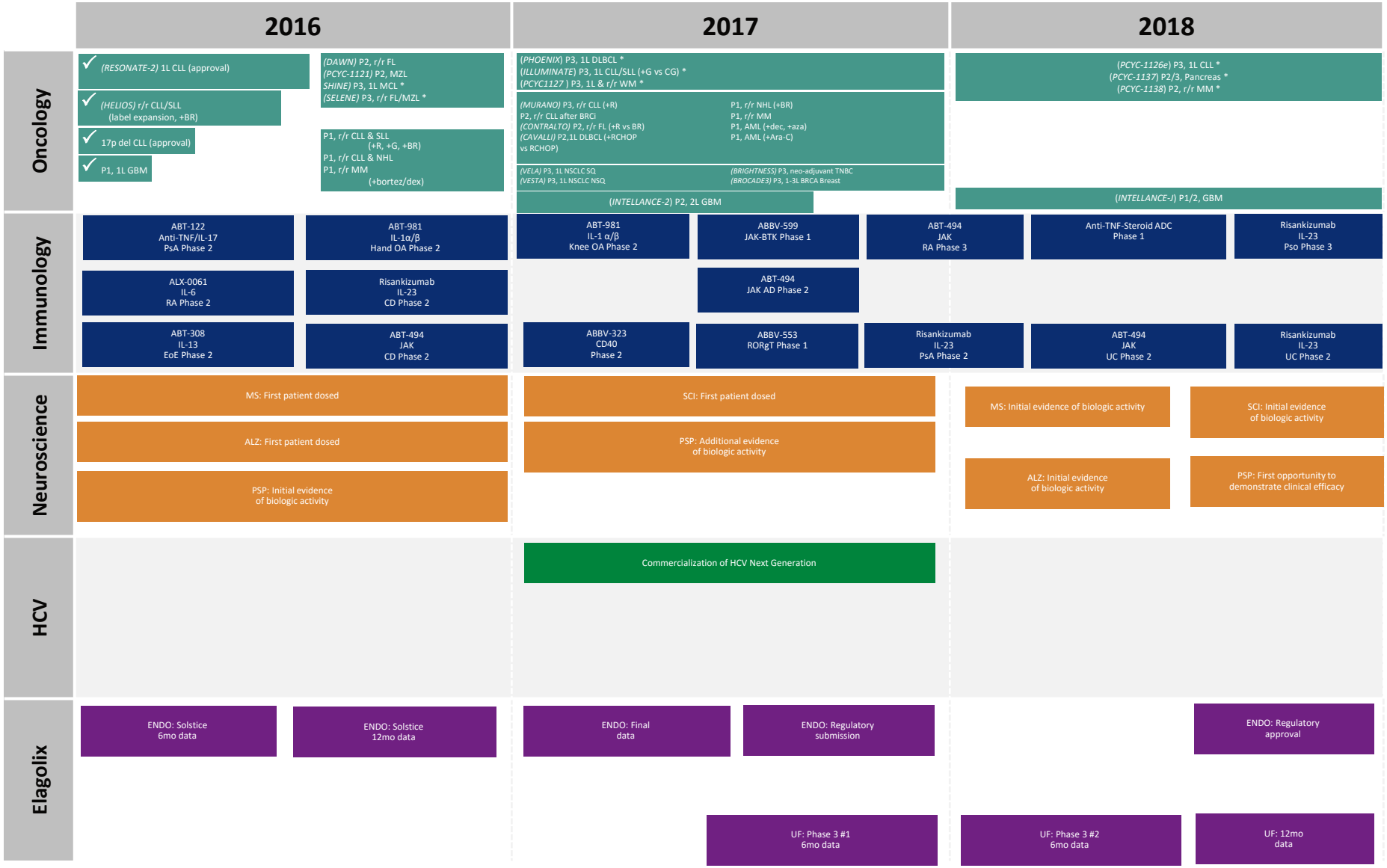
Zinbryta

Next-Generation HCV

ABT-494

Risankizumab

We'll See Continued Pipeline Advancement in the Years Ahead



What We Will Cover Today

Oncology	**Oncology Overview**	Michael Severino, M.D.
	Stemcentrx	Brian Slingerland
		Scott Dylla, Ph.D.
	Imbruvica	Danelle James, M.D., M.S.
	Venclexta, Veliparib and ABT-414	Gary Gordon, M.D., Ph.D.
	Discovery and Early Development	Thomas Hudson, M.D.
Immunology	**ABT-494 and Risankizumab**	Shao-Lee Lin, M.D., Ph.D.
	Highlights from Immunology Discovery	Lisa Olson, Ph.D.
HCV	**HCV**	Shao-Lee Lin, M.D., Ph.D.
Elagolix	**Elagolix**	Shao-Lee Lin, M.D., Ph.D.
Neuroscience	**Zinbryta and ABT-555**	Laura Gault, M.D., Ph.D.
	Alzheimer's Disease and the Foundational Neuroscience Center	Eric Karran, Ph.D.

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BUILDING ONCOLOGY LEADERSHIP

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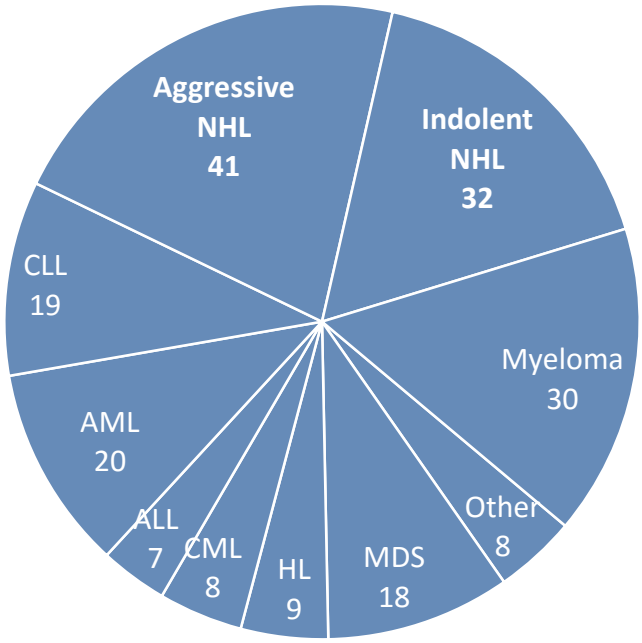
Oncology Overview

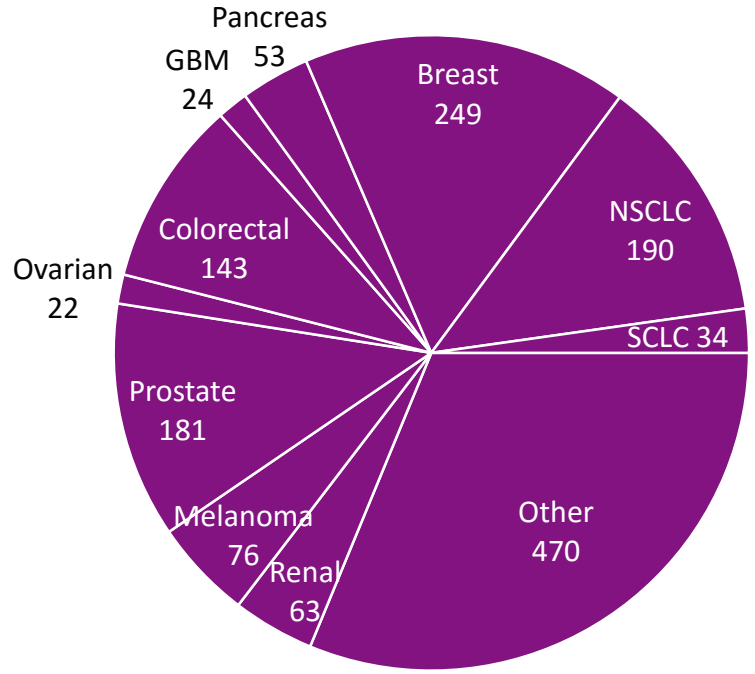
Michael Severino, M.D.

Despite Considerable Progress in Recent Years, Significant Unmet Medical Need Exists in Oncology

Hematologic Malignancies, 2016
U.S. Incidence (000's)



Solid Tumors, 2016
U.S. Incidence (000's)



Sources: American Cancer Society, SEER, Kantar Health.

- Growing patient population, ~21MM by 2030
  - ~ 40% life-time risk of being diagnosed with cancer
- ~30% of all patients diagnosed with cancer die within five years
- ~80% of patients with metastatic tumors die within five years

Our Oncology Efforts Are Guided by Three Strategic Imperatives

1. **Grow** our strong position in hematologic malignancies
2. **Establish** a foundation in solid tumors
3. **Leverage** our strength in immunology to develop next-generation immuno-oncology therapies

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Imbruvica and Venclexta Provide a Strong Foundation in Hematologic Malignancies

imbruvica™ (ibrutinib) 140mg capsules

VENCLEXTA™ venetoclax tablets

These agents have the potential to transform the treatment of CLL, MCL and Waldenström's macroglobulinemia

- Monotherapy
- Combination with existing therapies
- Novel/novel combinations

Clinical data show strong signs of activity across a wide range of other hematologic malignancies

Imbruvica
- NHL
- Multiple myeloma
- GVHD

Venclexta
- NHL
- Multiple myeloma
- AML

Our early pipeline provides additional opportunities based on our work in apoptosis and epigenetics

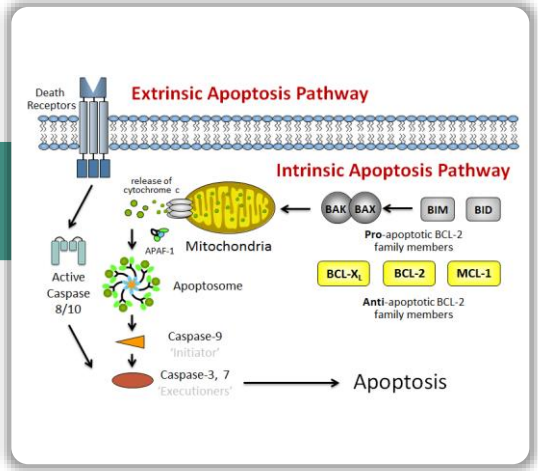
Our Oncology Efforts Are Guided by Three Strategic Imperatives

1. **Grow** our strong position in hematologic malignancies
2. **Establish** a foundation in solid tumors
3. **Leverage** our strength in immunology to develop next-generation immuno-oncology therapies

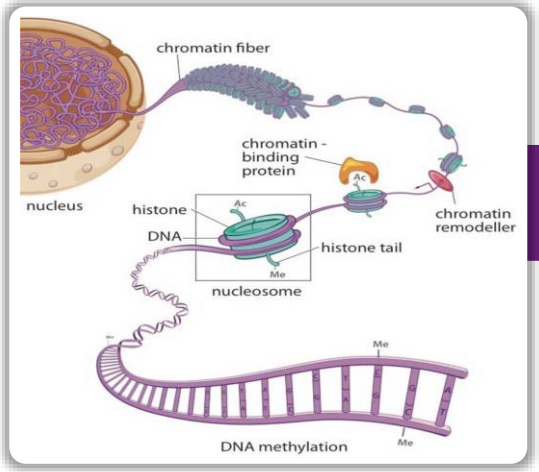
Building a Foundation in Solid Tumors

Our efforts are based on:

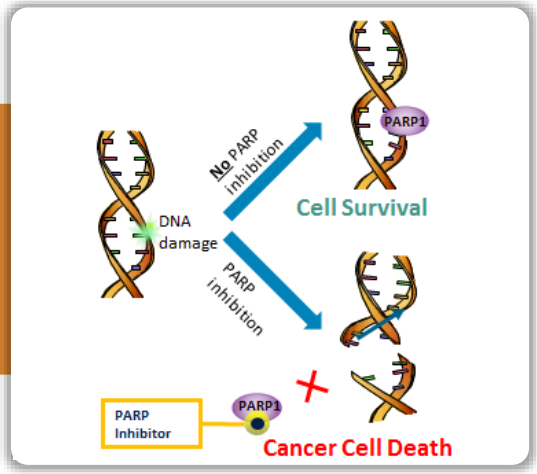
Apoptosis



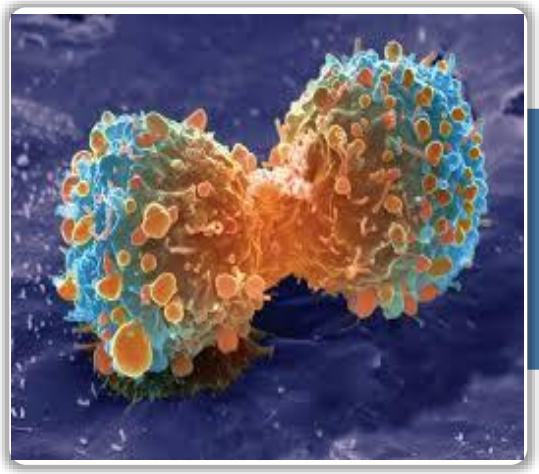
Epigenetics



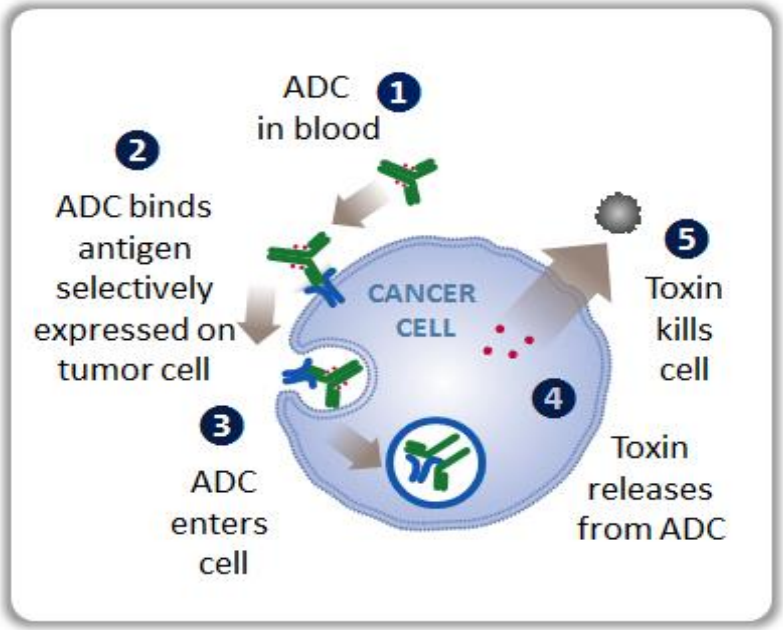
DNA Damage Repair



Emerging Areas in Cancer Biology



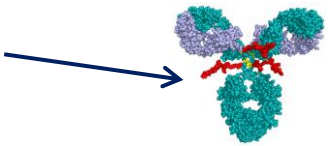
We Are Also Exploring New Technologies Designed to Extend our Reach



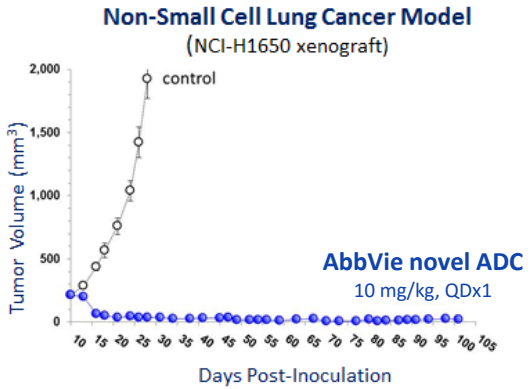
- Target Identification
- Antibody Engineering
- Linker Chemistry
- Toxin Technology
- Clinical Translation

ADCs with Novel Warheads

AbbVie proprietary warhead

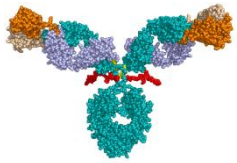


- We are developing novel warheads that leverage our experience in apoptosis, tumor energetics, and other areas
- Potent anti-tumor activity demonstrated in a range of tumor models
- ADC approach circumvents mechanism-based toxicity of novel warheads in preclinical models



Our Bispecific Platform has the Potential to Create Novel Biology

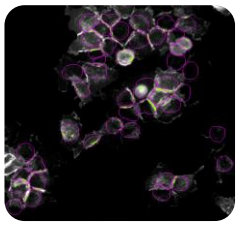
Bispecific ADCs



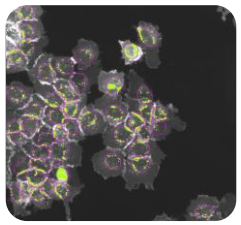
Targets two antigen

- Unique properties of bispecific ADCs can be used for multiple approaches:
  - Targeting two epitopes on single cancer target
  - Targeting two distinct antigens on the same tumor cell
  - Targeting two antigens on different cells within the tumor microenvironment

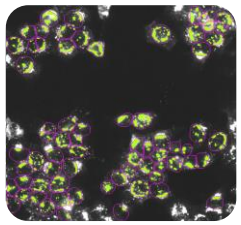
Bispecific Shows Enhanced Internalization in Cancer Cells



Antibody to epitope 1

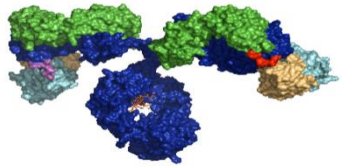


Antibody to epitope 2

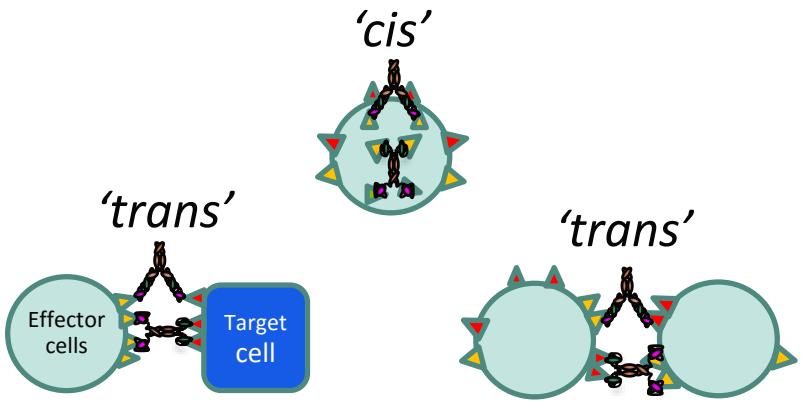


Bispecific to epitopes 1 & 2

Bispecifics Can Direct Cellular Activation



- Different formats can be constructed to:
  - Direct protein-protein interactions by targeting different proteins on the same cell
  - Activate cells in a specific setting by targeting two targets on different cell types

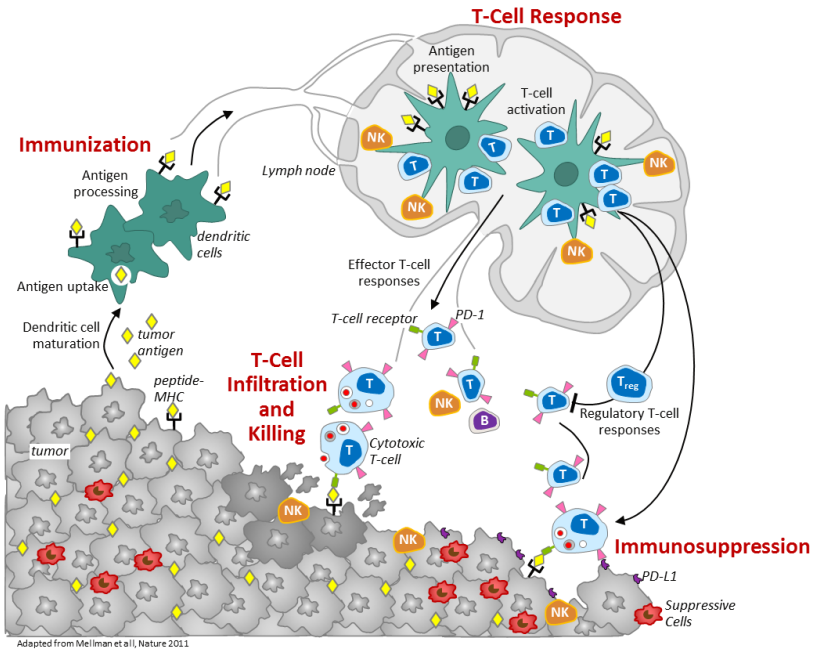


Our Oncology Efforts Are Guided by Three Strategic Imperatives

1. **Grow** our strong position in hematologic malignancies
2. **Establish** a foundation in solid tumors
3. **Leverage** our strength in immunology to develop next-generation immuno-oncology therapies

AbbVie's Immuno-Oncology Strategy Leverages our Strengths in Immunology and Protein Sciences

Generation and Regulation of Antitumor Immunity



AbbVie Approaches

Emerging Areas:
Suppressive Tumor Microenvironment
e.g., anti-GARP antibodies, CD40 agonists

Emerging Biology:
T Cell Agonists & T Cell Activation
e.g., OX40 agonists

Disruptive Technologies:
T Cell Receptor-based Biologics & Cell-based Therapies
e.g., soluble TCR bispecifics

Enabling Collaborations

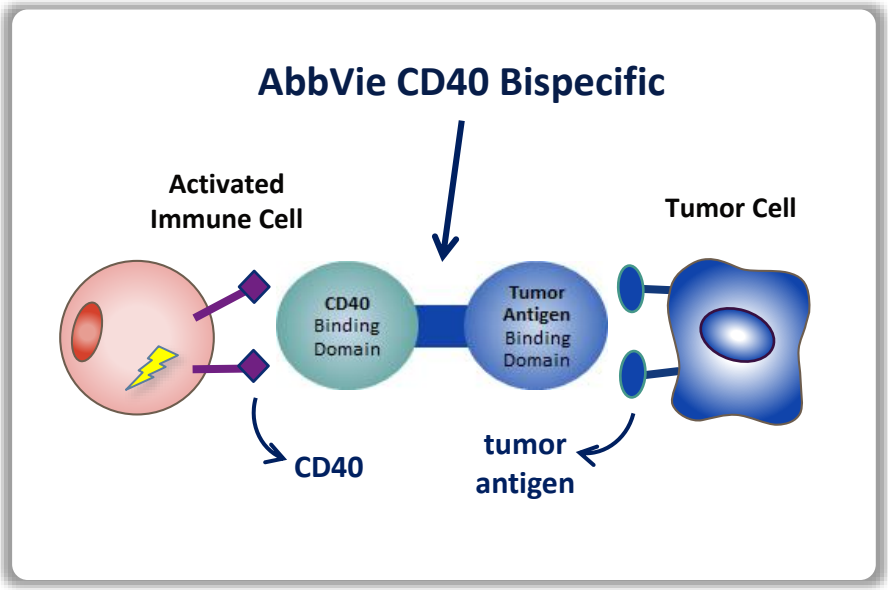
MD Anderson Cancer Center

UCSF University of California San Francisco

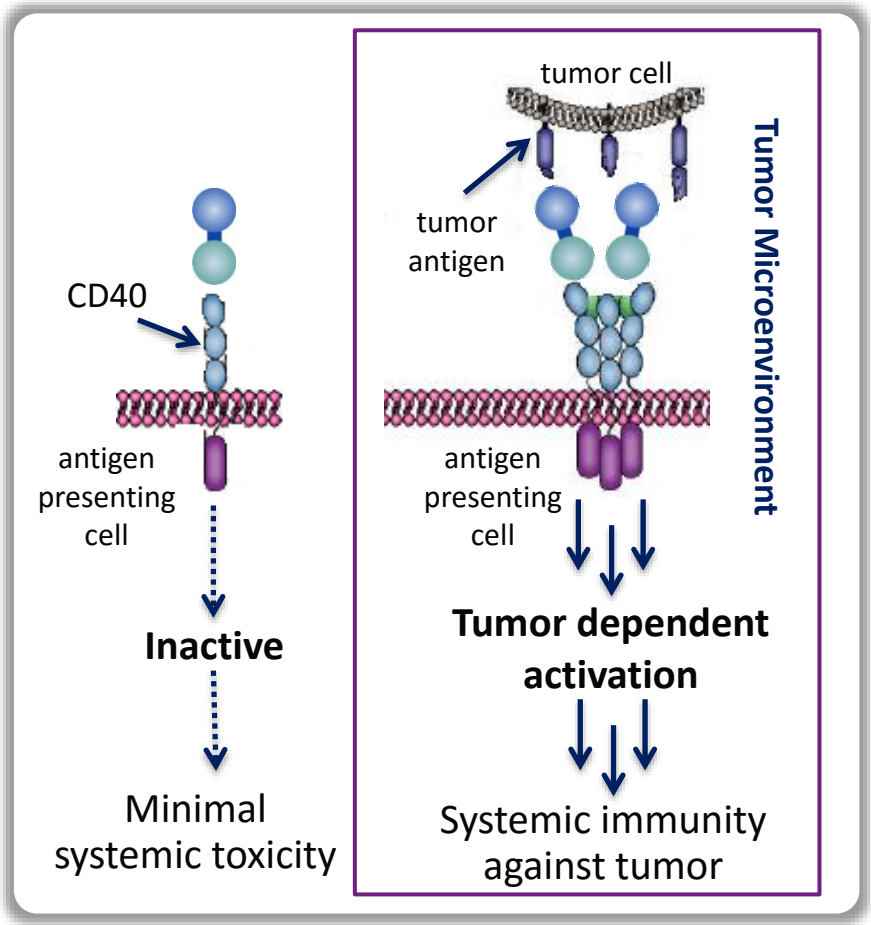
The University of Chicago

An Early Immuno-Oncology Program Targets a Central Pathway of the Immune System: CD40

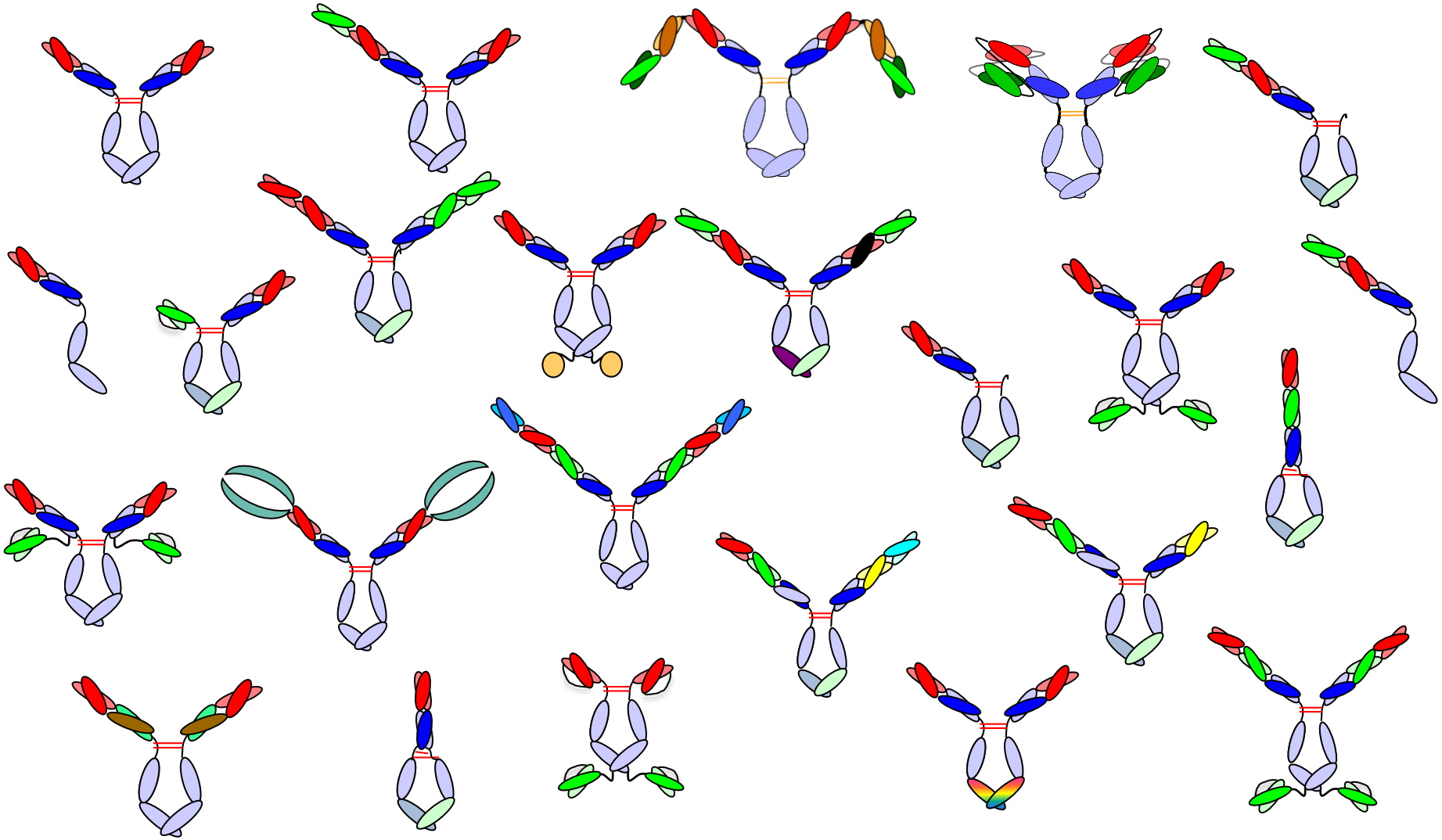
- Tumor microenvironment blunts the immune response
- Activation of CD40 restores cell-mediated immune responses
- However, systemic toxicity has been a challenge for the clinical development of CD40 agonists



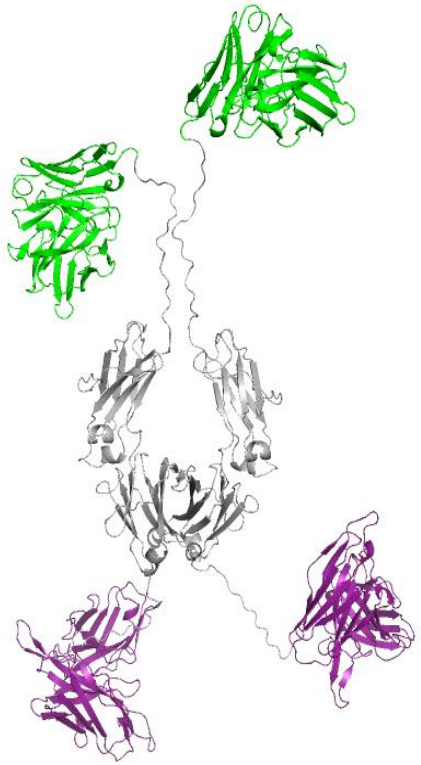
AbbVie's bispecific platform has the potential to deliver tumor-specific immune activation

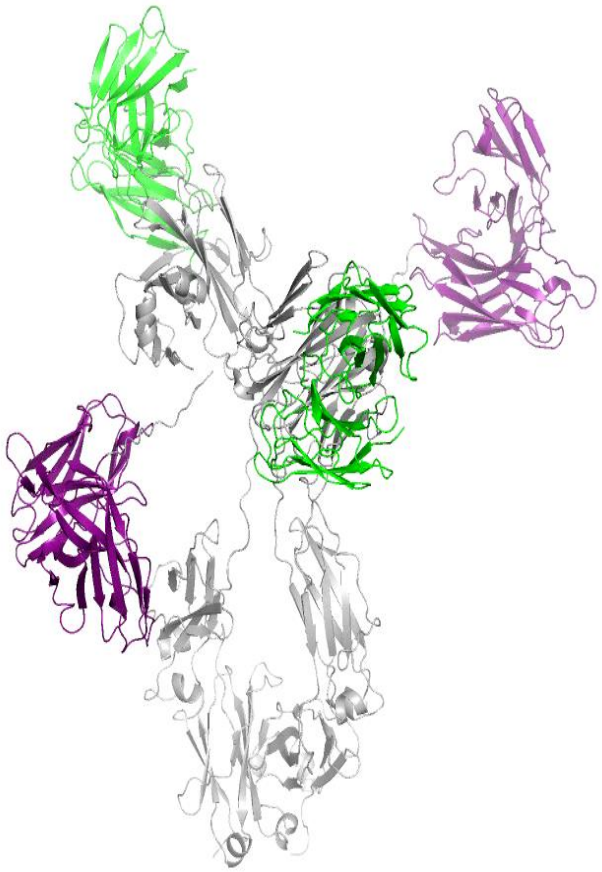


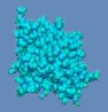
AbbVie's Bispecific Platform Can Be Used to Create a Wide Range of Formats, Leading to New Biology



Different Formats Allow for Differing Mechanisms of Action







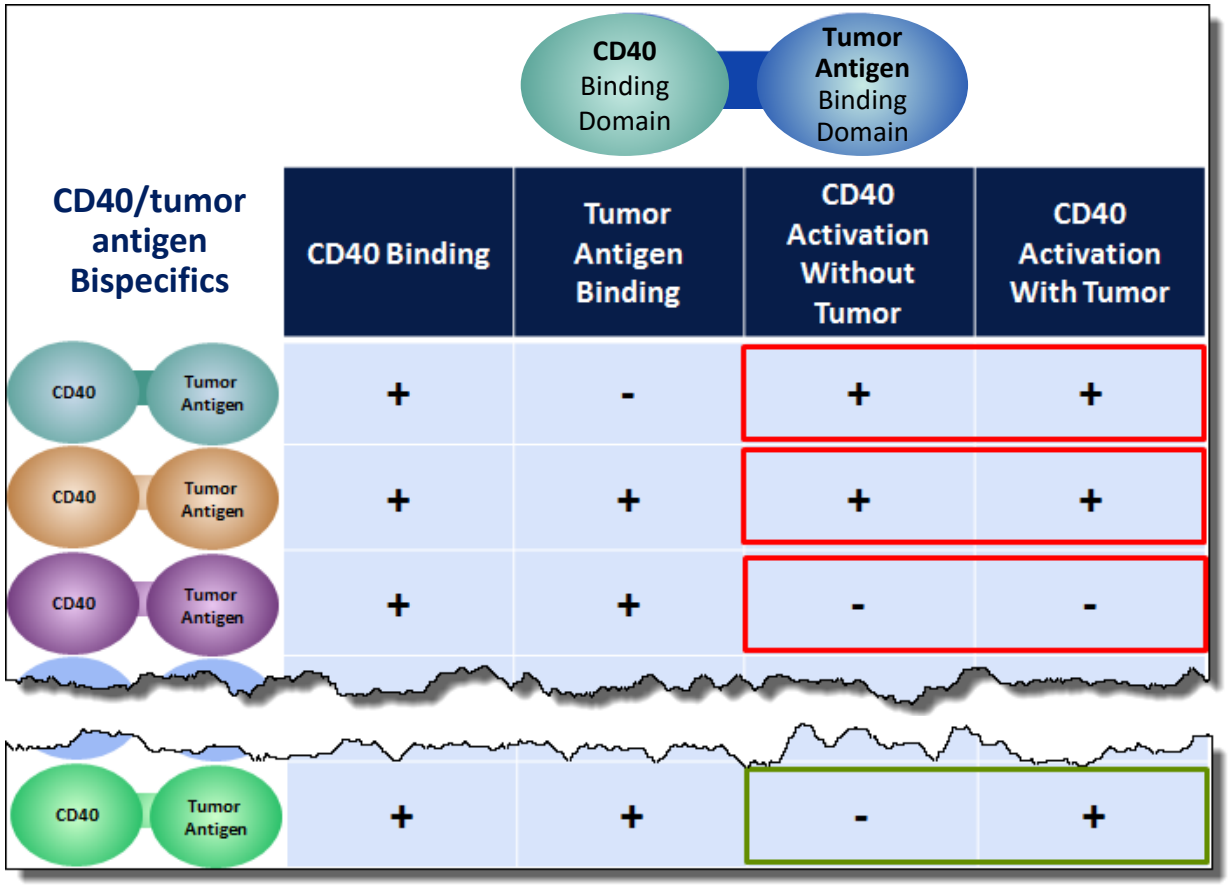
Protein 1

Protein 2

We Created More than 50 Unique Structures to Engineer a Molecule with the Right Properties

In Vitro Testing of CD40/Tumor Antigen Bispecific Formats

>50 bispecific constructs prepared and screened



Multiple bispecific formats tested…

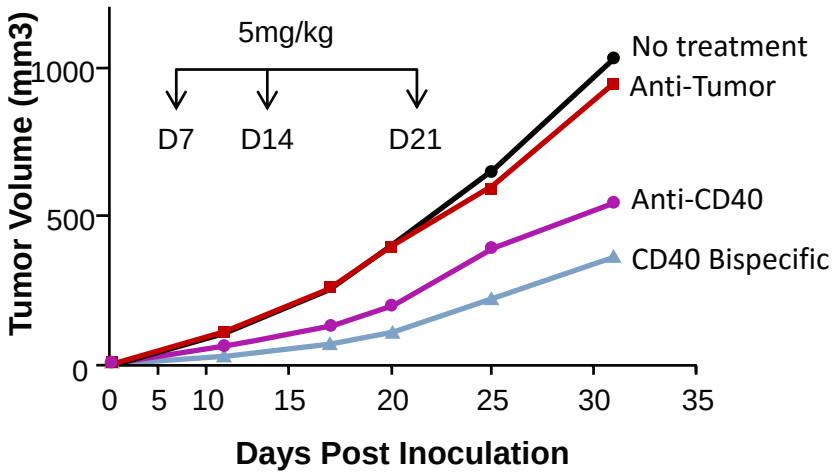
…but only the ABBV-428 structure leads to conditional activation

ABBV-428: AbbVie's lead CD40 Bispecific

Our Lead CD40 Candidate Inhibits Tumor Growth Without Toxicity in Preclinical Models

Efficacy

Preclinical Breast Cancer Model



Toxicity

Toxicity

	No Treatment	Anti-CD40	CD40 Bispecific
Liver Toxicity (ALT)	-	+	-
Systemic Inflammatory Response	-	+	-

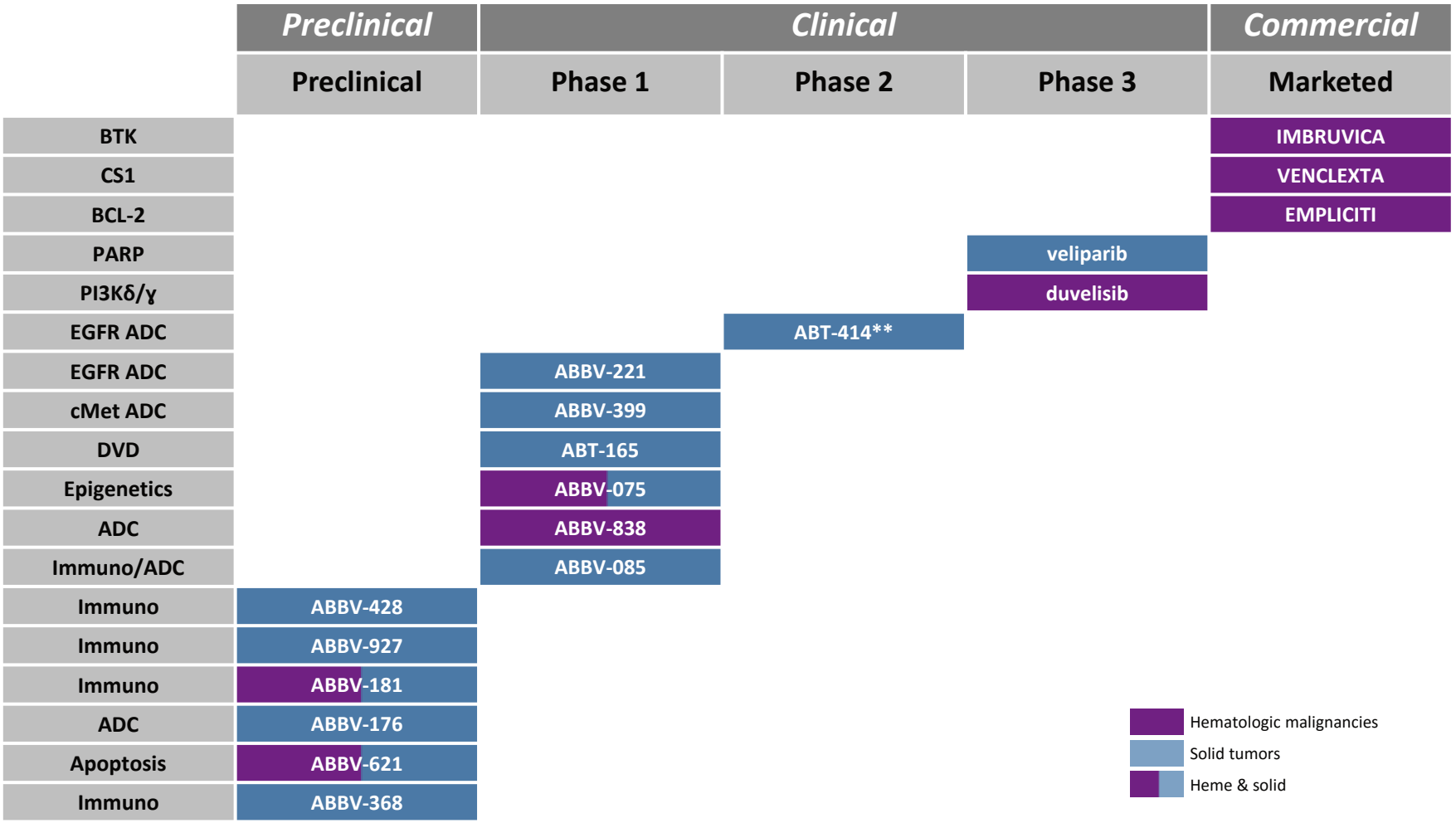
Conditional activation of CD40 by bispecific leads to efficacy

Bispecific avoids toxicity of systemic CD40 agents

Program is on track for human studies in 2016

Our Efforts Have Produced a Strong Oncology Pipeline

AbbVie's Oncology Pipeline



** Registration-enabling studies

AbbVie Oncology Pipeline with Stemcentrx

	Preclinical	Clinical			Commercial
	Preclinical	Phase 1	Phase 2	Phase 3	Marketed
BTK					IMBRUVICA
CS1					VENCLEXTA
BCL-2					EMPLICITI
PARP				veliparib	
PI3Kδ/γ				duvelisib	
EGFR ADC			ABT-414**		
DLL-3 ADC			Rova-T**		
EGFR ADC		ABBV-221			
cMet ADC		ABBV-399			
DVD		ABT-165			
Epigenetics		ABBV-075			
ADC		ABBV-838			
Immuno/ADC		ABBV-085			
DLL-3 ADC		SC-002			
DPEP3 ADC		SC-003			
EFNA4 ADC		Anti-EFNA4-calicheamicin*			
PTK7 ADC		Anti-PTK7-auristatin*			
Immuno	ABBV-428				
Immuno	ABBV-927				
Immuno	ABBV-181				
ADC	ABBV-176				
Apoptosis	ABBV-621				
Immuno	ABBV-368				
ADC	IND-1				
ADC	IND-2				
ADC	IND-3				
ADC	IND-4				
ADC	IND-5				

Hematologic malignancies
Solid tumors
Heme & solid
Stemcentrx

* Partnered with Pfizer (PF06647263, PF06647020)
** Registration-enabling studies

abbvie

Stemcentrx

Brian Slingerland

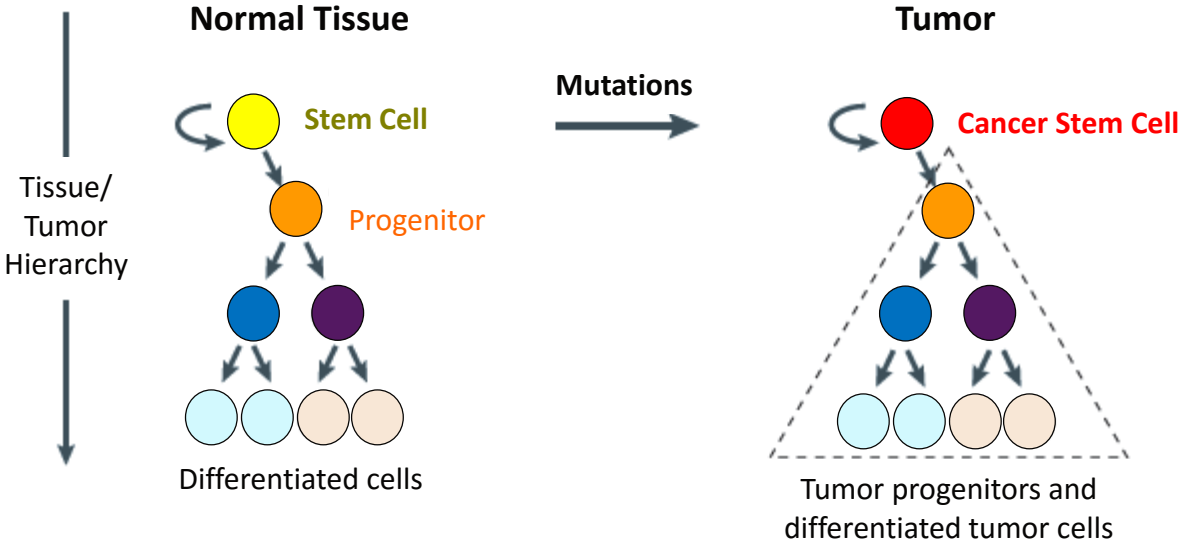
Scott Dylla, Ph.D.

Our Mission

Discover and Develop Cancer Therapies That Cure and Significantly Improve Survival

The Cancer Stem Cell (CSC) Paradigm

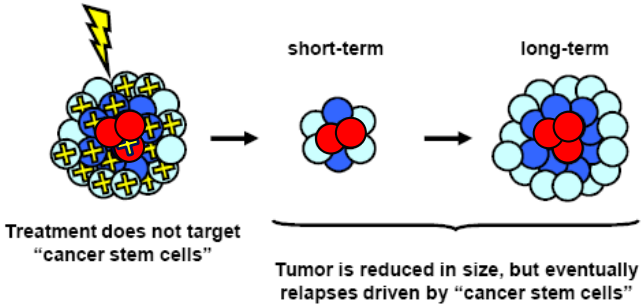
1. **Only stem cells accumulate compounding mutations**
2. **Only CSC are capable of fueling continued tumor growth**



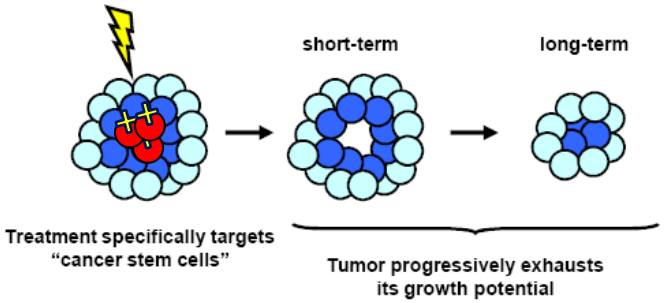
The Cancer Stem Cell (CSC) Paradigm

1. Only stem cells accumulate compounding mutations
2. Only CSC are capable of fueling continued tumor growth
3. **CSC are minimally impacted by current therapeutic regimens**

Traditional Approach



Stemcentrx



Stemcentrx®

- Founded in 2008 in South San Francisco, CA
- Core research platforms for novel target discovery
  - 706 patient-derived xenograft tumor bank across major cancer subtypes

Focus on Solid Tumor Disease Subtypes

Patient Tumor	PDX
Lung	154
Colorectal	131
Ovarian	88
Pancreatic	80
AML	47
Melanoma	47
Breast	39
Endometrial	25
Gastric	19
Bladder	19
Lymphoma	17
Kidney	13
Liver (HCC)	11
Other Solid Tumors	16
	706

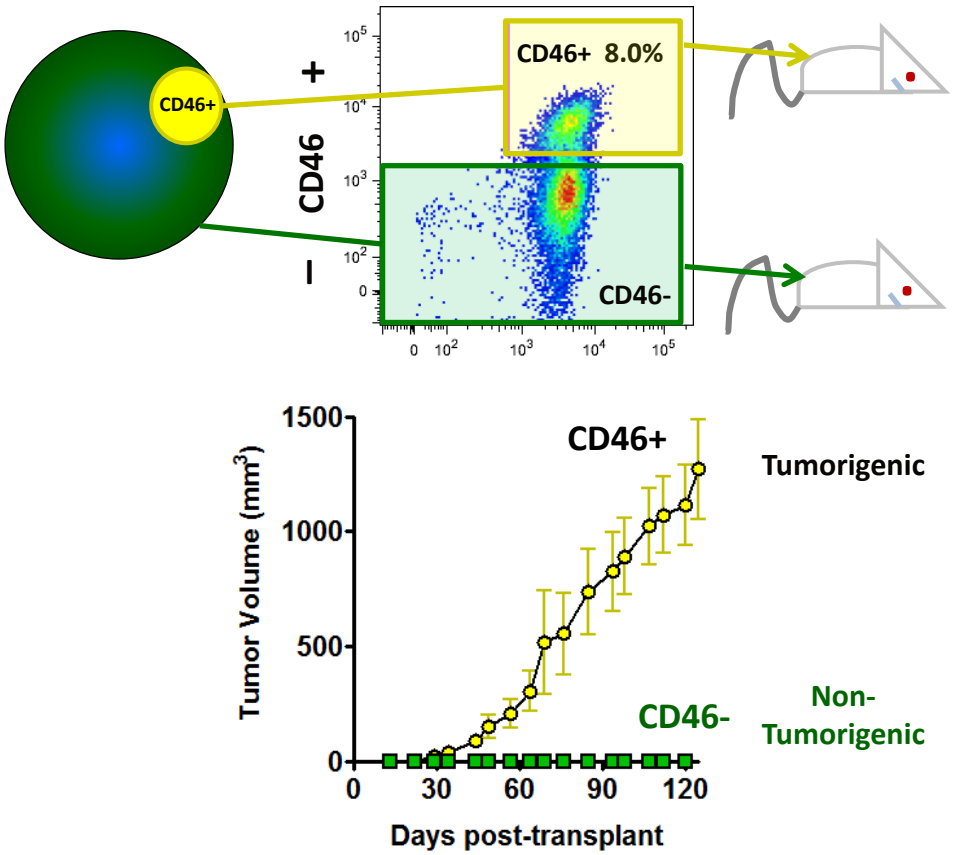
- Small Cell Lung Cancer (SCLC)
- NSCLC Adenocarcinoma subtypes (3)
- NSCLC Squamous cell subtypes (2)
- NSCLC Large Cell Neuroendocrine
- Carcinoids (typical, atypical)

- Serous
- Papillary Serous
- Endometroid
- MMMT
- Clear Cell
- Mucinous
- Neuroendocrine

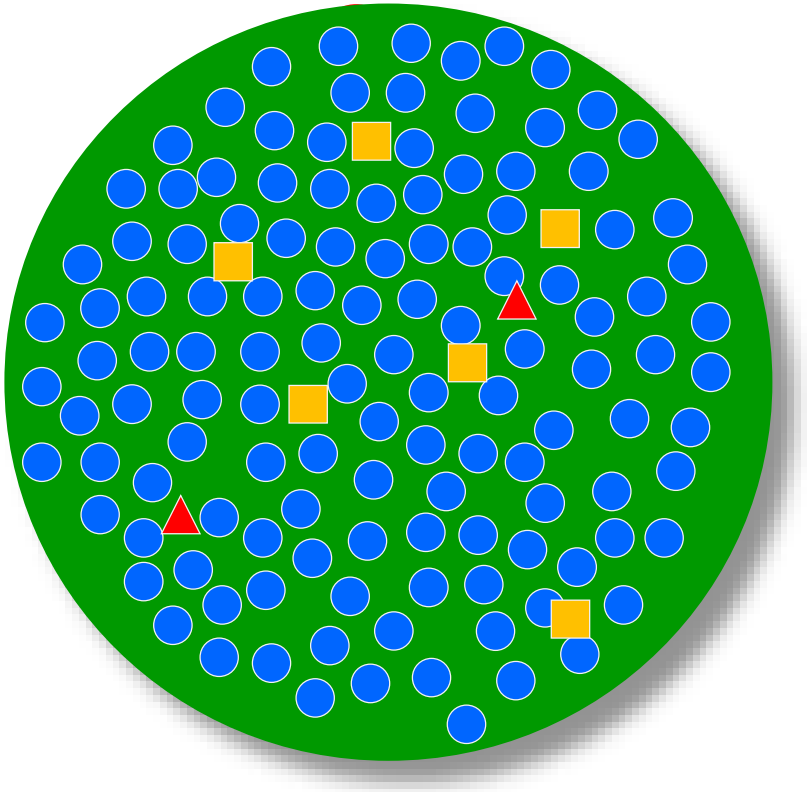
- Triple Negative (non-claudin low)
- Triple Negative (claudin low)
- Luminal B
- Luminal A
- Her2+

PDX Are used to Identify Tumorigenic Subpopulations

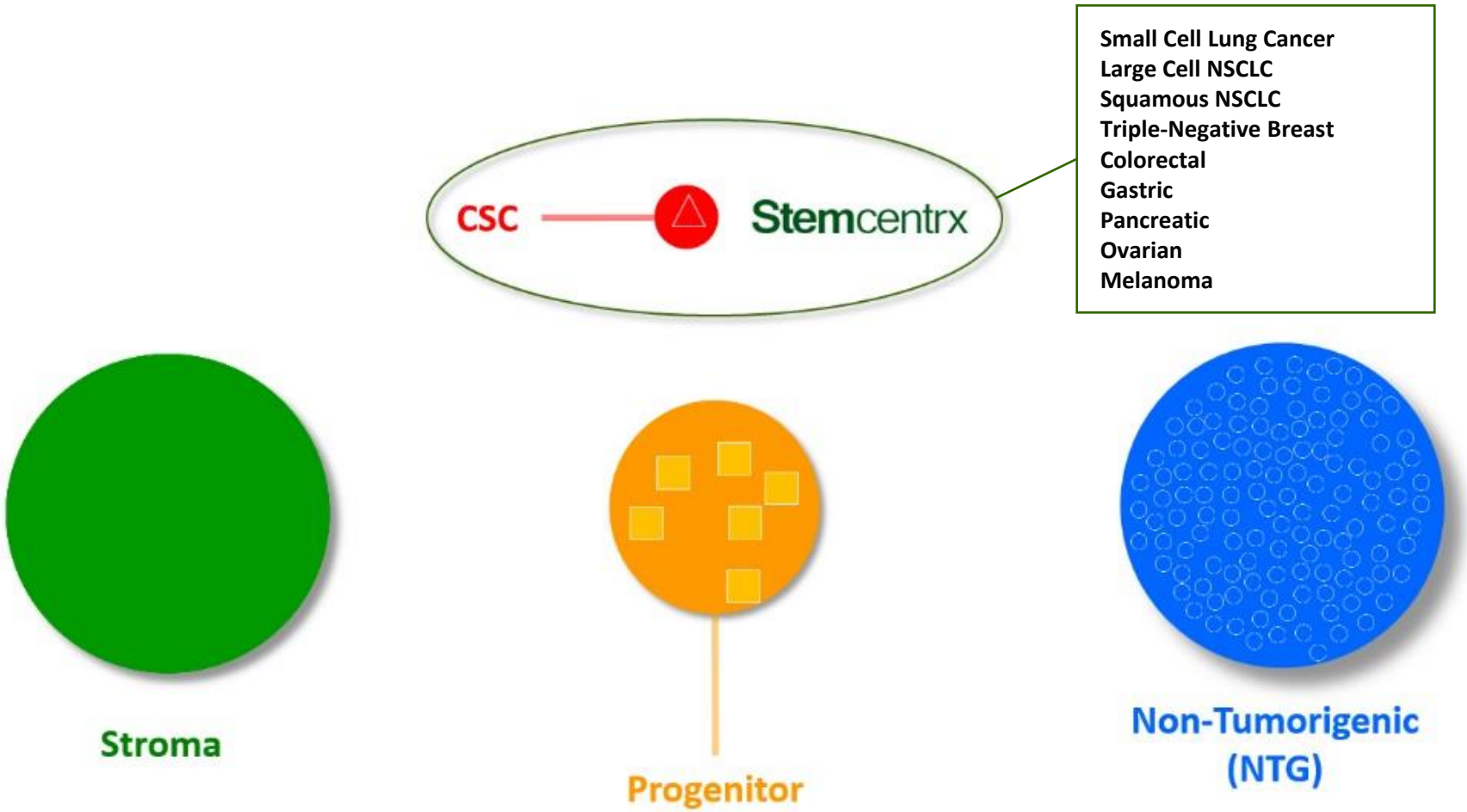
Patient Tumor	PDX
Lung	154
Colorectal	131
Ovarian	88
Pancreatic	80
AML	47
Melanoma	47
Breast	39
Endometrial	25
Gastric	19
Bladder	19
Lymphoma	17
Kidney	13
Liver (HCC)	11
Head & Neck	5
Glioblastoma	3
Other	8
	706



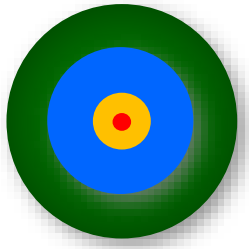
Stemcentrx Discovers Drug Targets Expressed on CSC



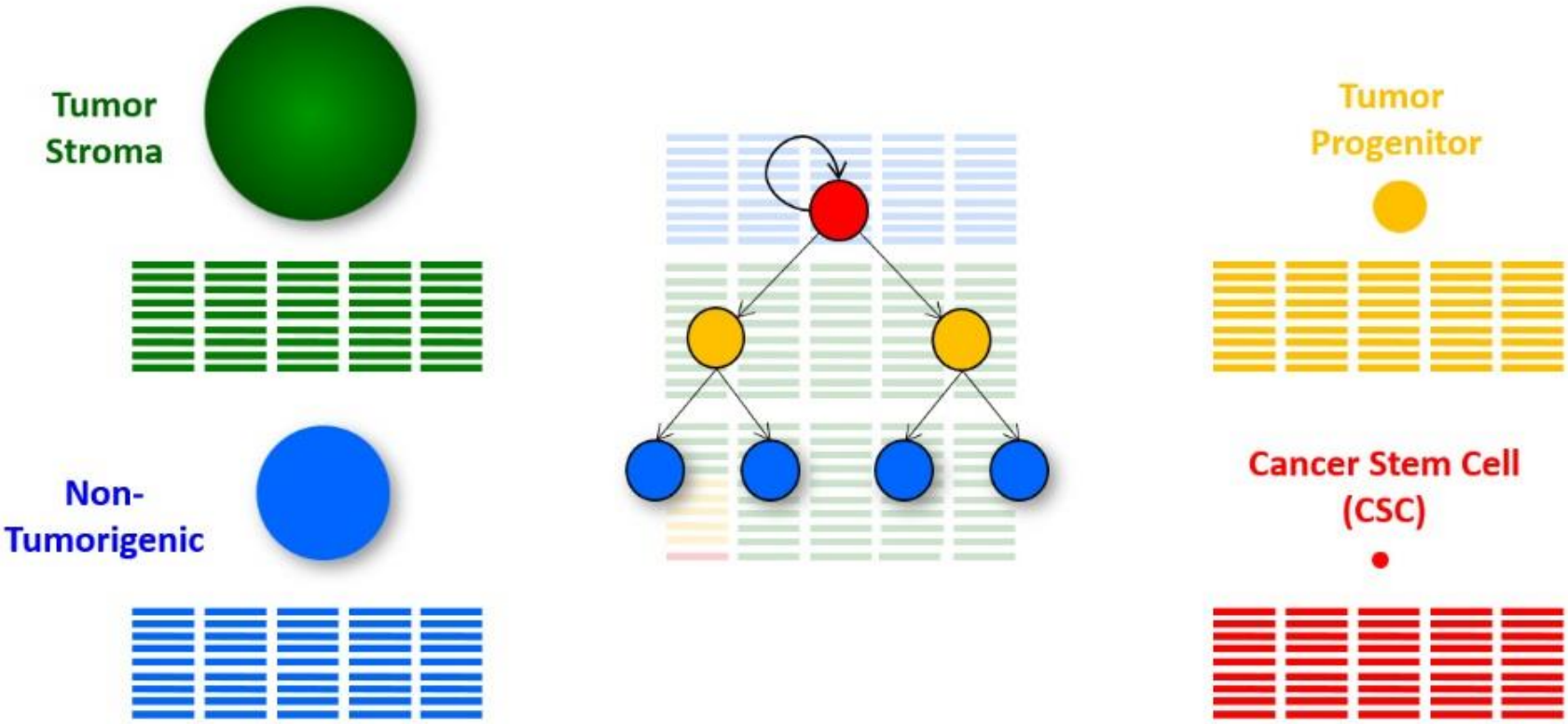
Stemcentrx Discovers Drug Targets Expressed on CSC



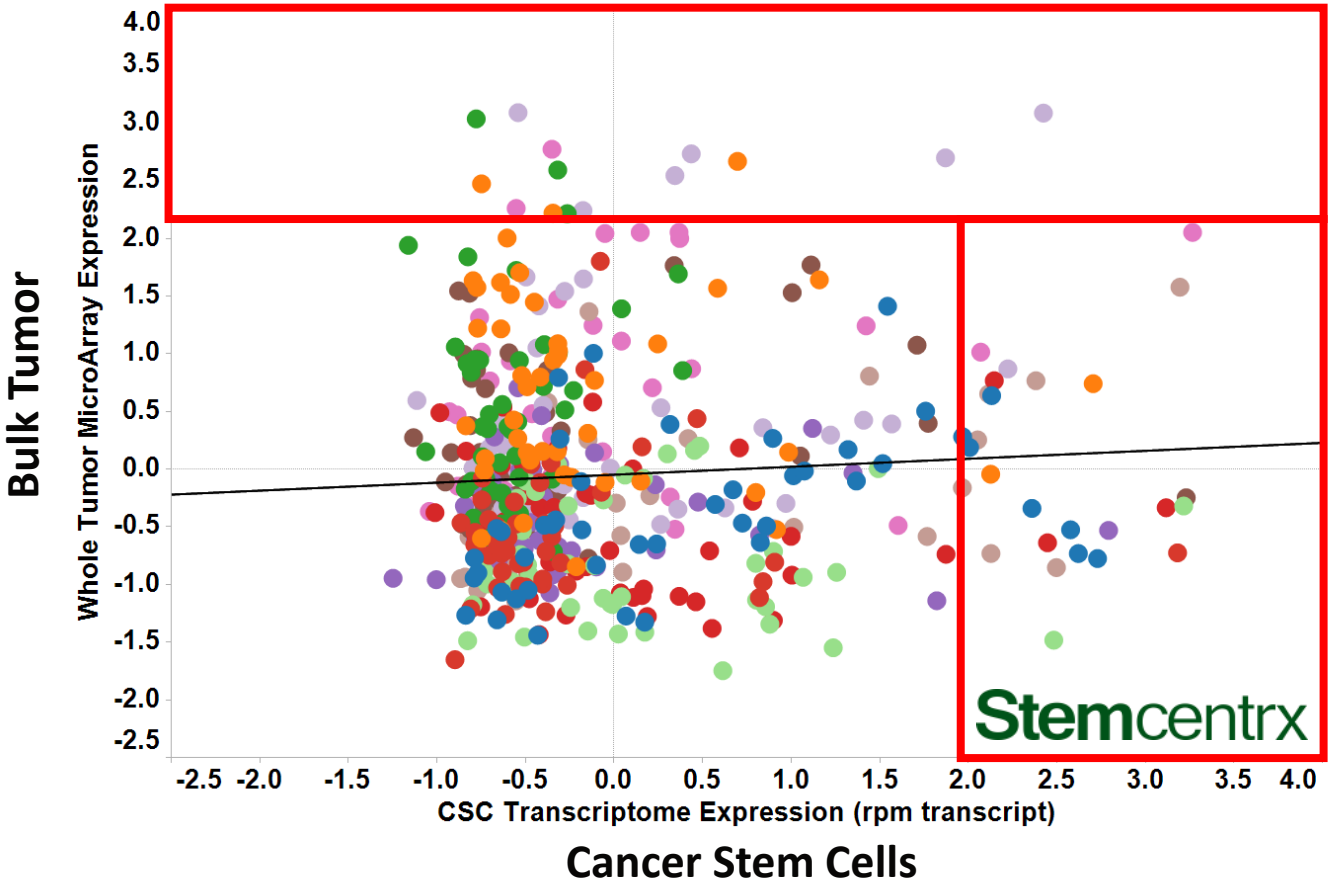
Leveraging CSC Identity to Find Targets



Leveraging CSC Identity to Find Targets



Stemcentrx Targets Have Often Been Overlooked

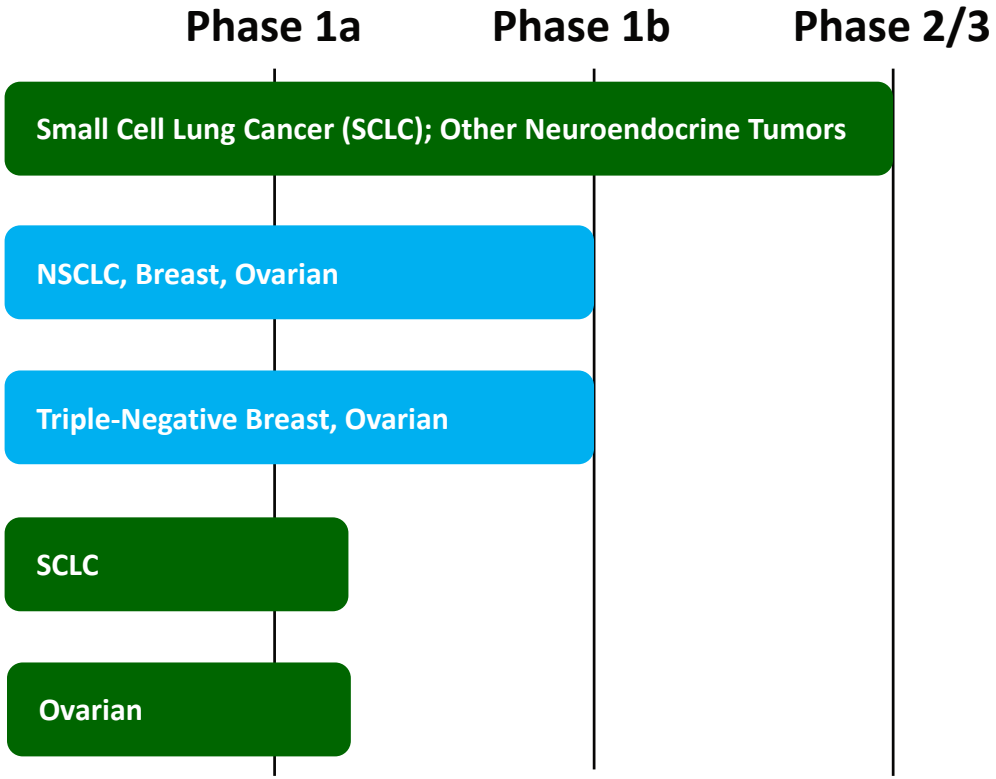


Stemcentrx®

- Founded in 2008 in South San Francisco, CA
- Core research platforms for novel target discovery
  - 706 patient-derived xenograft tumor bank across major cancer subtypes
  - Proteomic and genetic platforms for cancer stem cell and target identification
  - Bioinformatics software and IT tools for target discovery and validation
- Fully integrated company with 180+ employees
  - 110+ in target/biomarker discovery and validation
  - GMP antibody, chemistry and ADC manufacturing on-site (+ process sciences, QC, QA, regulatory)
  - 5 drugs targeting novel antigens in clinical trials (SCLC, Triple-Negative Breast, Ovarian, NSCLC)
  - Pipeline of CSC-associated targets in NSCLC, pancreatic, colorectal, gastric, melanoma, AML

Stemcentrx Drugs in Human Clinical Trials

1. **DLL3-PBD ADC**
   Rovalpituzumab Tesirine (Rova-T™)
2. **PTK7-Auristatin ADC**
   (PF-06647020)
3. **EFNA4-Calicheamicin ADC**
   (PF-06647263)
4. **SC-002 (Undisclosed Target)**
5. **SC-003 (Undisclosed Target)**



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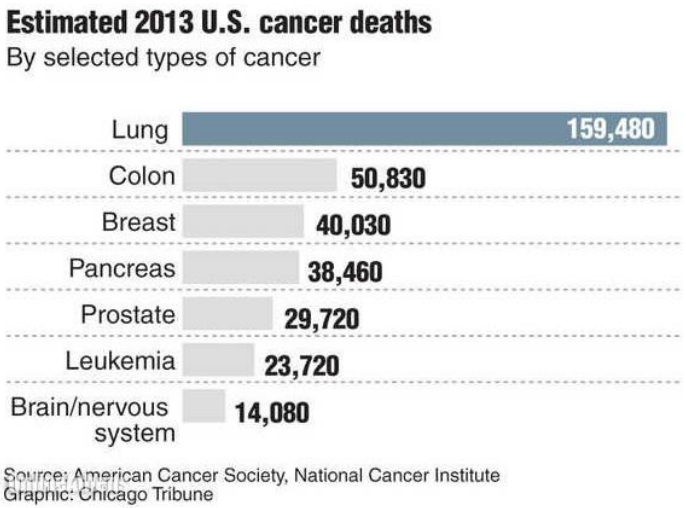
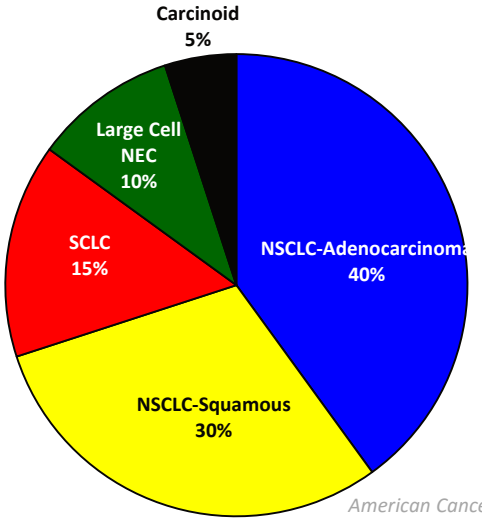
Rovalpituzumab Tesirine (Rova-T™) Targeting DLL3

SCLC & Other Neuroendocrine Cancers

Lung Cancer Statistics

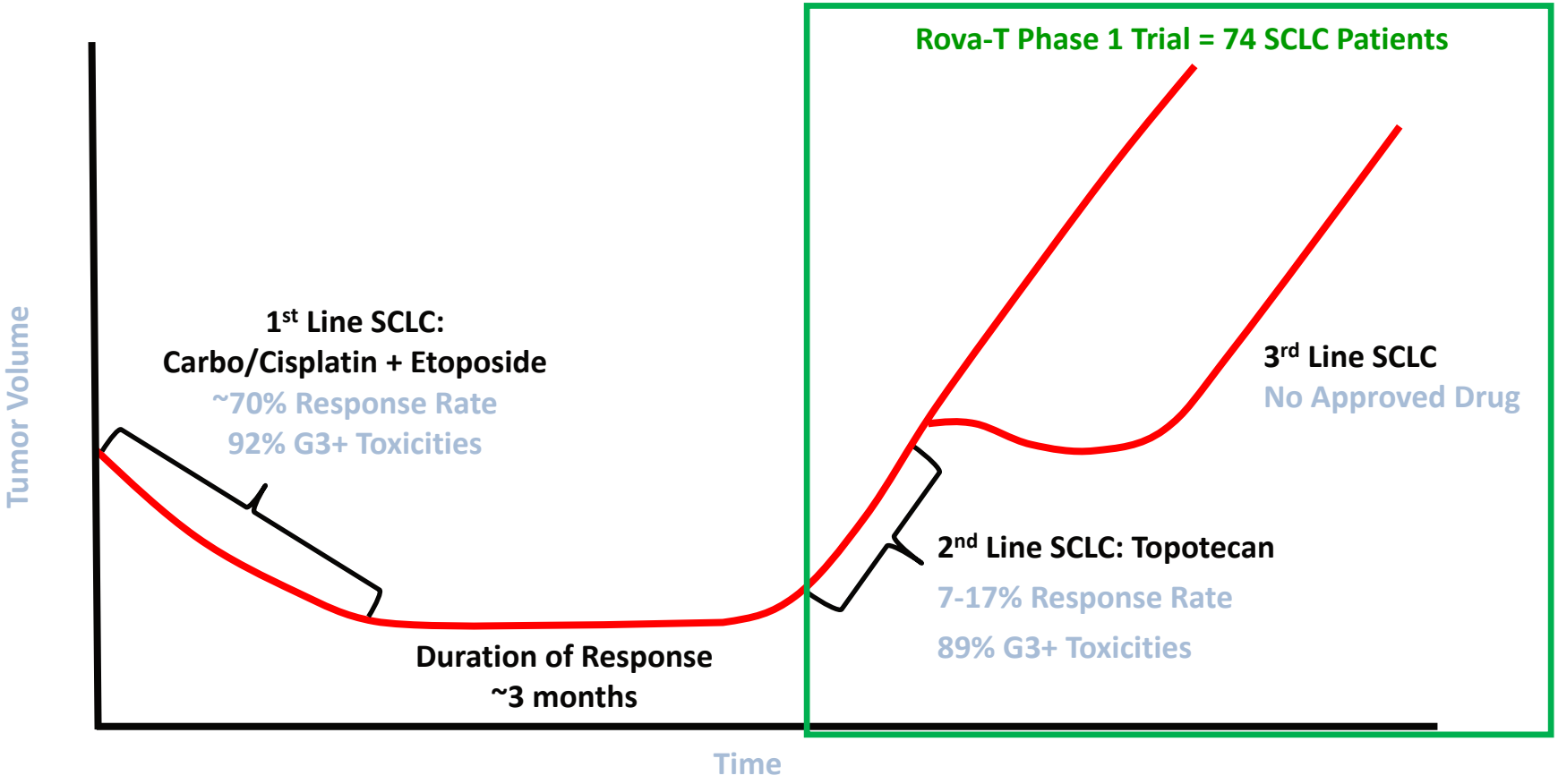




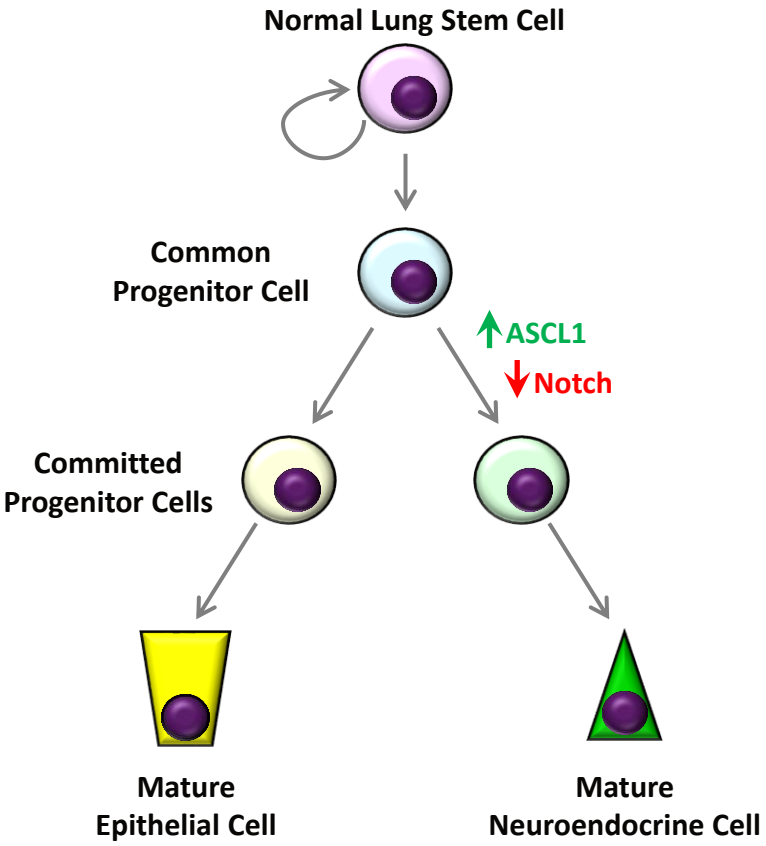
American Cancer Society

	All Lung Cancer	SCLC
Newly Diagnosed – US, EU, Japan	540,000	81,000
Newly Diagnosed – Worldwide	1,825,000	274,000
5-Year Survival	18%	3%

Small Cell Lung Cancer



ASCL1 and Notch Inhibition Promote Neuroendocrine Cell Fates

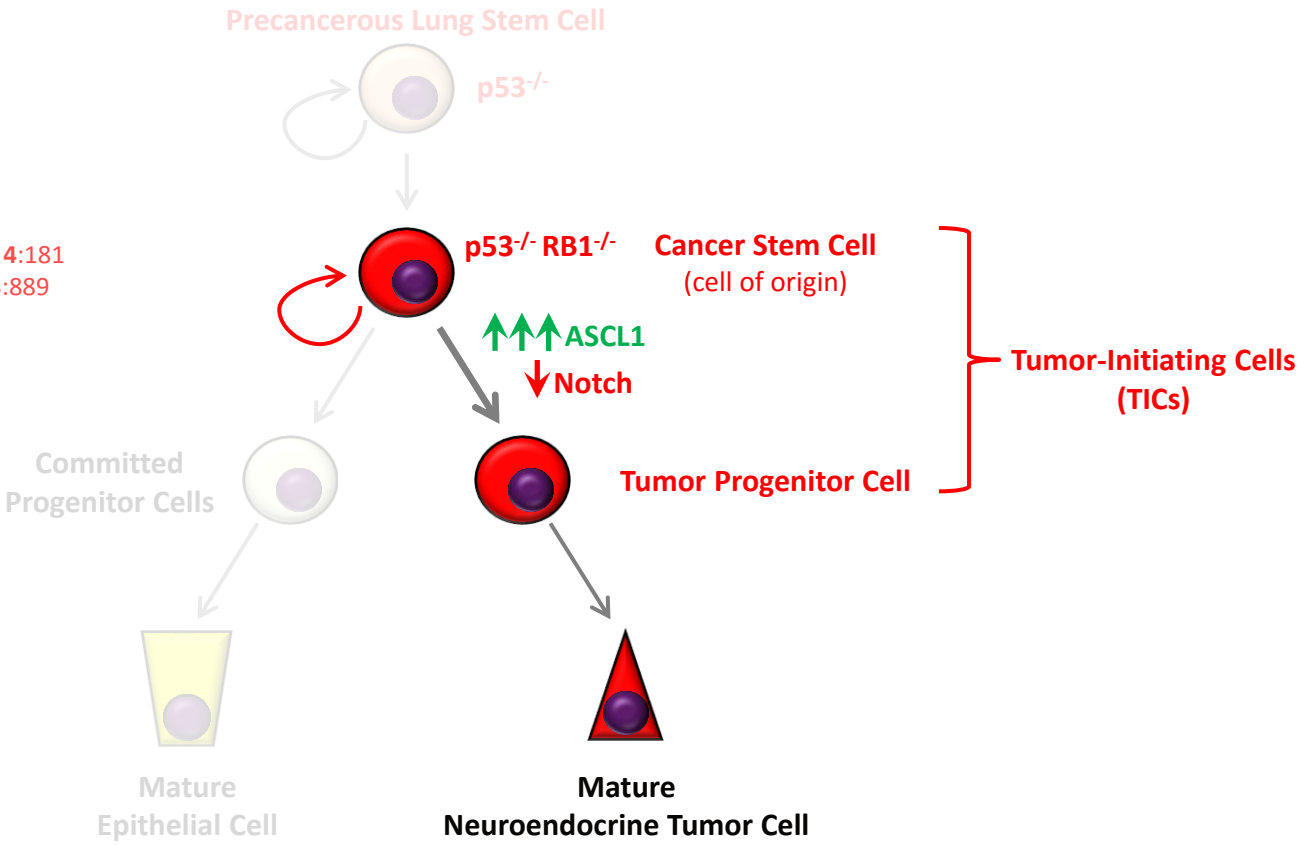


Borges (1997) *Nature* **386**:852
Li (2012) *Am J. Respir Cell Mol Biol* **47**:768

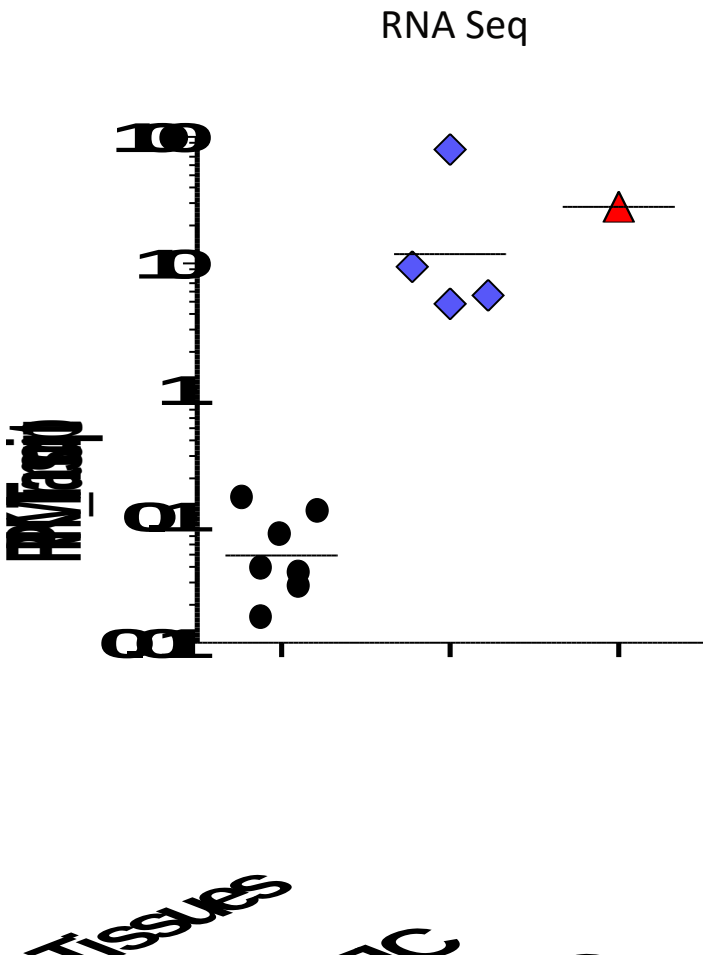
Kunnimalaiyaan (2007) *Oncologist* **12**:535
Morimoto (2012) *Development* **139**:4365

RB1 Mutations in the Lung Induce Neuroendocrine Tumors

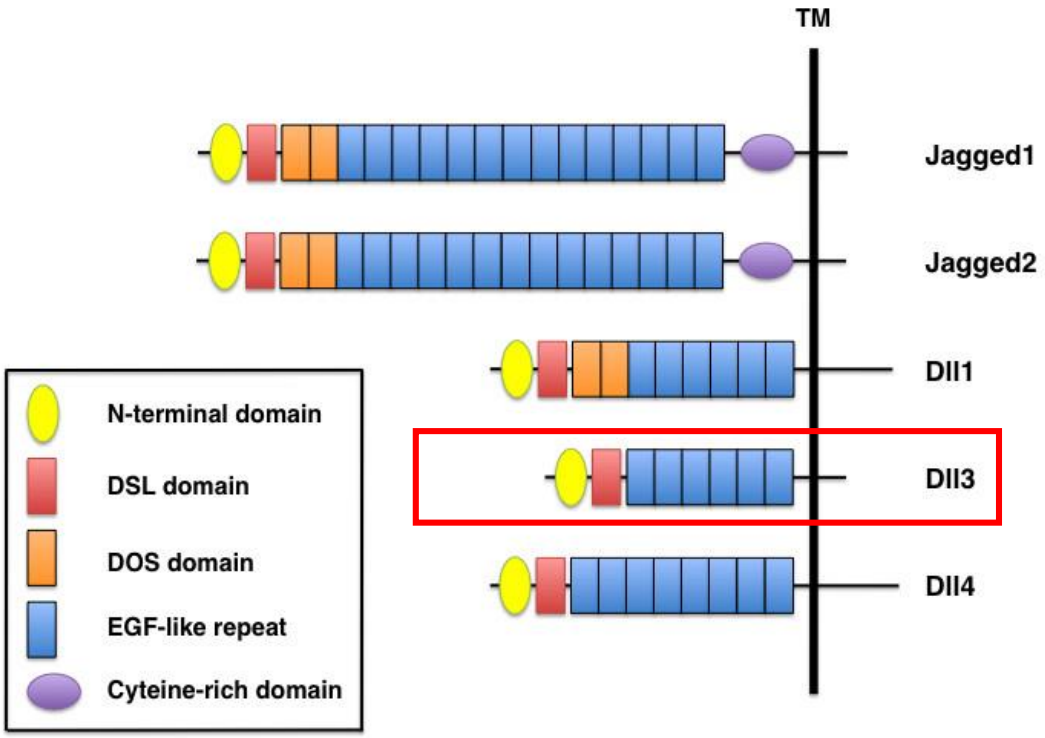
Meuwissen (2003) *Cancer Cell* **4**:181
Moreira (2010) *Mod Pathol* **23**:889



Delta-Like Protein 3 (DLL3) Is Overexpressed in High Grade Pulmonary Neuroendocrine Tumor-Initiating Cells



DLL3 Is a Dominant Inhibitor of Notch Signaling

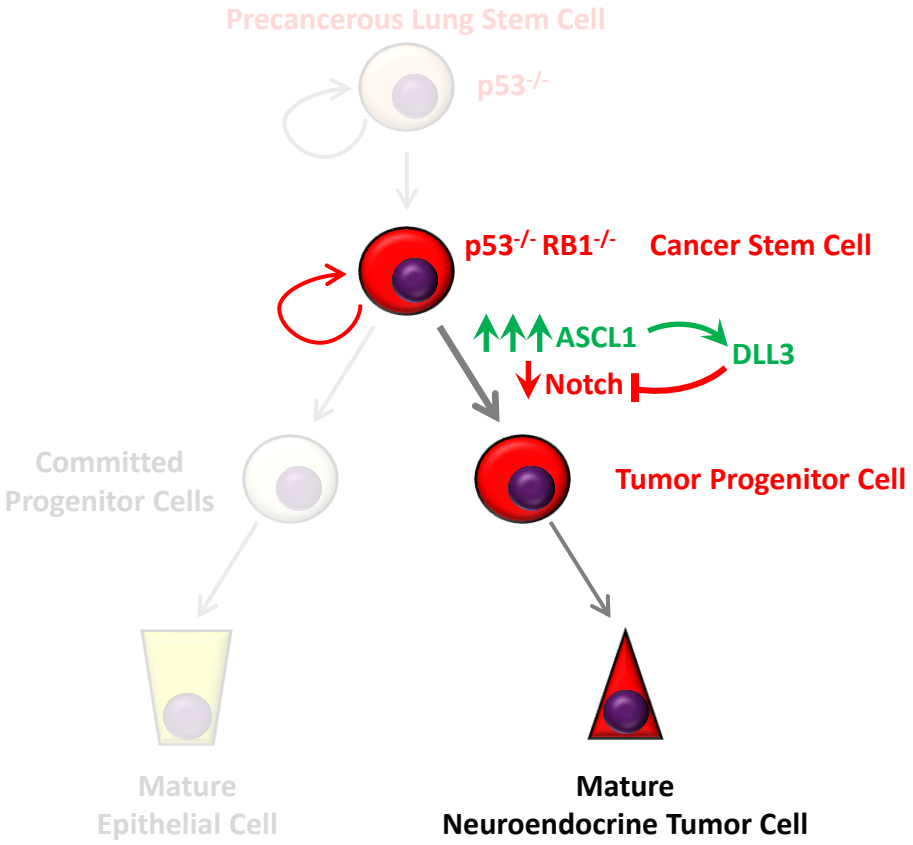


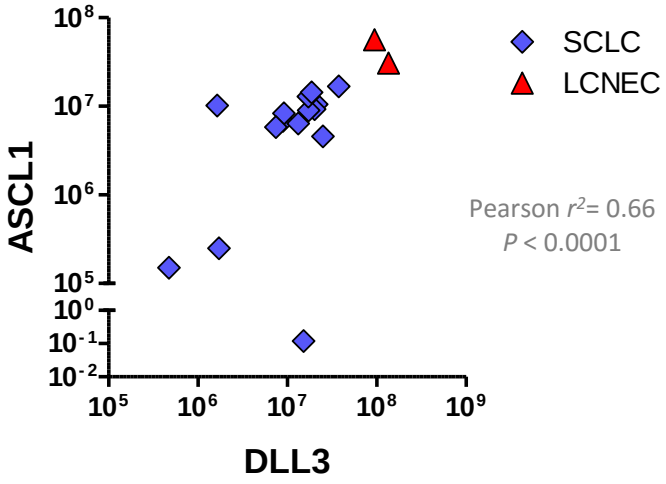
Kume T. (2009) *Journal of Angiogenesis Research* **1**:8

- Normally expressed during development and localized to Golgi intracellular compartment
- Interacts with and inhibits Notch1 localization to the cell surface
- Mediates DLL1 intracellular retention in concert with LFNG, inhibiting Notch activation in trans

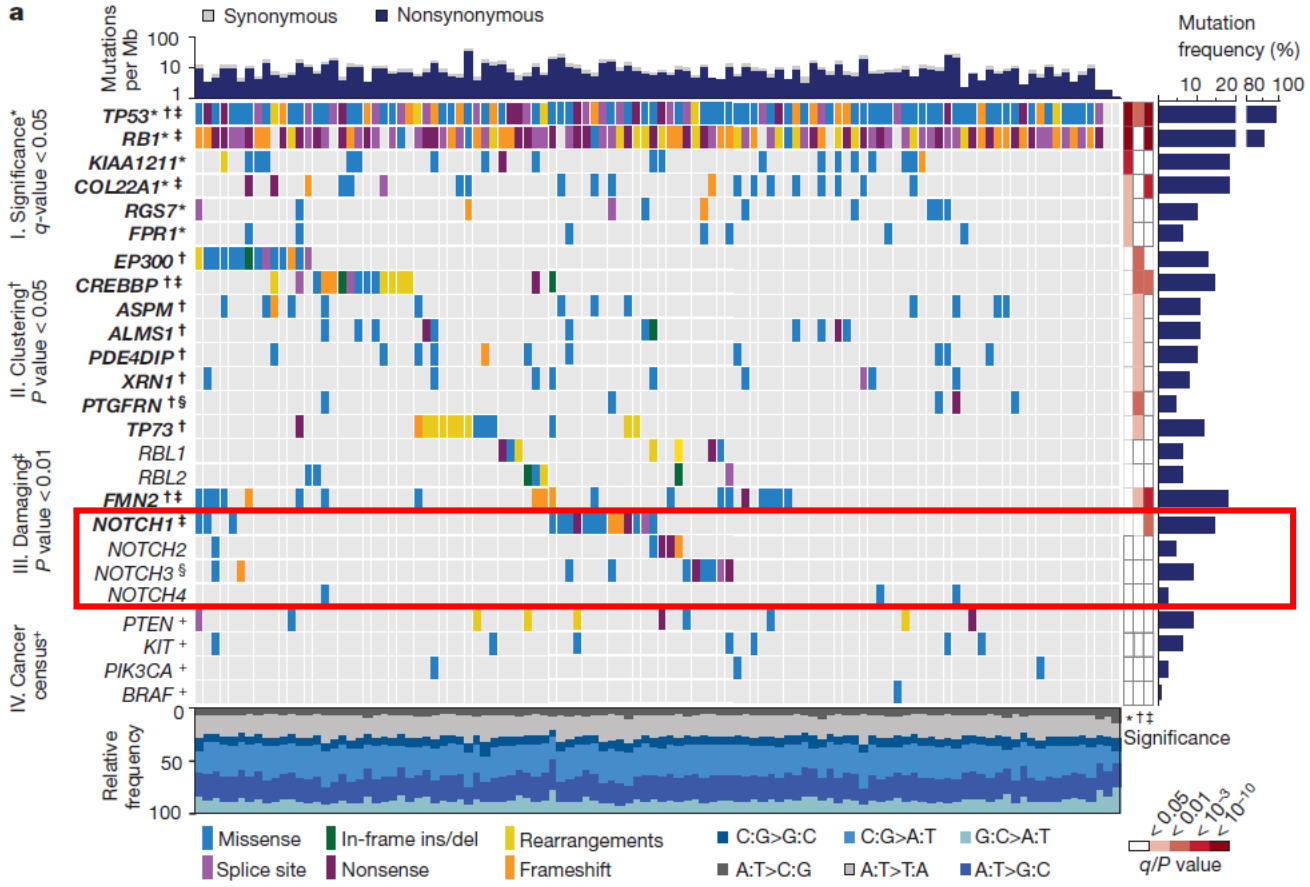
Geffers *et al*. (2007) *J Cell Biol* **178**:465.
Chapman *et al.* (2011) *Human Mol Genetics* **20**:905.
Serth *et al.* (2015) *PLoS ONE* **10**:e0123776.

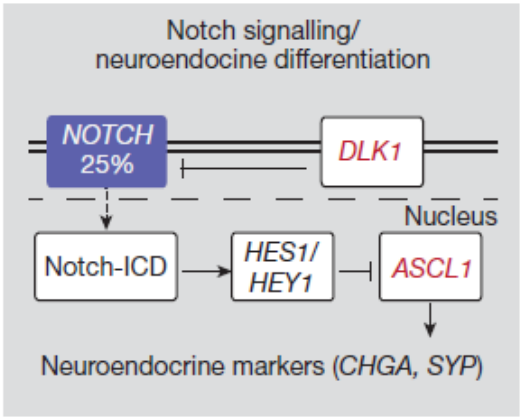
DLL3 Elevations May Drive Neuroendocrine Tumorigenesis





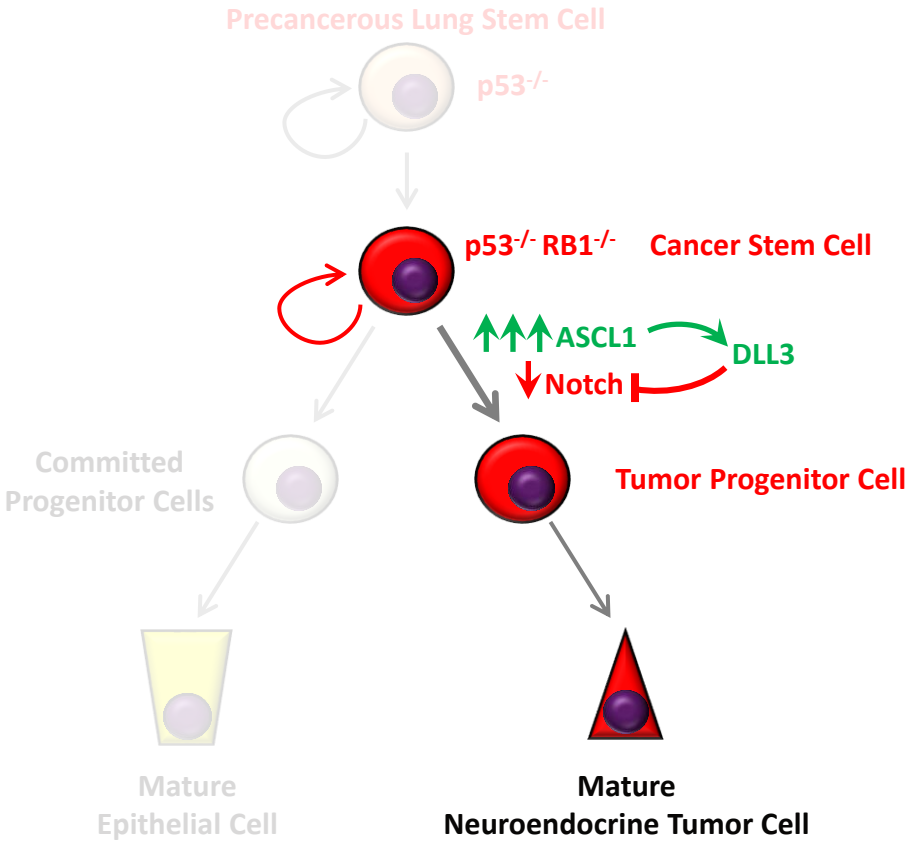
Notch Receptor Mutations May Contribute to Tumorigenesis in a Subset of SCLC

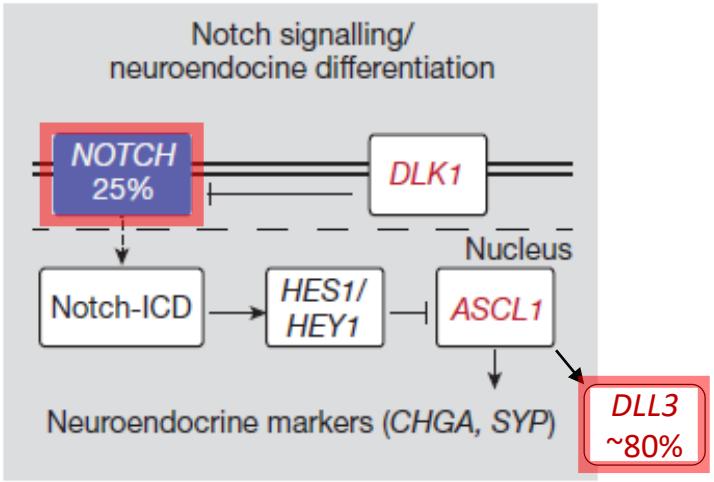




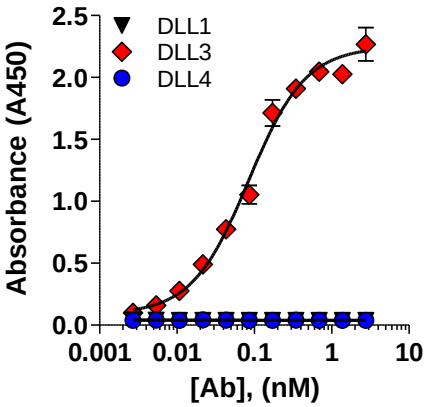
George J. *et al.* (2015) *Nature* **524**:47-53.

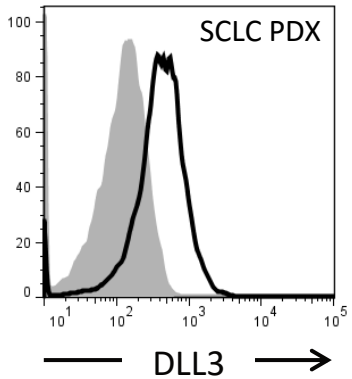
DLL3 Elevations May Drive Neuroendocrine Tumorigenesis

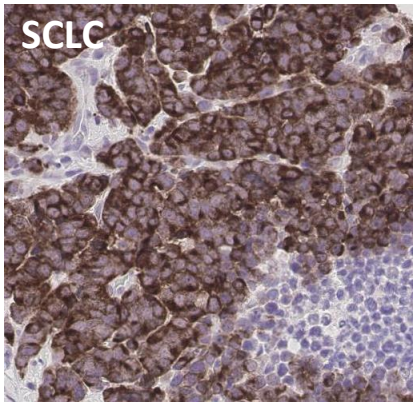


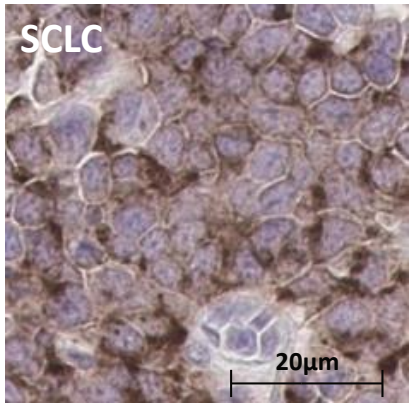


DLL3 Is on the Surface of SCLC Tumor Cells

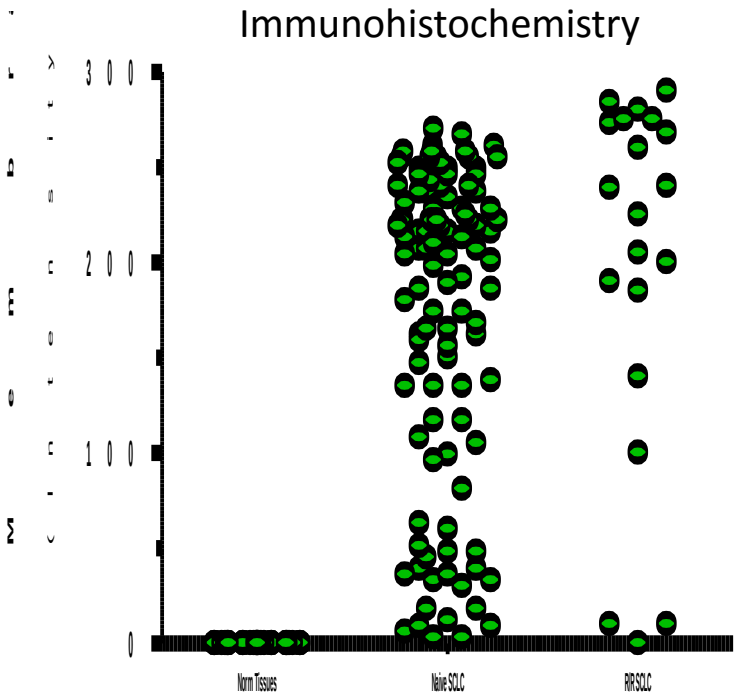








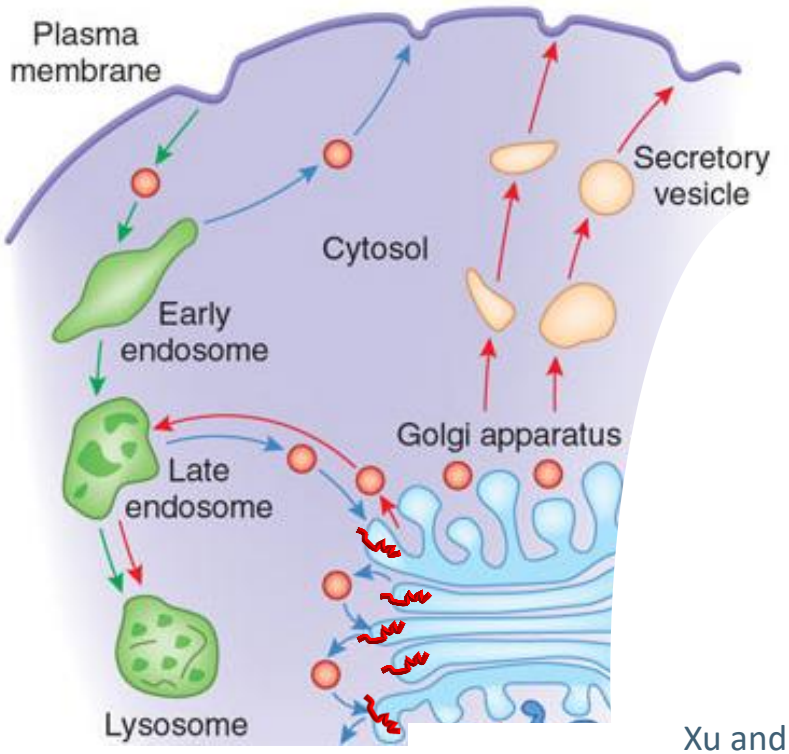
Saunders *et al.* (2015) *Sci Transl Med* 302ra136.



Courtesy of Pierre Massion (Vanderbilt)

Courtesy of Afshin Dowlati (Case Western U.)

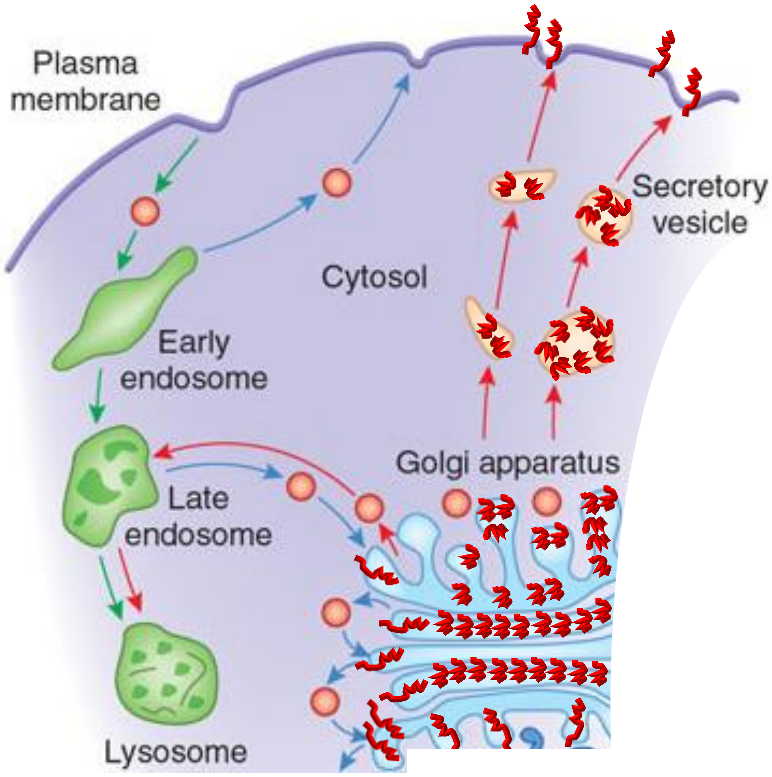
DLL3 Is Normally Retained in the Golgi



= DLL3

Xu and Esko, *Nat Chem Biol* 2009

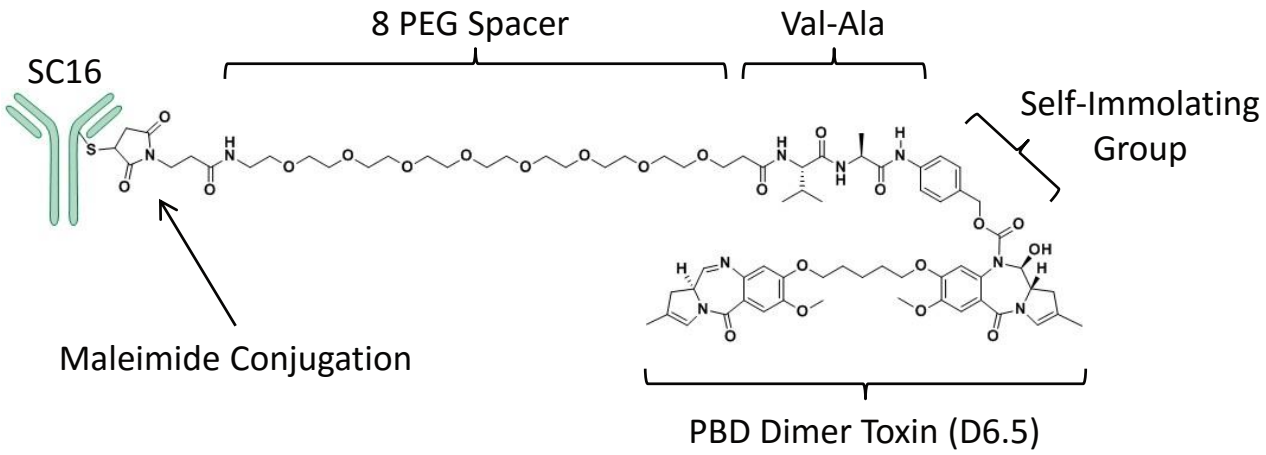
DLL3 Reaches the Cell Surface When Overexpressed in SCLC



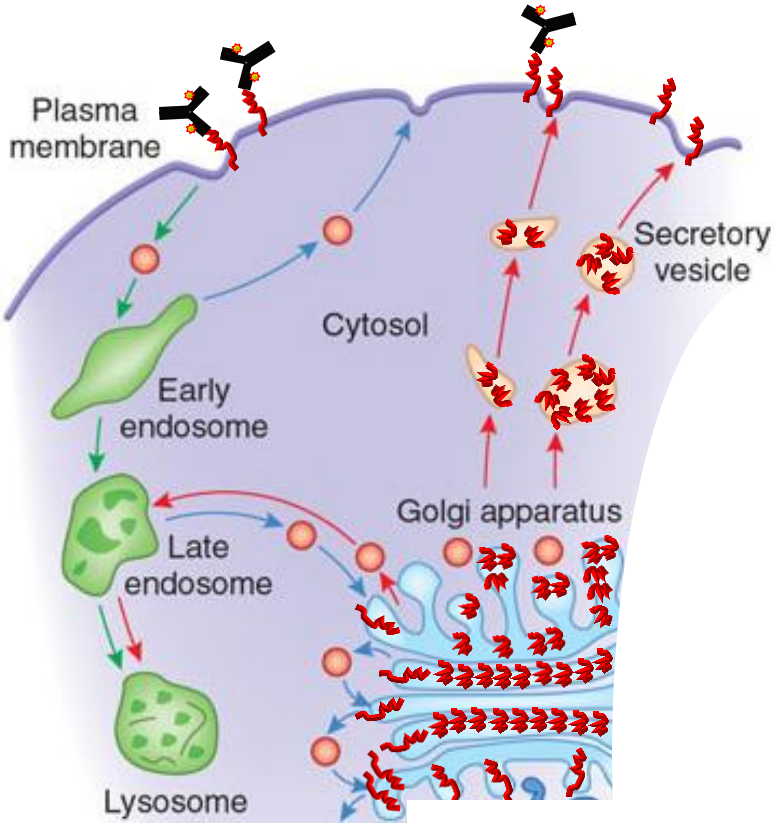
= DLL3

Rovalpituzumab Tesirine (Rova-T™; SC16LD6.5)

Drug-to-Antibody Ratio (DAR) = 2



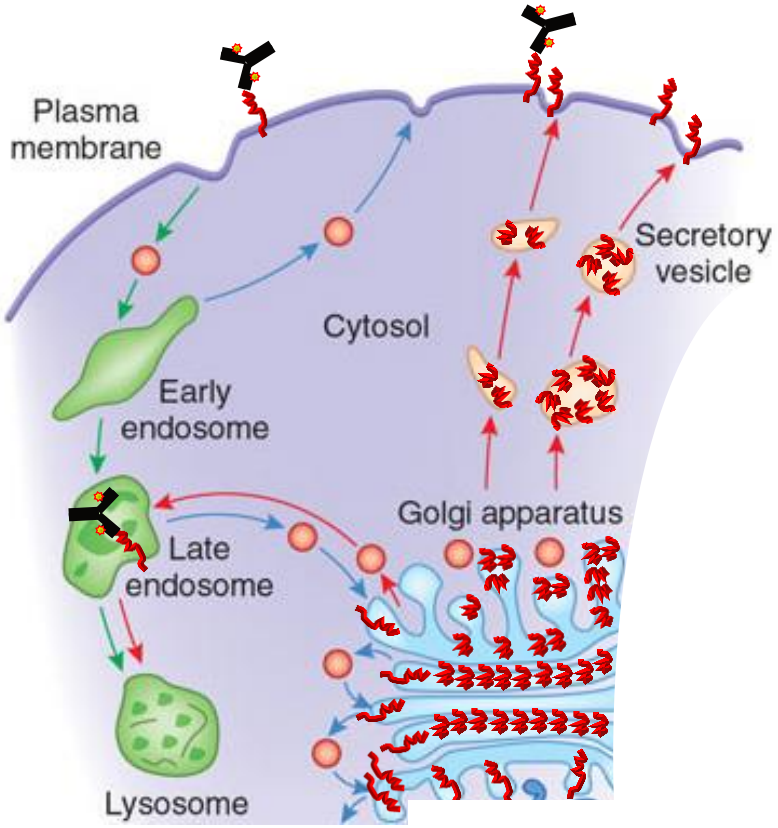
Rova-T Leverages Surface DLL3 to Deliver PBD Toxin



= DLL3

Rova-T (SC16LD6.5)

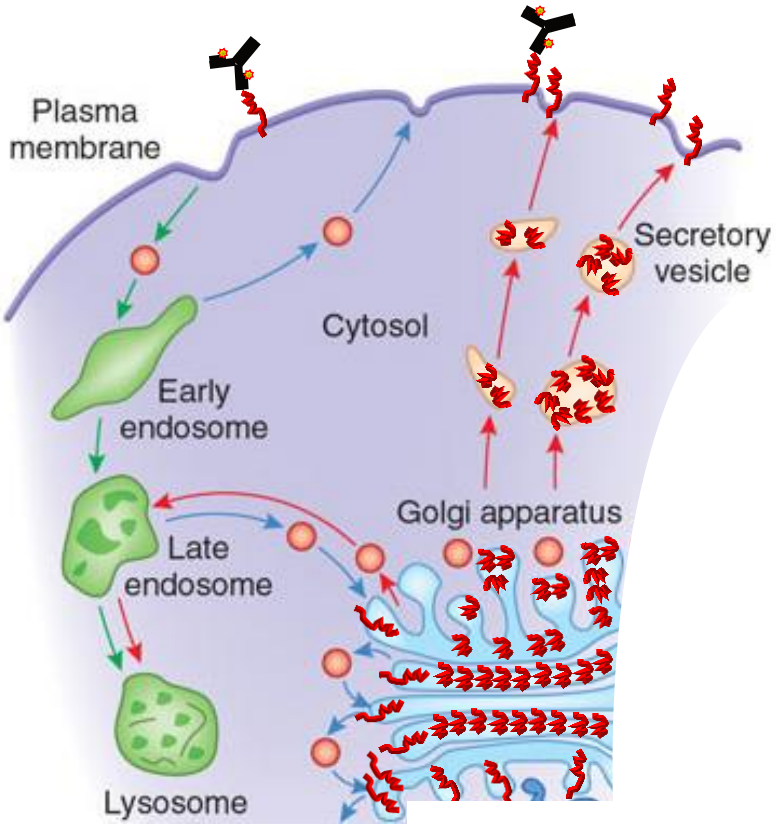
Rova-T Leverages Surface DLL3 to Deliver PBD Toxin



= DLL3

Rova-T (SC16LD6.5)

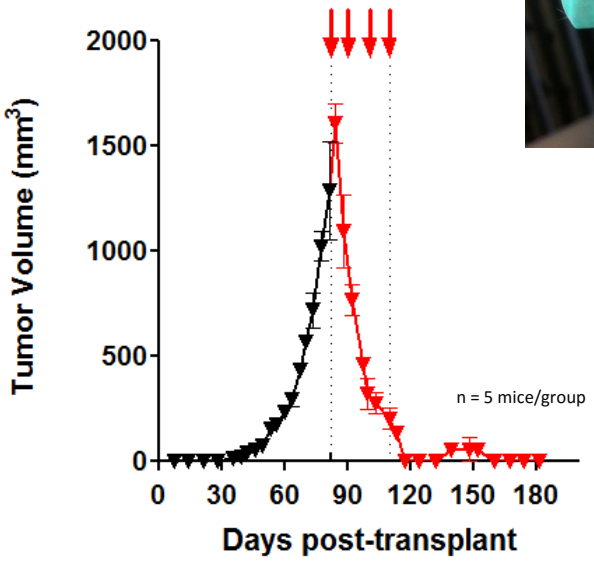
PBD Dimer Toxin Mediates Tumor Cell Killing

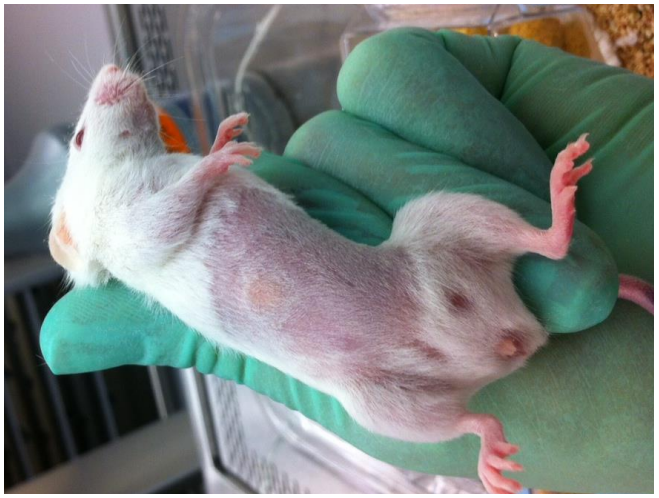


= DLL3

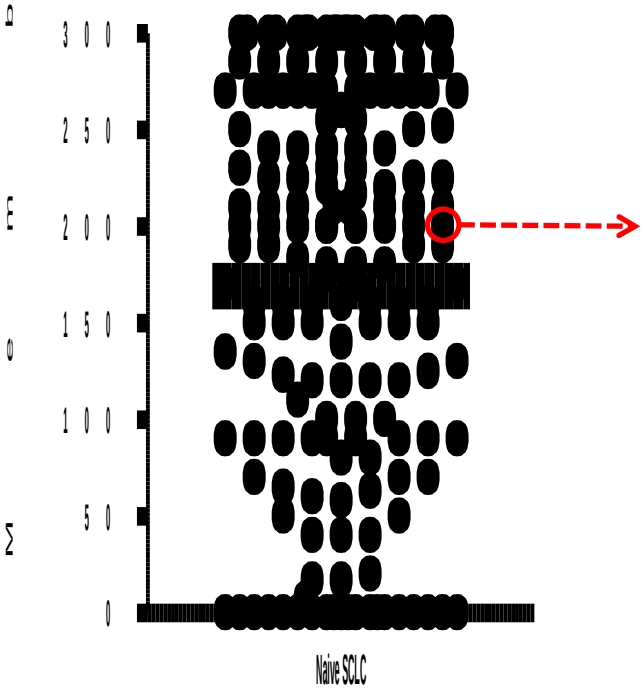
Rova-T (SC16LD6.5)

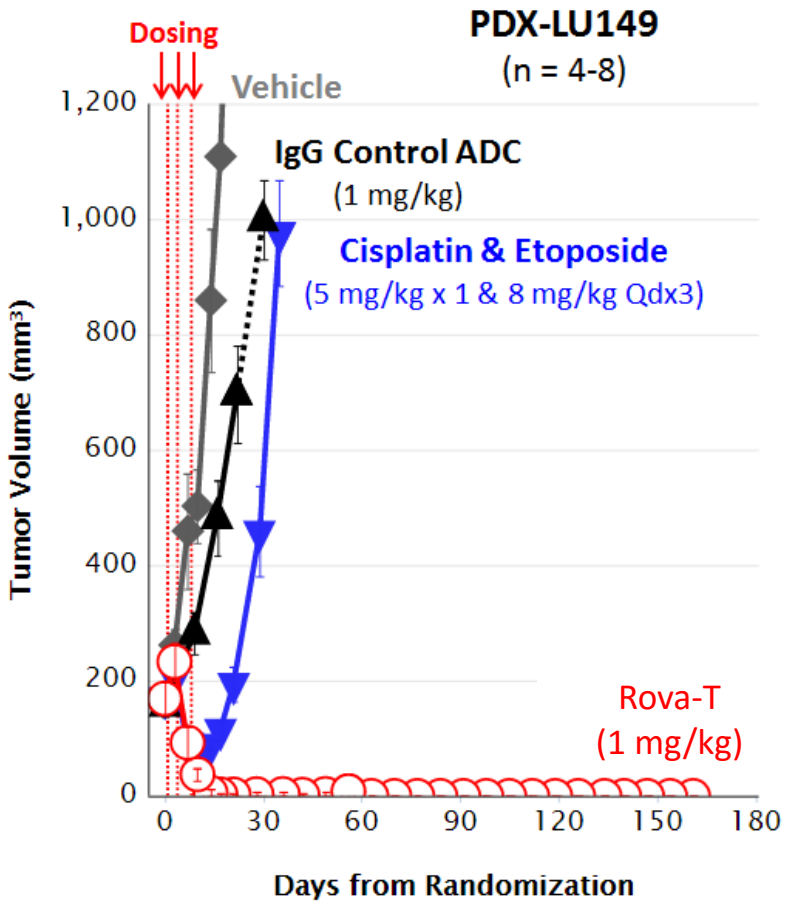
Stemcentrx ADCs Eliminate Large Solid PDX Tumors



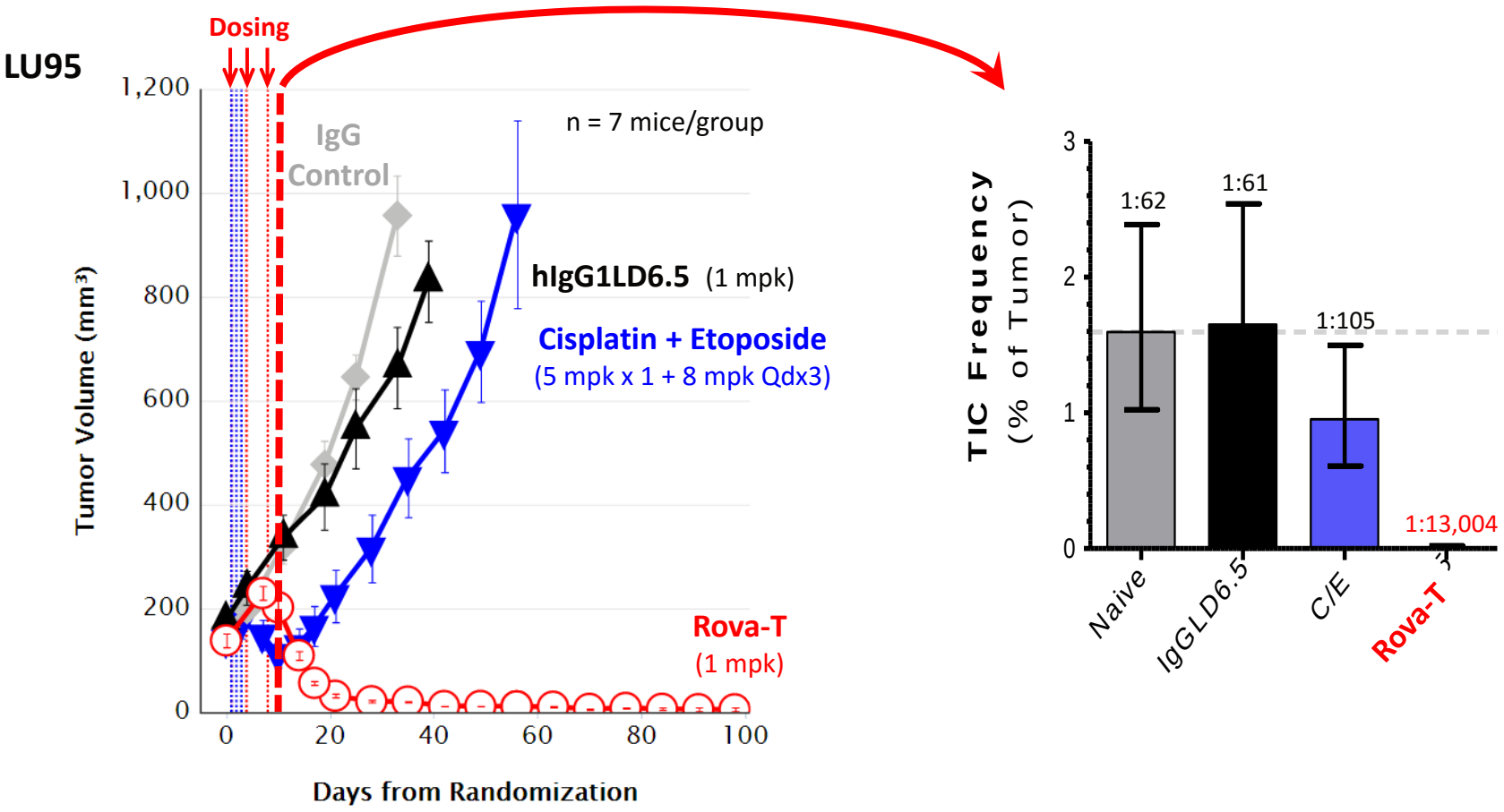


Rova-T Is Efficacious in DLL3+ SCLC PDX Tumors



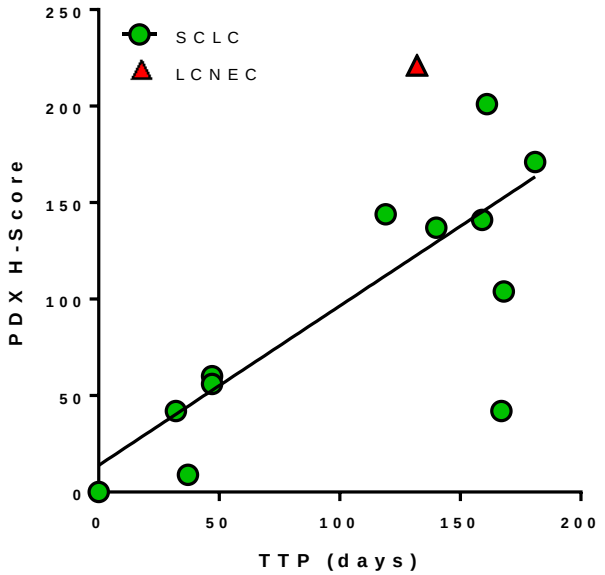


Rova-T Eliminates Tumor-Initiating Cells; Chemo Does Not



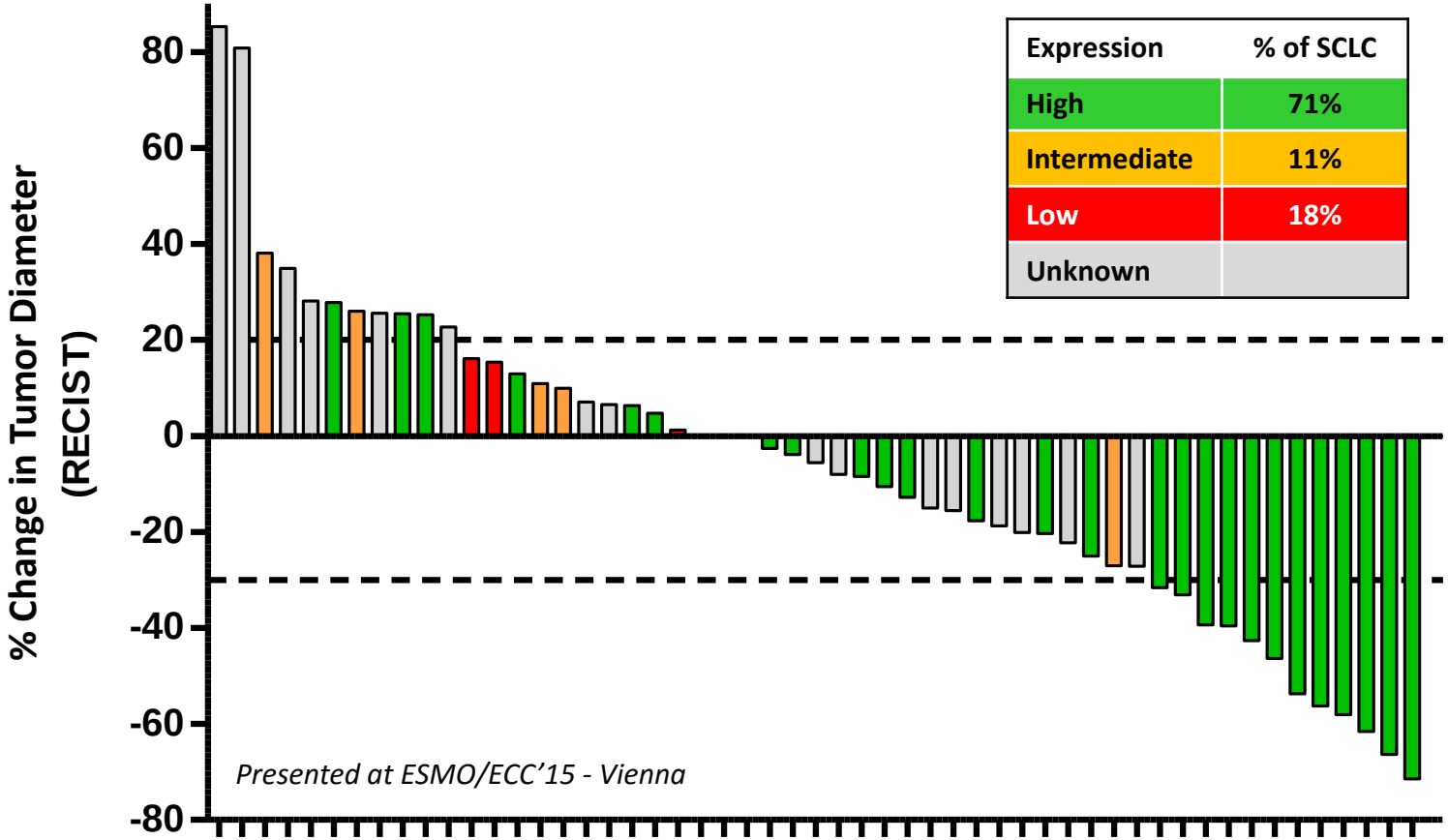
Rova-T vs. SOC in SCLC & LCNEC PDX Tumors

	Cisplatin/Etoposide (5 mpk x 1, 8 mpk Qdx3)		Single Agent Rova-T (1 mpk q4d x 3)		DLL3 Expression
	%TGI	TTP (days)	%TGI	TTP (days)	IHC H-Score
LU102	97%	28	100%	> 181	171
LU95	56%	2	100%	> 168	104
LU117	98%	21	100%	> 167	42
LU149	90%	18	100%	> 161	201
LU129	87%	52	100%	> 159	141
LU111	84%	22	100%	> 140	137
LU37	60%	4	100%	> 132	221
LU64	78%	12	100%	> 119	144
LU124	83%	19	88%	47	60
LU73	85%	28	75%	47	56
LU80	75%	15	75%	37	9
LU86	26%	0	95%	32	42
LU100	100%	63	0%	0	0
Avg	**78%**	**22**	**87%**	**> 107**	

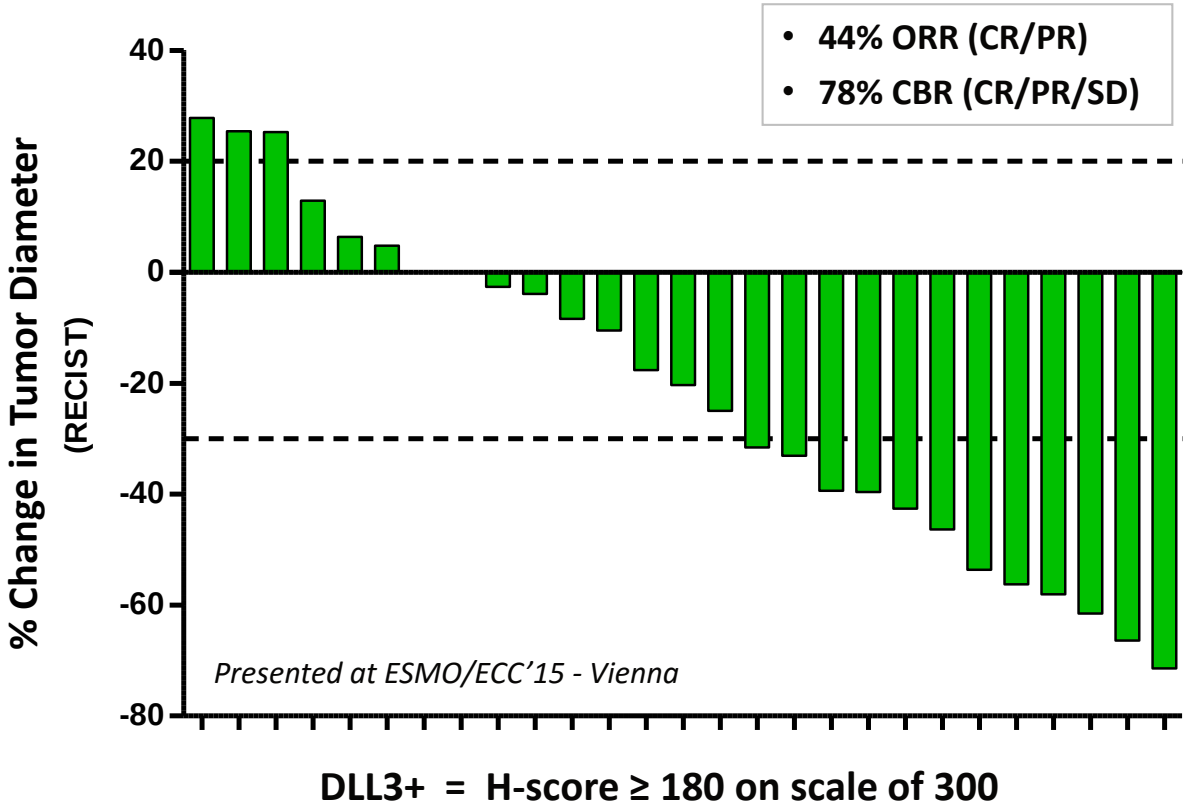


Number of XY Pairs	13
Pearson r	0.7296
95% confidence interval	0.2985 to 0.9134
P value (two-tailed)	0.0046
P value summary	**
Is the correlation significant? (alpha=0.05)	Yes
R square	0.5323

Rova-T: Best Response Data in Evaluable SCLC Patients 0.2 mg/kg q3w and 0.3 mg/kg q6w cohorts (n=53)

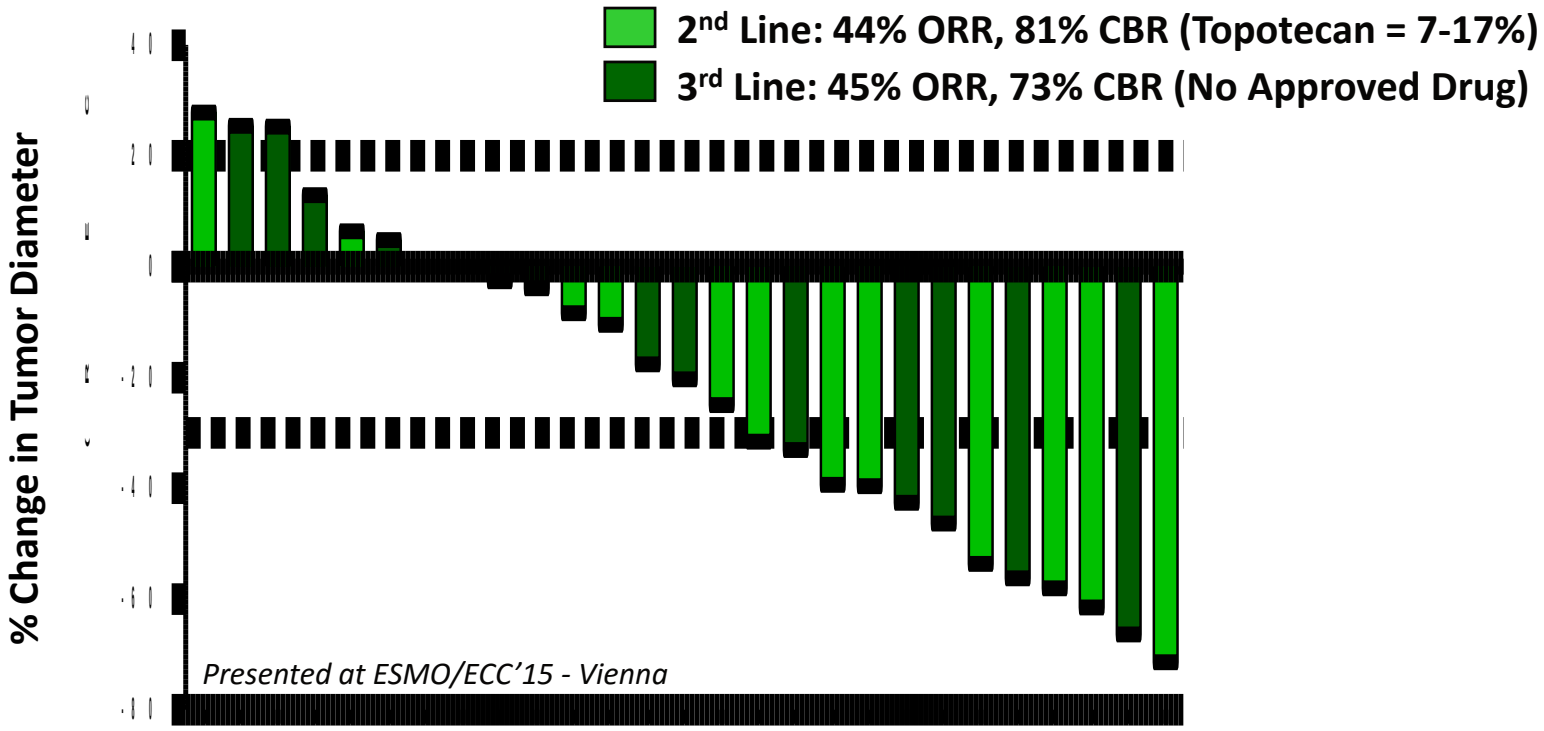


Rova-T: Best Response Data in Evaluable DLL3hi Patients 0.2 mg/kg q3w and 0.3 mg/kg q6w cohorts (n=27)



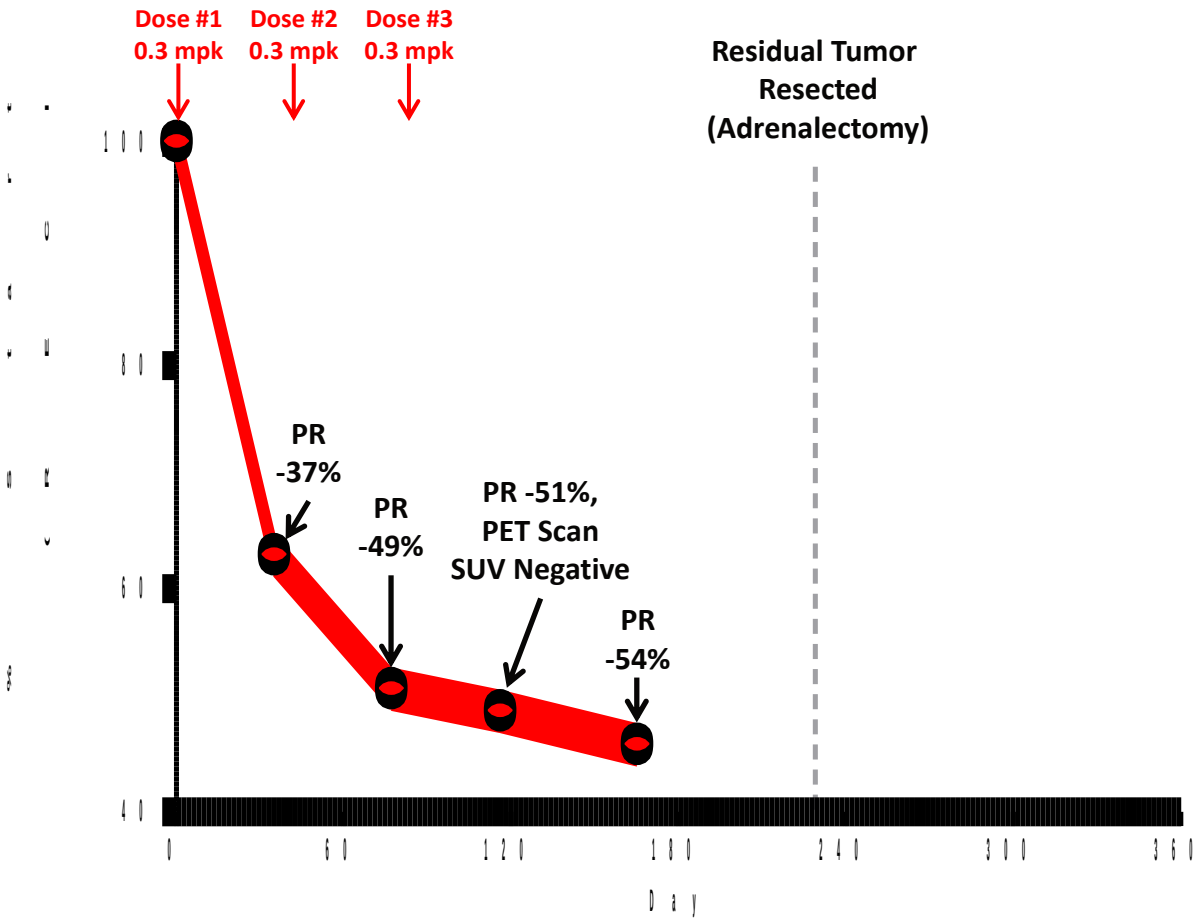
^3 Pts whose target lesions were noted as SD or better by RECIST had clinical progression

Efficacy in the 3rd Line Setting, Where No Standard of Care Exists

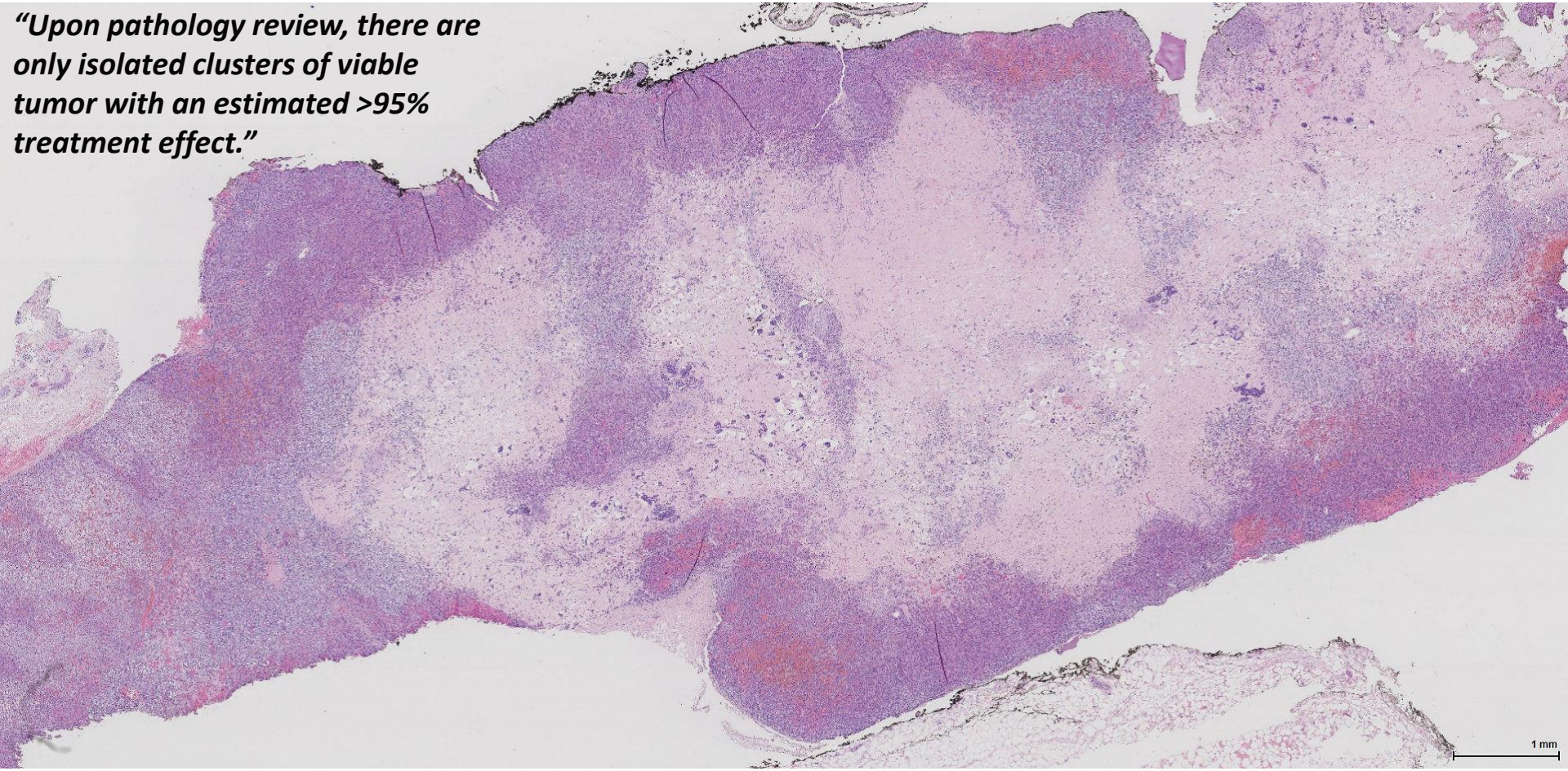


DLL3+ = H-score ≥ 180 on scale of 300

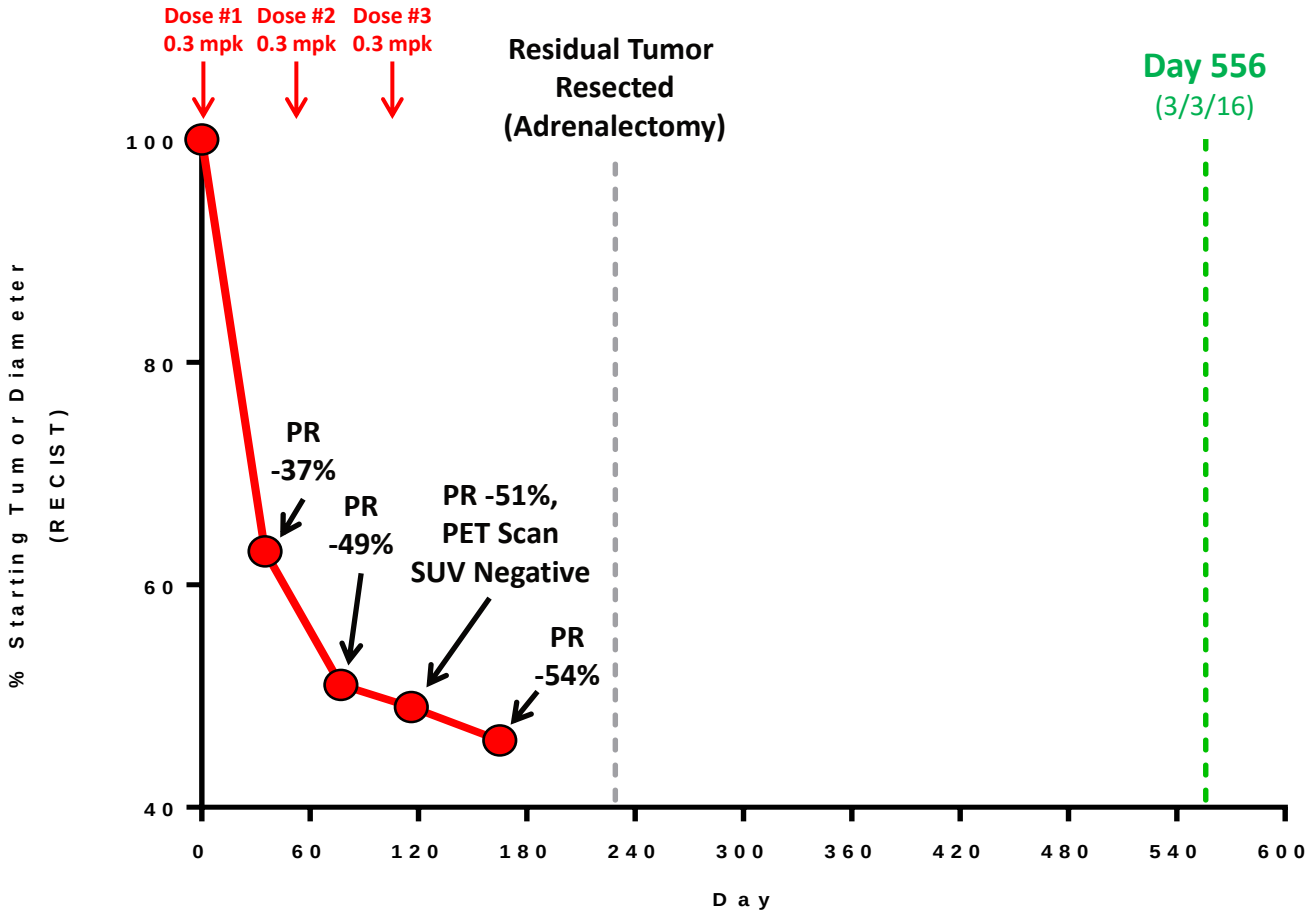
3rd Line Case Study #1: 54 Year Old Male



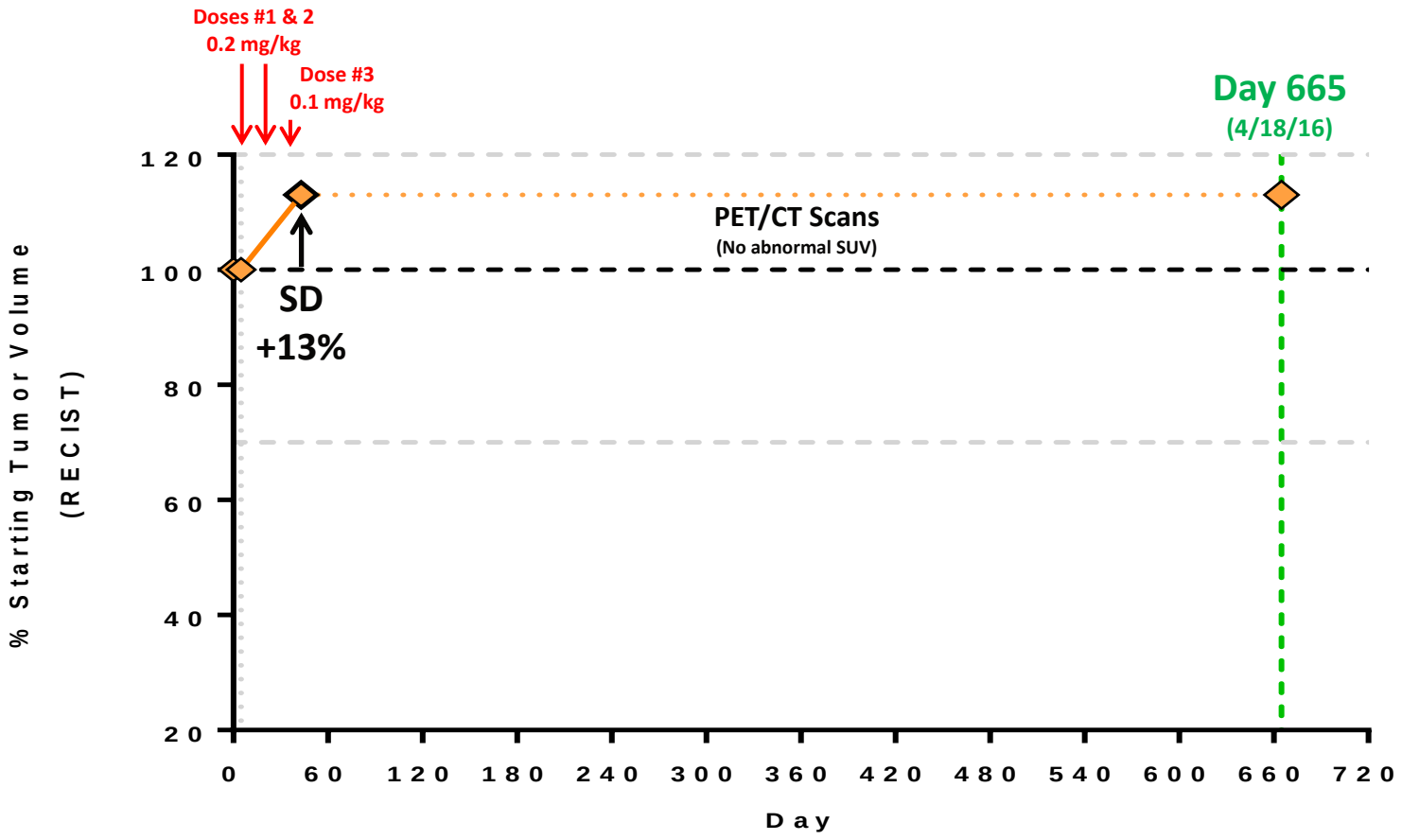
Residual Metastatic Tumor Mass After Rova-T



3rd Line Case Study #1: 54 Year Old Male

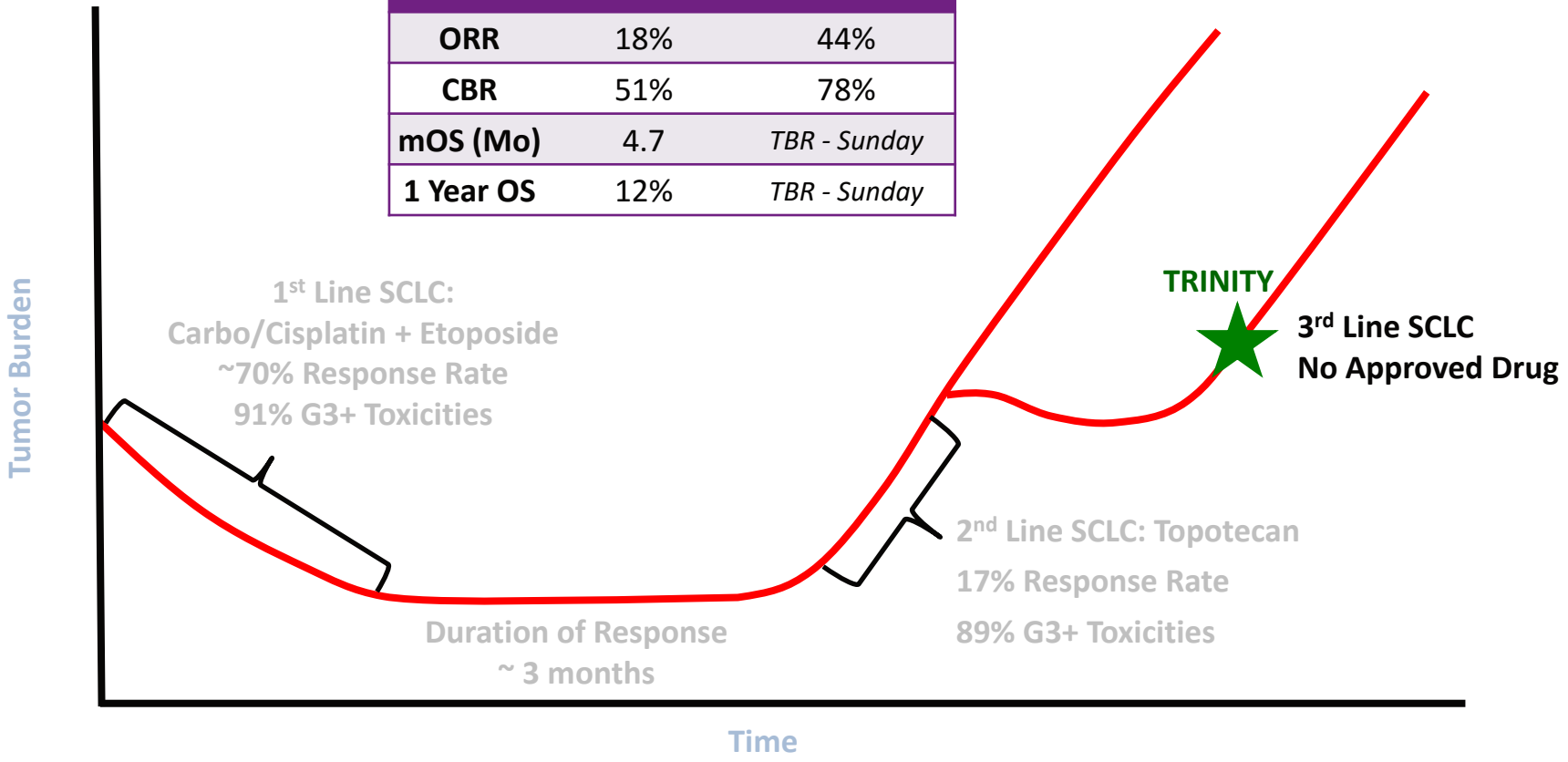


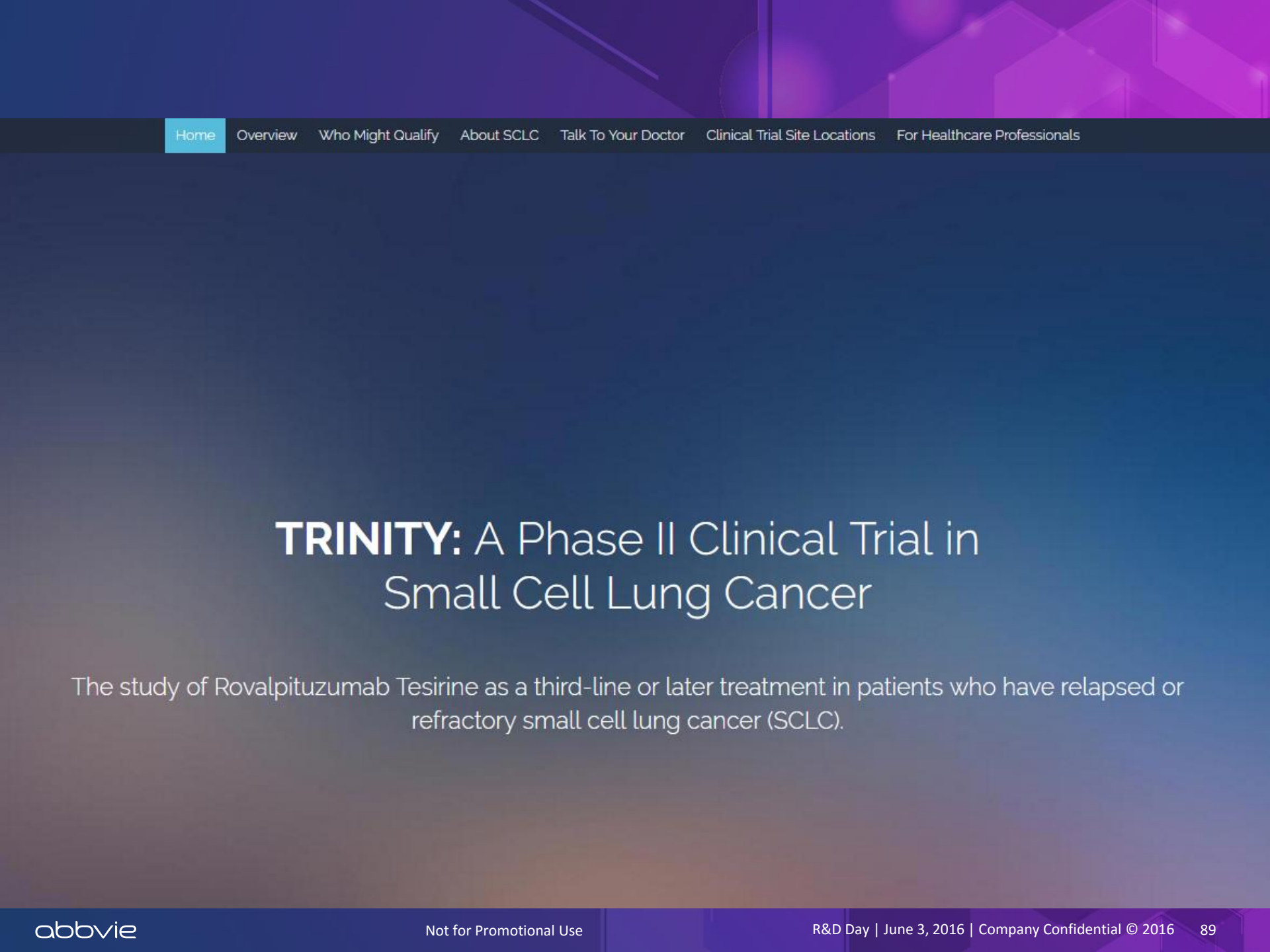
3rd Line Case Study #2: 60 Year Old Female



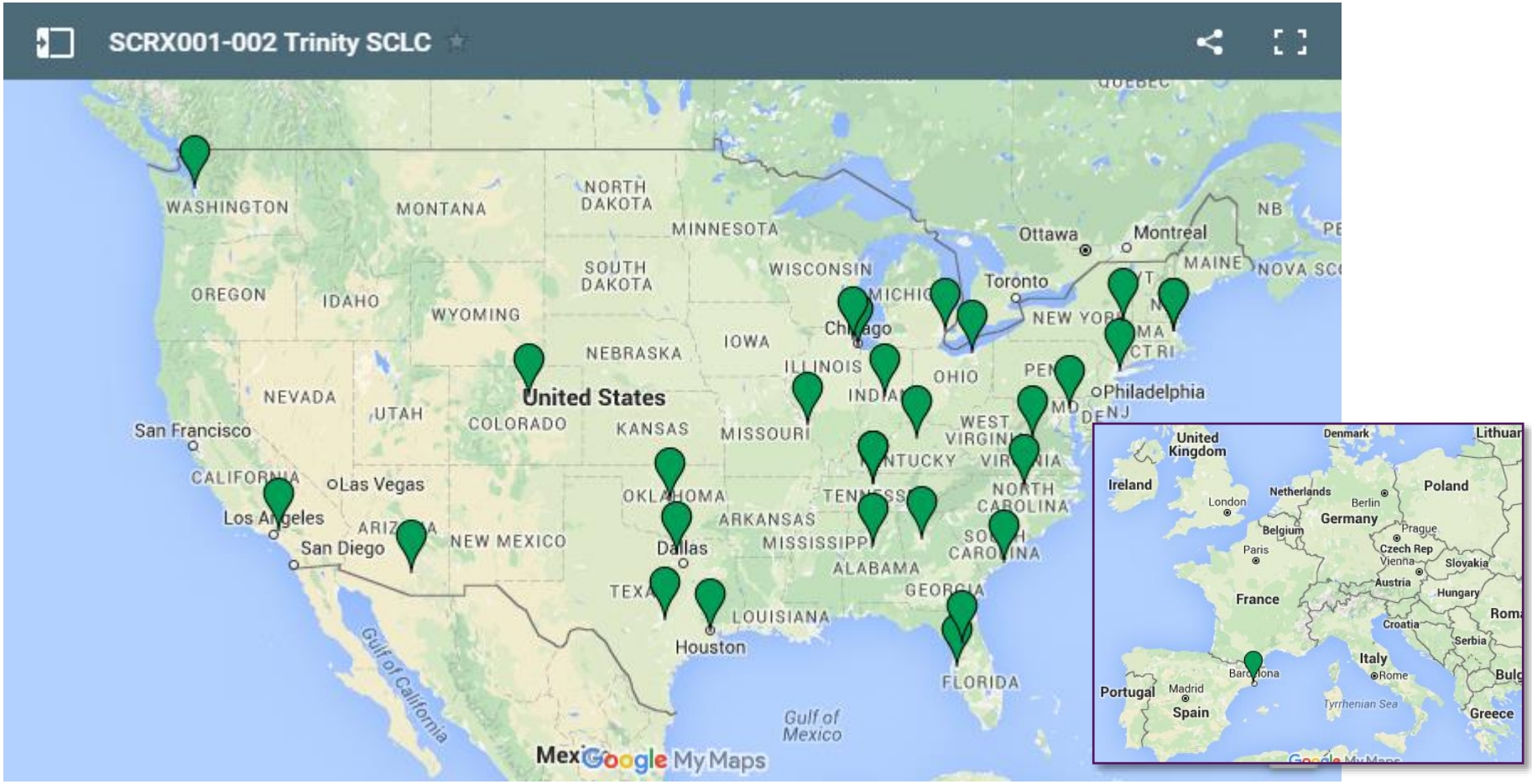
Rova-T Pivotal Study in 3rd Line SCLC

	Historical (n = 120) Simos'14	Rova-T DLL3^{Hi} (n = 27)
ORR	18%	44%
CBR	51%	78%
mOS (Mo)	4.7	*TBR - Sunday*
1 Year OS	12%	*TBR - Sunday*

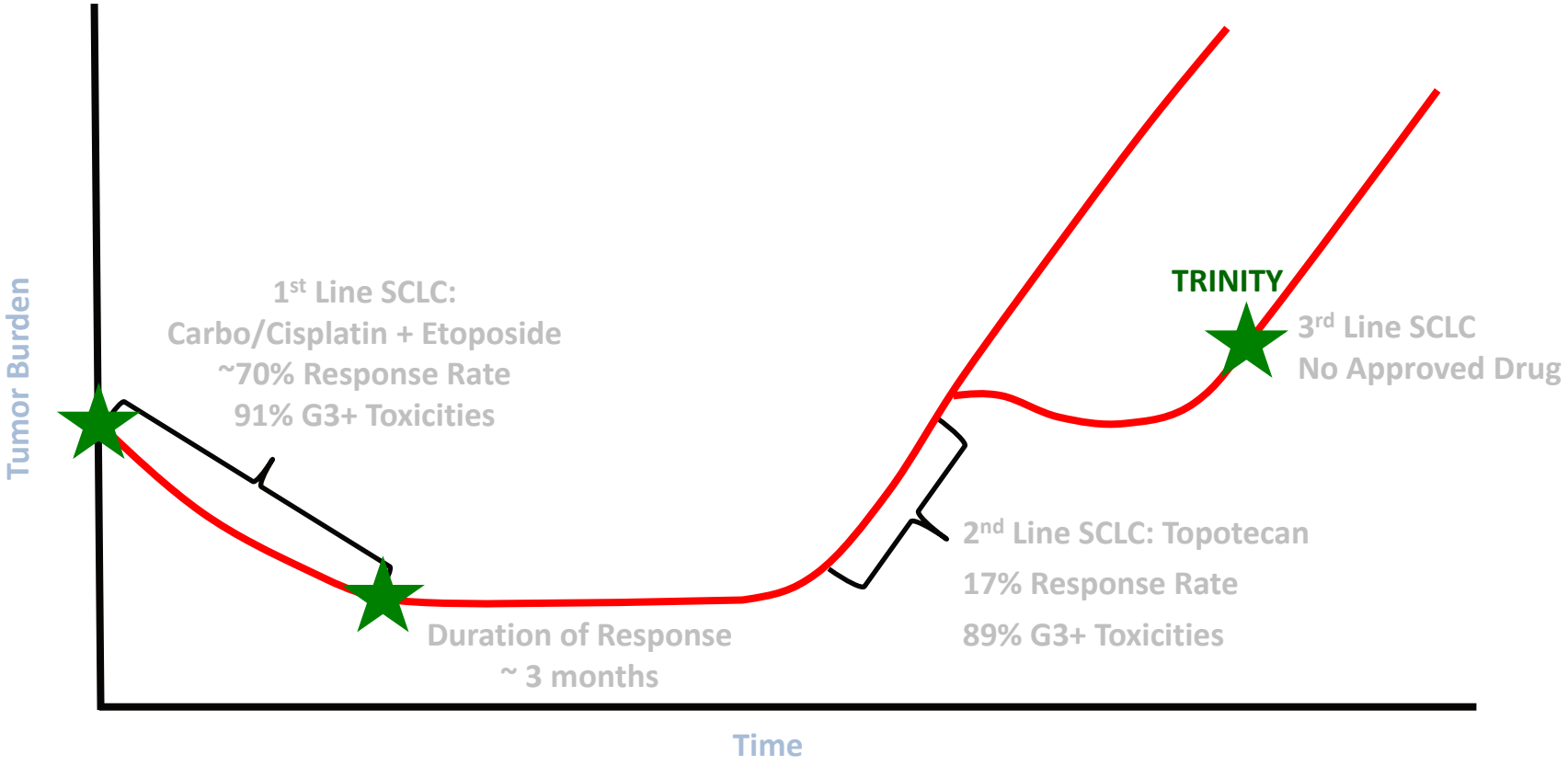



Home
Overview
Who Might Qualify
About SCLC
Talk To Your Doctor
Clinical Trial Site Locations
For Healthcare Professionals
TRINITY: A Phase II Clinical Trial in Small Cell Lung Cancer
The study of Rovalpituzumab Tesirine as a third-line or later treatment in patients who have relapsed or refractory small cell lung cancer (SCLC).

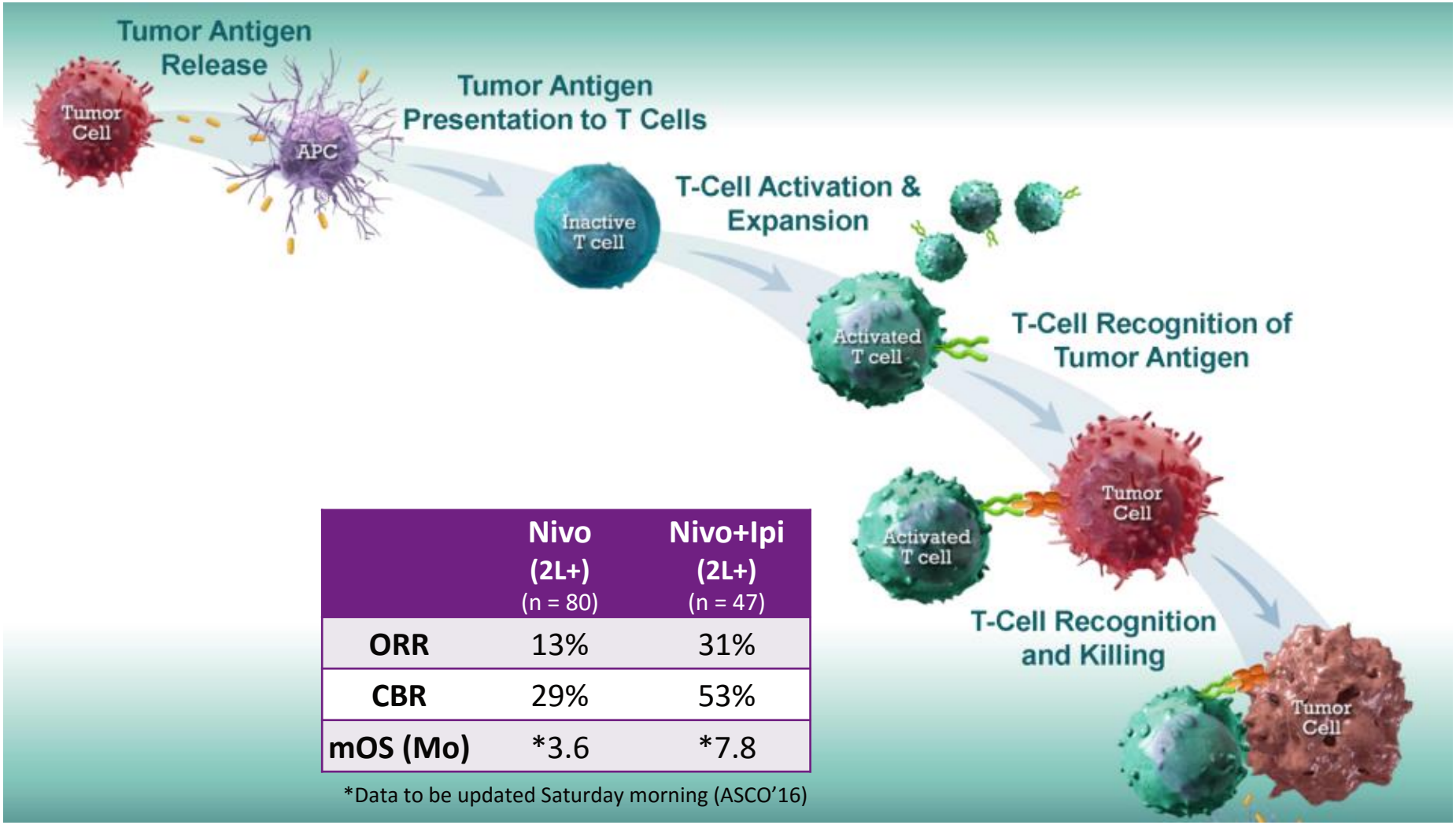
28 Sites in the U.S. and Europe Currently Enrolling TRINITY



1st Line SCLC Strategy



Additive Activities of ADCs and Checkpoint Inhibitors



	Nivo (2L+) (n = 80)	Nivo+Ipi (2L+) (n = 47)
ORR	13%	31%
CBR	29%	53%
mOS (Mo)	*3.6	*7.8

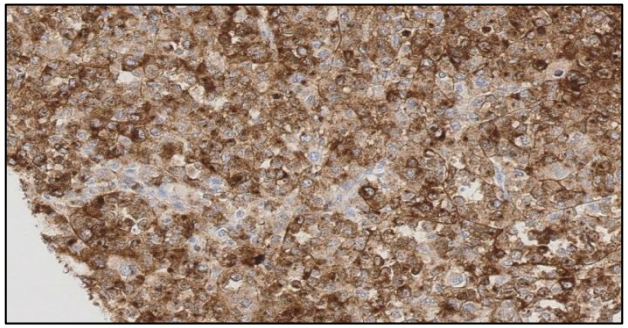
*Data to be updated Saturday morning (ASCO'16)

BMS, Immuno-Oncology, 201x

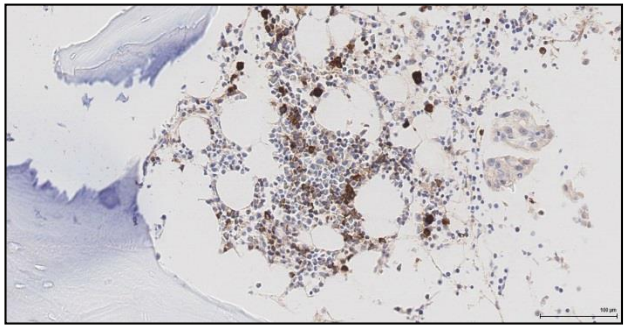
Other Indications for Rova-T

DLL3 Is Expressed in Extrapulmonary Neuroendocrine Tumors

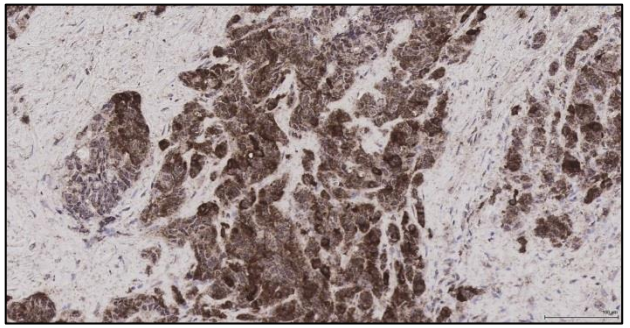
Metastatic Melanoma



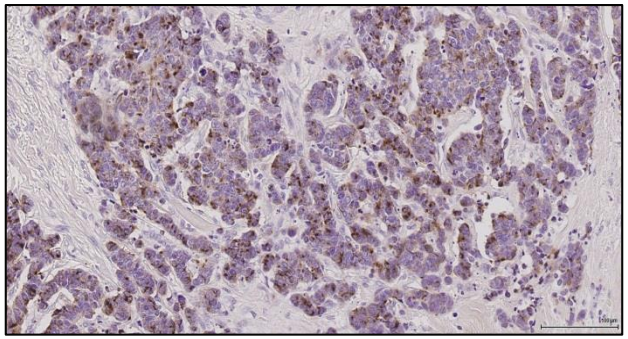
NE Prostate



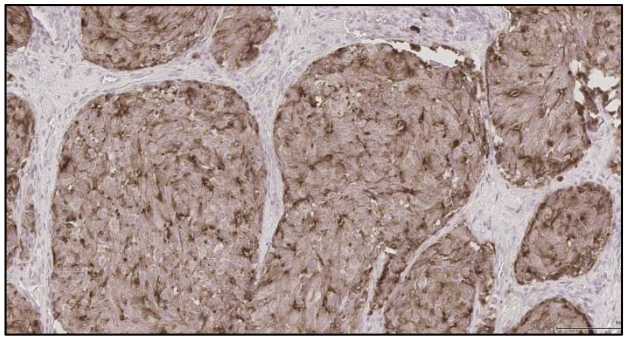
NE Pancreatic



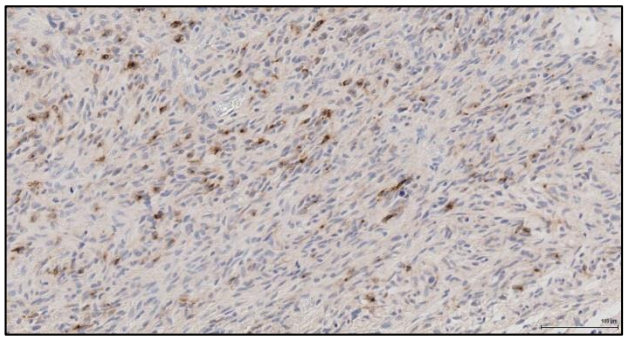
NE Colorectal



Medullary Thyroid

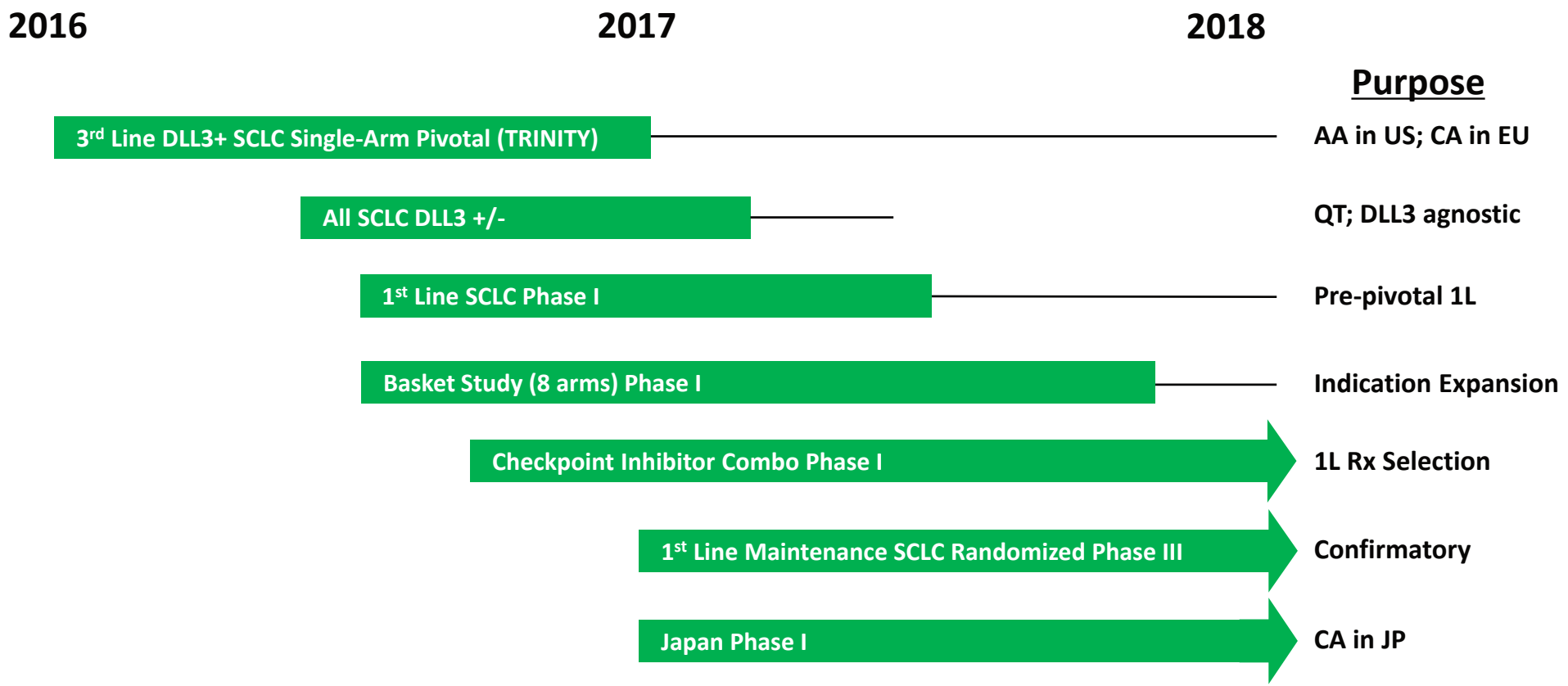


Glioblastoma



Abstract 11611, Poster Board: #308 – Tumor Biology, Hall A, 1-4 PM, Jun 6th

Rova-T Clinical Development



Other Clinical & Pipeline Drugs

abbvie

Other Clinical & Pipeline Drugs

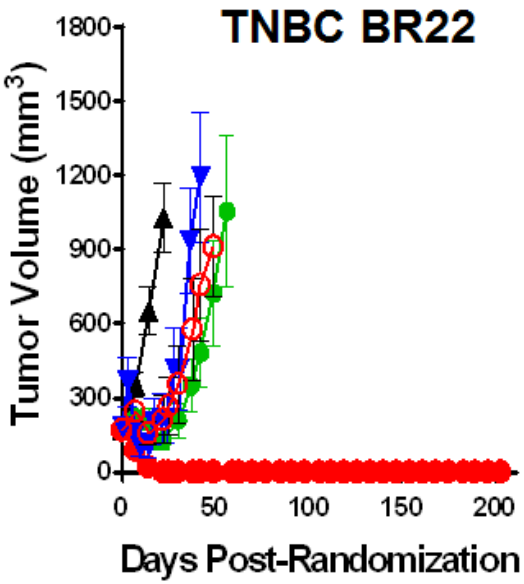
Clinical Drug #2: αPTK7-Auristatin

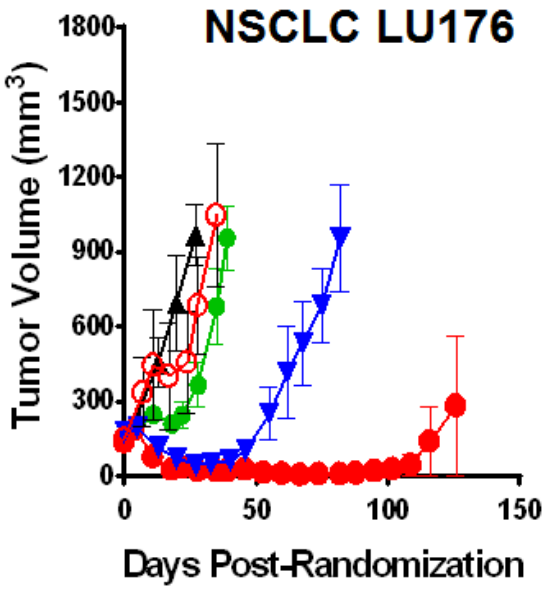
(PF-06647020)

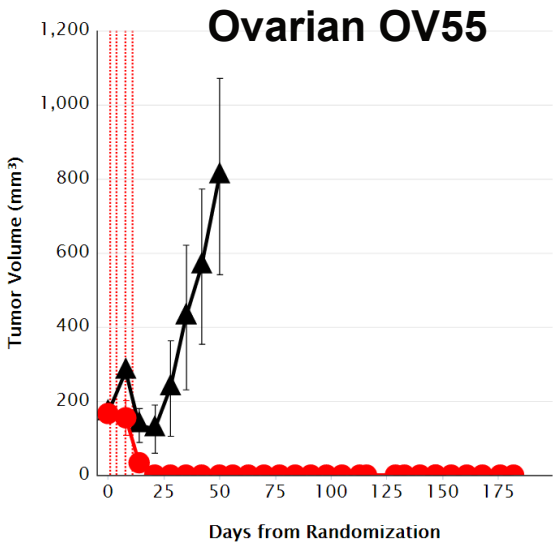
Non-Small Cell Lung, Breast and Ovarian Cancer

Pfizer

Preclinical Efficacy with PTK7-ADC







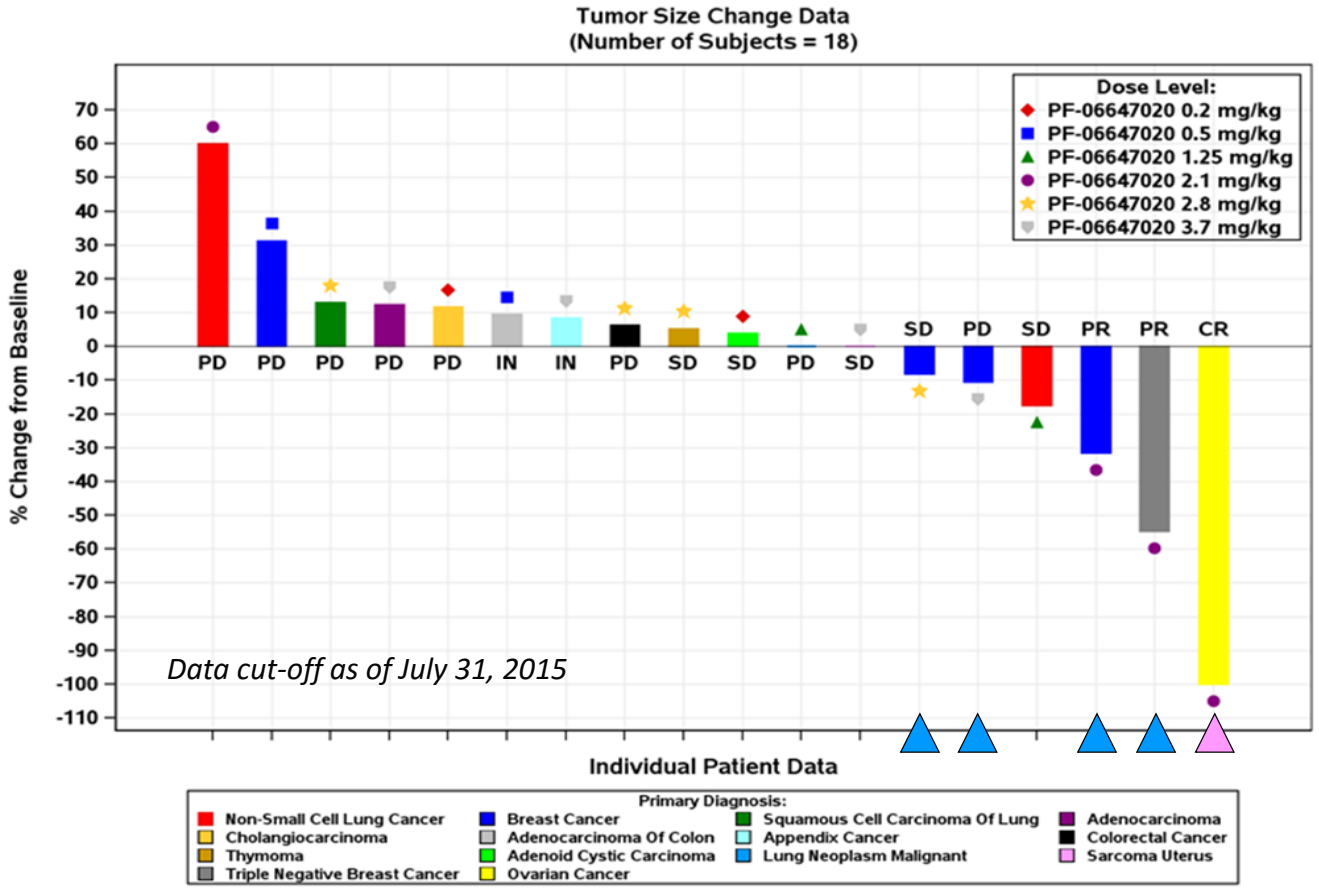
PTK7-ADC, 3 mpk
PTK7-ADC, 1 mpk
Standard of care
Vehicle

A Phase I Study of PF-06647020, an Antibody-Drug Conjugate Targeting Protein Kinase 7 (PTK7), in Patients with Advanced Solid Tumors

Tolcher AW[1], Calvo E[2], Doger B[2], Maitland ML[3], Gibson B[4], Xuan D[4], Joh T[4], Jackson-Fisher A[5], Damelin M[5], Barton J[4], Xin X[4], Sachdev JC[6]

[1]South Texas Accelerated Research Therapeutics, [2]South Texas Accelerated Research Therapeutics Madrid, [3]University of Chicago Medicine, [4]Pfizer Biotechnology Clinical Development, La Jolla, CA, [5]Pfizer Oncology Research Unit, [6]TGen – Virginia G. Piper Cancer Center at Scottsdale Healthcare

PF-06647020 Is Efficacious as a Single Agent in Humans



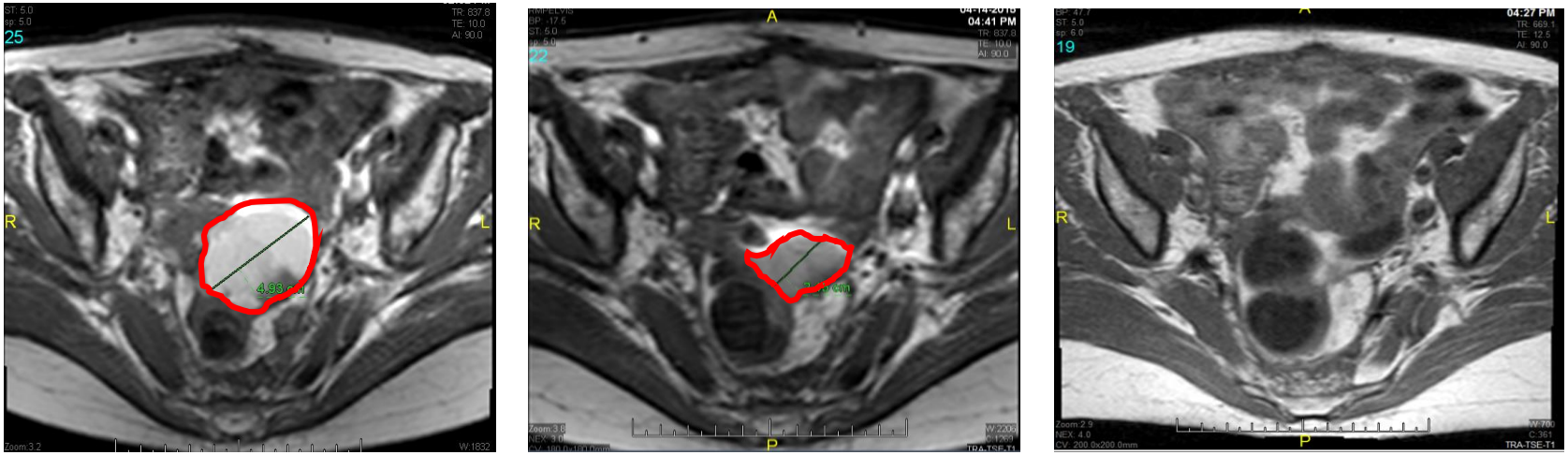
Breast cancer ≥ 2.1 mg/kg

Ovarian cancer ≥ 2.1 mg/kg

Tolcher AW et al. ESMO'15 - Vienna

Confirmed Complete Response in Ovarian Cancer Patient

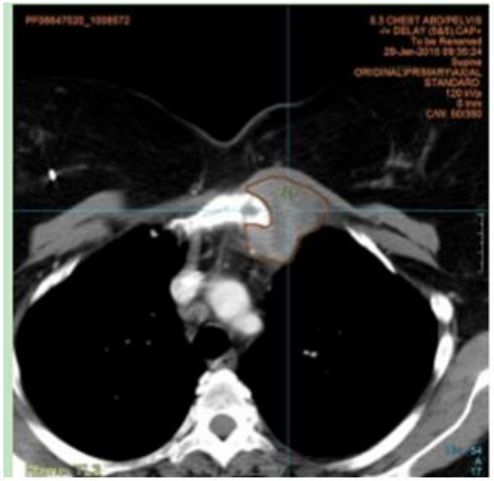
Baseline | **After 2 cycles →PR** | **After 4 cycles →CR**

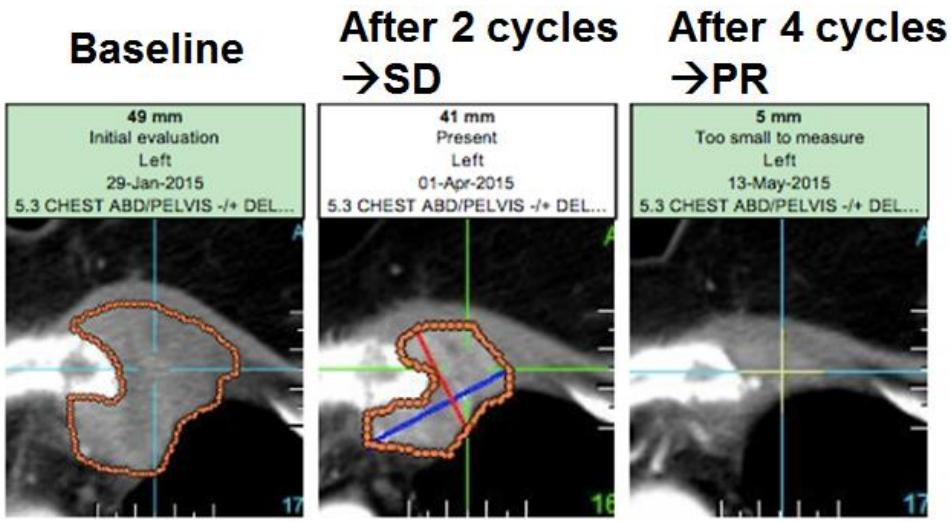


- 52 yo woman with advanced ovarian cancer (serous papillary carcinoma) previously treated with multiple lines of chemotherapies including carboplatin/taxol, cisplatin/gemcitabine, carboplatin/pegylated liposomal doxorubicin, and nab paclitaxel (the last immediate therapy) →Progressive Disease
- Patient received PF-06647020 at 2.1 mg/kg IV, q3w
- The CR was confirmed, and she has been in the study for 6 months

Tolcher AW et al.
ESMO'15 - Vienna

Confirmed Partial Response in a Patient with TNBC





- 49 yo woman with advanced TNBC previously treated with multiple lines of chemotherapies and investigational agents (the last immediate therapy) →Stable Disease
- Patient received PF-06647020 at 2.1 mg/kg IV, q3w
- The PR was confirmed, and treatment duration was 6 months

Tolcher AW et al.
ESMO'15 - Vienna

PF-06647020 Is Well Tolerated

	Grade 1		Grade 2		Grade 3		Grade 4		Grade 5		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Any AEs	5	(25.0)	6	(30.0)	4	(20.0)	0	(0.0)	0	(0.0)	15	(75.0)
Fatigue	4	(20.0)	2	(10.0)	1	(5.0)	0	(0.0)	0	(0.0)	7	(35.0)
Headache	0	0.0)	6	(30.0)	1	(5.0)	0	(0.0)	0	(0.0)	7	(35.0)
Nausea	5	(25.0)	2	(10.0)	0	(0.0)	0	(0.0)	0	(0.0)	7	(35.0)
Alopecia	2	(10.0)	3	(15.0)	0	(0.0)	0	(0.0)	0	(0.0)	5	(25.0)
Vomiting	1	5.0)	4	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	5	(25.0)
Chills	3	(15.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(15.0)
Diarrhea	2	(10.0)	1	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(15.0)
Neutropenia	0	0.0)	1	(5.0)	2	(10.5)	0	(0.0)	0	(0.0)	3	(15.0)
Pruritus	2	(10.0)	1	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(15.0)
Rash maculo-pap	2	(10.0)	1	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(15.0)
Hypomagnesaemia	2	(10.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(10.0)
Myalgia	1	(5.0)	1	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(10.0)

Data cut-off as of July 31, 2015

Tolcher AW et al. ESMO'15 - Vienna

abbvie

Other Clinical & Pipeline Drugs

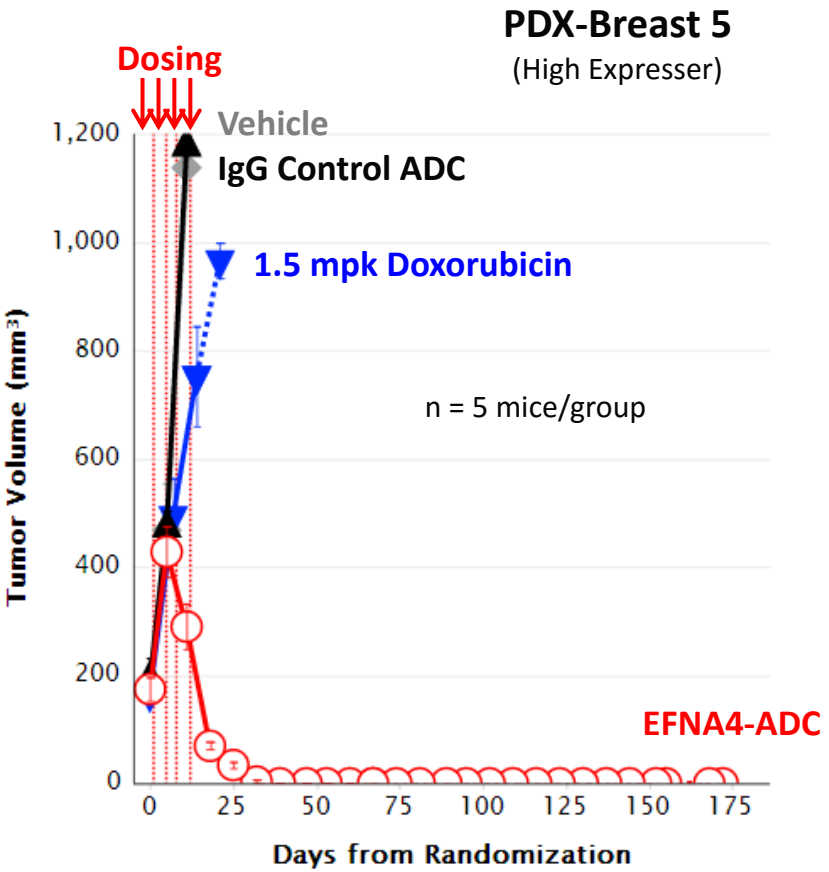
Clinical Drug #3: αEFNA4-Calicheamicin

(PF-06647263)

Triple-Negative Breast and Ovarian Cancer

Pfizer

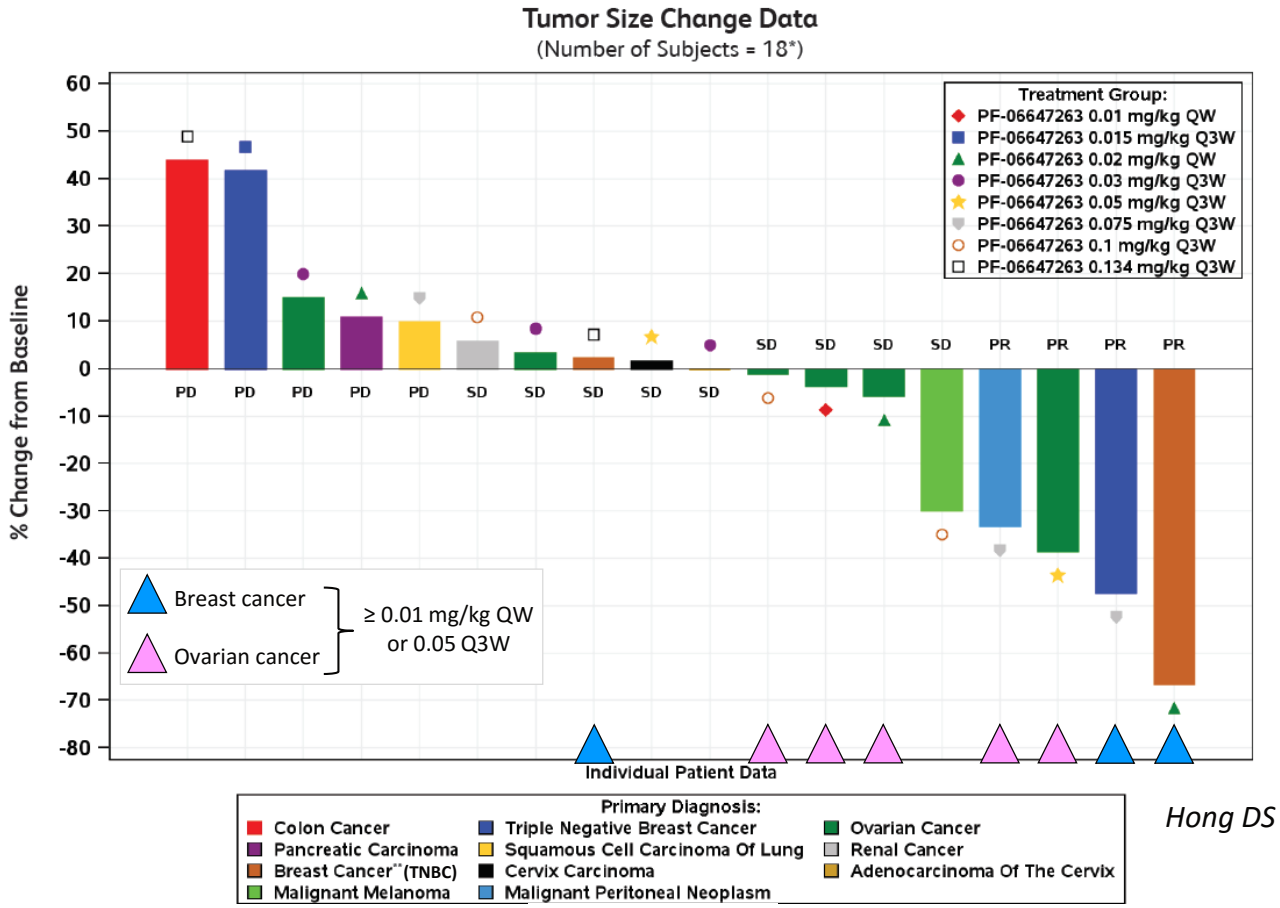
90% of TNBC PDX Express and Respond to EFNA4-ADC



Tumor (Subtype)	%TGI (0.3 mpk)	TTP (0.3 mpk)
BR5 (Basal)	**100%**	**172+**
BR31 (Basal)	**100%**	**147**
BR56 (Basal)	**98%**	**63**
BR13 (Bas/Lum)	**99%**	**97**
BR22 (Bas/Lum)	**90%**	**43**
BR25 (Claudin low)	**27%**	--
BR64 (Claudin low)	**0%**	--
BR17 (Her2+)	**0%**	--

~90% TNBC

PF-06647263 Is Efficacious as a Single Agent



Hong DS et al. ASCO 2015 poster

PF-06647263 Adverse Event Profile

Treatment-Emergent AEs (≥ 20%) Q3W

	All Causality n=17 (%)		Treatment-Related n=17 (%)	
	All Gr	Gr 3*	All Gr	Gr 3*
Fatigue	13 (77)	1 (6)	12 (71)	0
Decreased appetite	12 (71)	0	9 (53)	0
Nausea	11 (65)	1 (6)	10 (59)	0
Dysgeusia	8 (47)	0	8 (47)	0
Thrombocytopenia	8 (47)	1 (6)	8 (47)	1 (6)
Abdominal pain	7 (41)	0	4 (24)	0
Skin hyperpigmentation	7 (41)	0	7 (41)	0
Mucosal inflammation	6 (35)	3 (18)	6 (35)	3 (18)
Vomiting	6 (35)	1 (6)	5 (29)	0
Back pain	5 (29)	0	0	0
Constipation	5 (29)	0	1 (6)	0
Diarrhea	5 (29)	1 (6)	4 (24)	0
Dry mouth	5 (29)	0	4 (24)	0
Oedema Peripheral	5 (29)	0	2 (12)	0
Pyrexia	5 (29)	1 (6)	2 (12)	0
Stomatitis	5 (29)	1 (6)	5 (29)	1 (6)
Headache	4 (24)	0	2 (12)	0
Hypomagnesemia	4 (24)	0	1 (6)	0
Rash	4 (24)	1 (6)	4 (24)	1 (6)

* No Gr 4-5

Other ≥Gr 3 AEs [Treatment-Related]:

- Gr 3 (all n=1): **[anaemia, blood bilirubin increased, platelet count decreased, AST increased]**
- Gr 4 (all n=1): **[Neutropenia]**

Treatment-Emergent AEs (≥ 20%) QW

	All Causality n=13 (%)		Treatment-Related n=13 (%)	
	All Gr	Gr 3*	All Gr	Gr 3*
Nausea	8 (62)	0	8 (62)	0
Fatigue	6 (46)	0	6 (46)	0
Vomiting	6 (46)	0	5 (39)	0
Decreased appetite	5 (38)	0	4 (31)	0
Diarrhea	5 (38)	1 (7)	4 (31)	0
Thrombocytopenia	4 (31)	1 (7)	4 (31)	1 (7)
Dysgeusia	3 (23)	0	3 (23)	0
Mucosal inflammation	3 (23)	0	3 (23)	0
Constipation	3 (23)	0	0	0
Headache	3 (23)	0	0	0

* No Gr 4-5

Other ≥Gr 3 AEs [Treatment-Related]:

- Gr 3 (all n=1): pyrexia, pain in extremity, hypotension, **[dehydration, asthenia]**
- Gr 4-None
- Gr 5 (n=1): death cause undetermined

Hong DS et al. ASCO 2015 poster

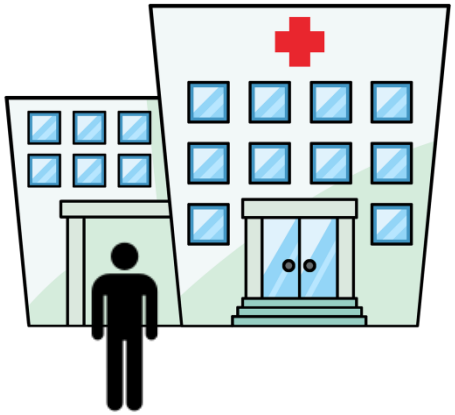
Stemcentrx Coverage of Major Cancers

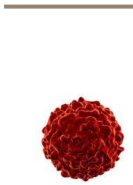
Target	SCLC	TNBC	OV	MEL	NSCLC
DLL3	Stemcentrx			Stemcentrx	
PTK7		Stemcentrx	Stemcentrx		Stemcentrx
EFNA4		Stemcentrx	Stemcentrx		
SC-002	Stemcentrx				
SC-003			Stemcentrx		

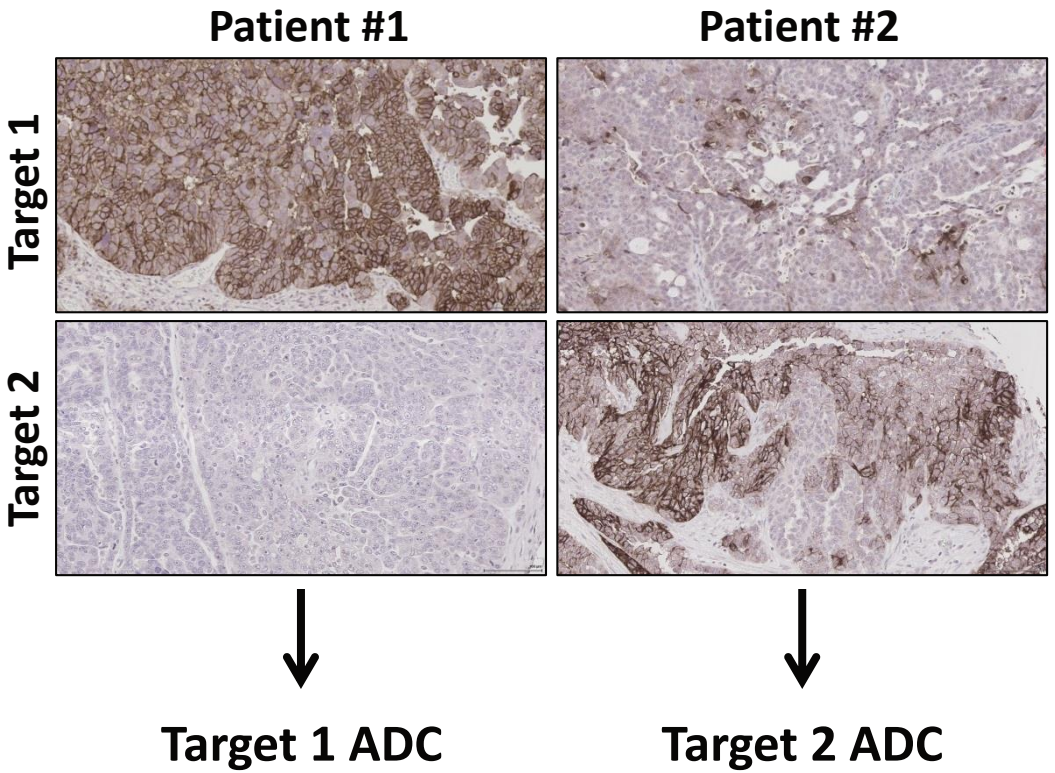
Stemcentrx Coverage of Major Cancers

Target	SCLC	TNBC	OV	MEL	NSCLC	PA	CR	GA	LumB BR	AML
DLL3	Stemcentrx			Stemcentrx						
PTK7		Stemcentrx	Stemcentrx		Stemcentrx					
EFNA4		Stemcentrx	Stemcentrx							
SC-002	Stemcentrx									
SC-003			Stemcentrx							
IND #6			Stemcentrx		Stemcentrx					
IND # 7										
IND # 8										
IND # 9										
IND # 10										

Our Vision: Provide Disease-Specific CSC-Targeted Therapies







Summary

- 3 of 3 first clinical drugs showing single-agent efficacy at tolerated doses
- All 3 targeting antigens (DLL3, PTK7, EFNA4) never before pursued clinically
- Discovery platform unveiling additional novel targets (ADC, CAR-T/NK/TCR, SM)
- 2016 Milestones
  - TRINITY pivotal study initiated
    - Continue to ensure rapid enrollment
  - Initiate 1st line SCLC induction studies for regimen selection
  - Initiate 1st line SCLC maintenance confirmatory study by 4Q'16/1Q'17
  - Initiate neuroendocrine basket study
  - Initiate checkpoint inhibitor combo studies

Stemcentrx

Science Company Join Us **Clinical Trials**

abbvie

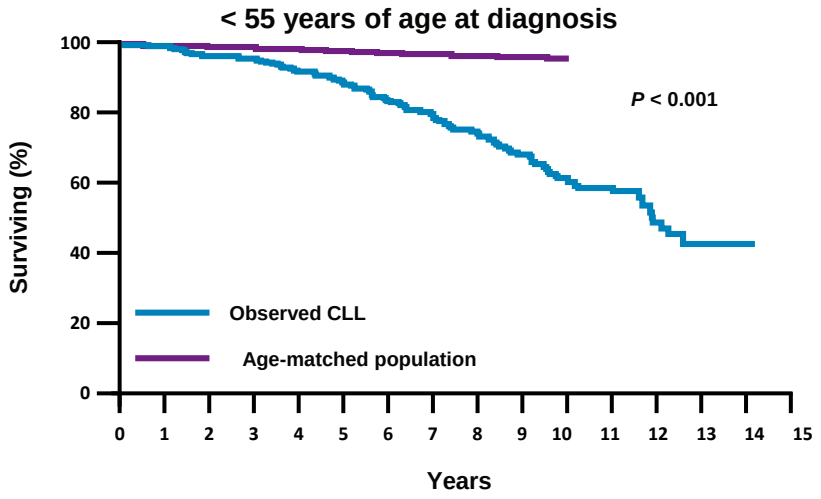
Imbruvica

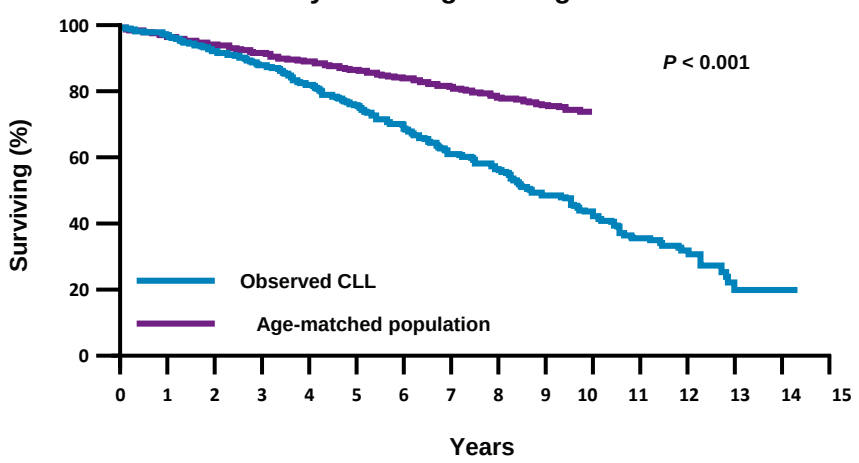
Danelle James, M.D., M.S.

REMARKABLE IMPACT ON PATIENTS' LIVES RIGHT STRATEGY STRONG TALENT TANGIBLE RES
STRONG EXECUTION IMMUNOLOGY ONCOLOGY VIROLOGY NEUROLOGY REMARKABLE IMPACT
ON PATIENTS' LIVES RIGHT STRATEGY STRONG TALENT TANGIBLE RESULTS STRONG EXECUT

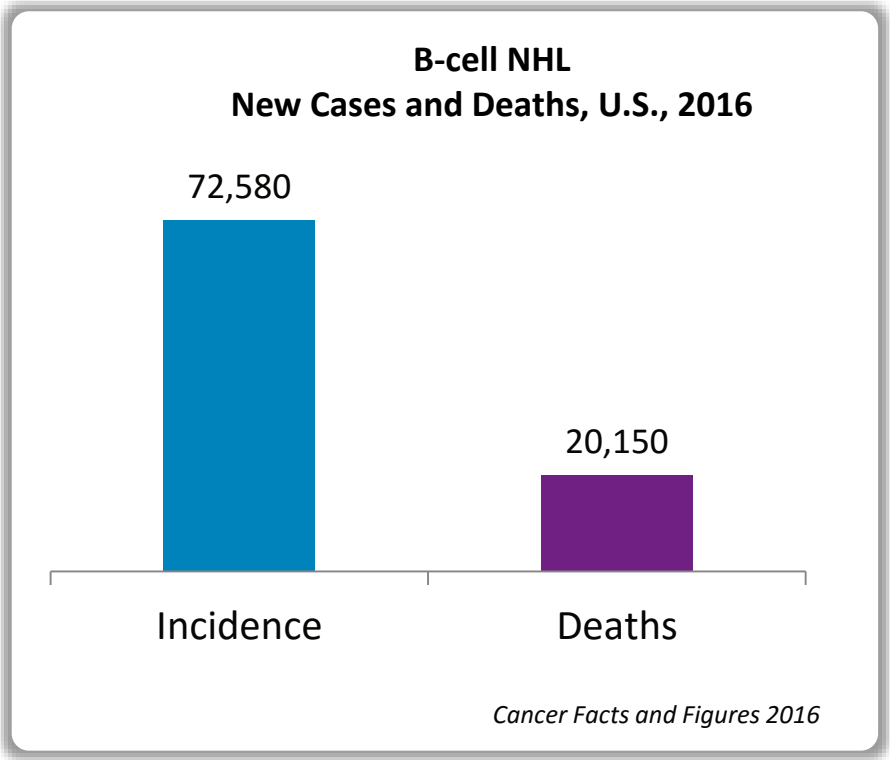
pharmacyclics®
An AbbVie Company

Despite Efficacy of Current Standard of Care, Unmet Need Remains in CLL and NHL





Shanafelt et al, *Cancer*, 2010;116:4777-4787



Cancer Facts and Figures 2016

From Target Validation to Front-line Indication:
Rapid Development of the First Inhibitor of Bruton Tyrosine Kinase (BTK), Ibrutinib

1952
Colonel Bruton described a genetic disorder, agammaglobulinemia

1993
BTK gene was cloned and characterized

2009
First human treated with ibrutinib

2013
Approved for MCL patients who received at least 1 prior therapy

2014
Approved for CLL patients who received at least 1 prior therapy

2014
Approved for CLL patients with deletion 17p

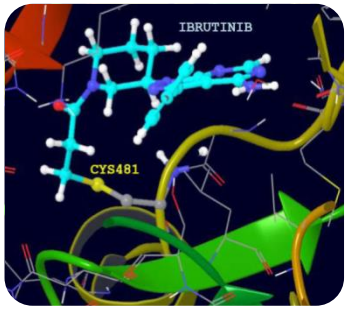
2015
Approved for WM patients

Oct 2015
sNDA Treatment Naïve submitted

FDA Approval in SLL
May 2016

2005 | 2010 | 2014 | 2015 | 2016

2005
First synthesis of ibrutinib (PCI-32765)



2013
NDA submitted for two R/R B-cell malignancy indications: MCL & CLL

Three Breakthrough Therapy Designations Received

2013
CLL & MCL top-line data published in NEJM

2014
RESONATE™ Data published in NEJM

Jan 2015
Treon paper on Waldenström's published in NEJM

Dec 2015
RESONATE-2 Data published in NEJM

Mar 2016
FDA approval for front-line. Extremely rapid development of First-in-Class BTK Inhibitor

Imbruvica (ibrutinib) Has the Potential to Broadly Transform the Management of Treatment-Naïve CLL/SLL

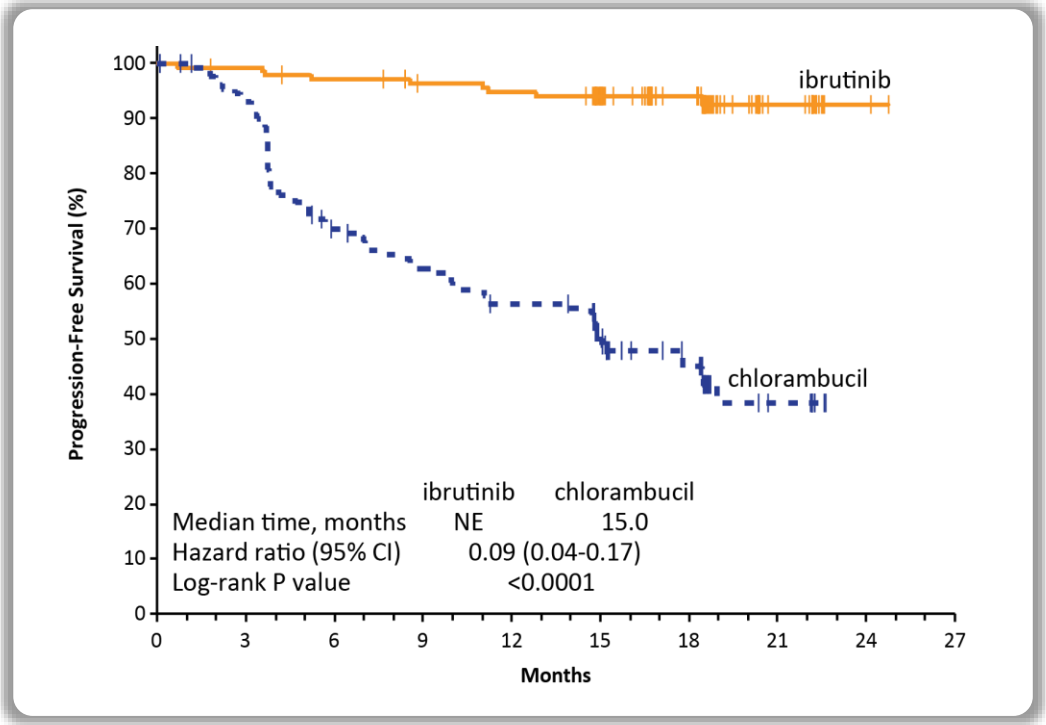
Study	RESONATE-2™ PCYC-1115	UK CLL NCRN & ECOG 1912	Alliance 041202	iLLUMINATE PCYC-1130	CLL 12
Patient Population	Age ≥ 65	Age < 70	Age ≥ 65	Age ≥ 65 or comorbidities	Watch & Wait
Regimen	**Ibr** vs **Chl**	**Ibr-Ritux** vs **FCR**	**Ibr** or **Ibr-Ritux** vs **BR**	**Ibr-obinutuz** vs **Chl-obinutuz**	**Ibr** vs **placebo**

FCR – fludarabine, cyclophosphamide, rituximab. Ibr – ibrutinib, ritux- rituximab. BR – bendamustine, rituximab. Obinutuz – obinutuzumab. Chl – Chlorambucil

RESONATE-2™

Data Supports Imbruvica and in First-line CLL/SLL

NEJM: Imbruvica Front-Line CLL Data (RESONATE-2)



- ➔ NCCN category 1 for key front-line patient segments in addition to all previously treated segments
- ➔ Full FDA approval for CLL/SLL (all lines of therapy and all genetic subgroups)
- ➔ EMEA review ongoing for first-line indication, positive opinion from CHMP received April 2016

- 91% reduction in risk of progression or death with Imbruvica
- 84% reduction in the risk of death compared to chlorambucil
  - With a median of 28.1 months of follow up and crossover of 41% of chorambucil patients a statistically significant 54% reduction in risk of death for Imbruvica arm

USPI Imbruvica May 2016

NEJM Burger 2016

Studying Imbruvica in a Comprehensive Development Program in Treatment-Naïve CLL/SLL

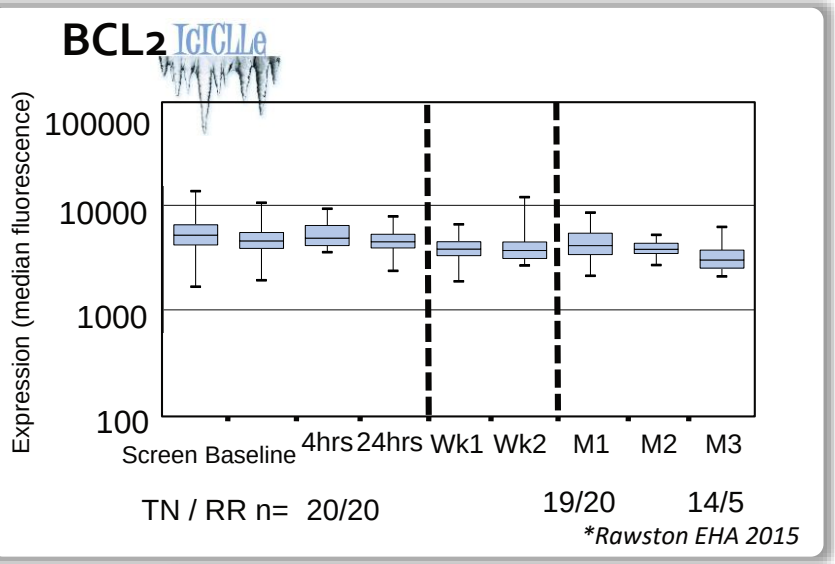
Study	RESONATE-2™ PCYC-1115	UK CLL NCRN & ECOG 1912	Alliance 041202	iLLUMINATE PCYC-1130	CLL 12
Patient Population	Age ≥ 65	Age < 70	Age ≥ 65	Age ≥ 65 or comorbidities	Watch & Wait
Regimen	Ibr vs Chl	**Ibr-Ritux** vs **FCR**	**Ibr** or **Ibr-Ritux** vs **BR**	**Ibr-obinutuz** vs **Chl-obinutuz**	**Ibr** vs **placebo**

We anticipate data from studies to read out from 2017 - 2019

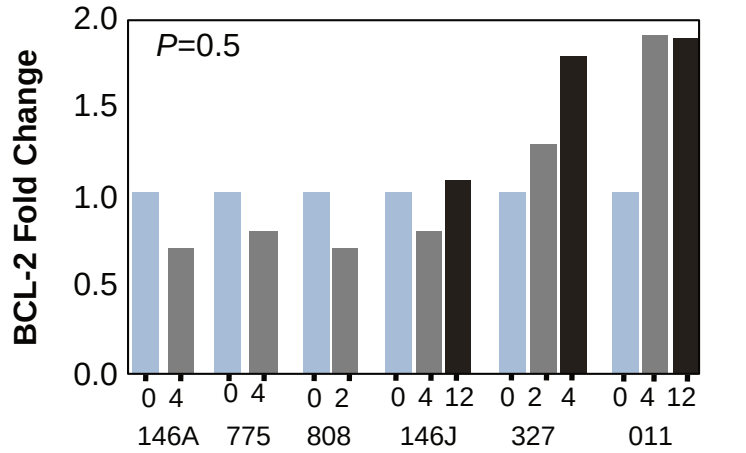
FCR – fludarabine, cyclophosphamide, rituximab. Ibr – ibrutinib, ritux- rituximab. BR – bendamustine, rituximab. Obinutuz – obinutuzumab. Chl – Chlorambucil

Rationale: Imbruvica + Venclexta Combination

Strong expression of BCL-2 observed throughout Imbruvica treatment

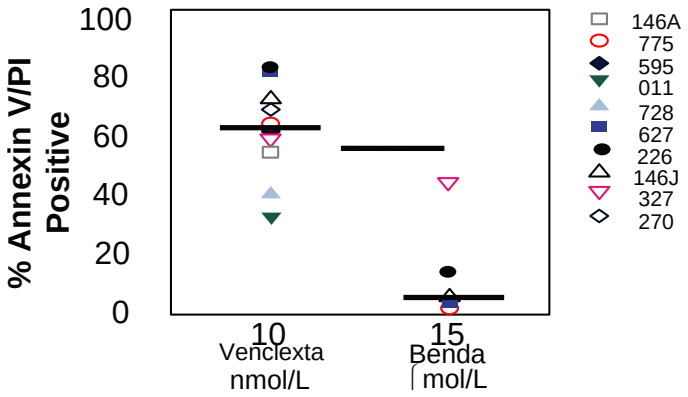


*Rawston EHA 2015



*Cervantes-Gomez Clin Can Res. Epub Mar 31, 2015

Leukemia cells from patients treated with Imbruvica are highly sensitive to apoptosis with Venclexta



Serial samples of CLL cells obtained before and 2, 4, or 12 weeks after the start of Imbruvica showed no reduction in BCL-2 protein, and sensitivity to Venclexta

*Cervantes-Gomez Clin Can Res. Epub Mar 31, 2015

Clinical Evaluation of the Combination of Imbruvica and Venclexta

CLL13 –OBVIOUS Study GCLLSG Phase 3 - TN CLL Ibr + Ve + Obinutuz *vs.* Ve + Obinutuz *vs.* Ve + Ritux *vs.* FCR/BR n = 920

CLL13b GCLLSG Phase 2 TN del 17p CLL Ibr + Ve + Obinutuz n = 60

CLARITY Study Phase 2 R/R CLL Ibr + Ve n = 100

PCYC-1142 Phase 2 TN CLL patients <70yrs Ibr + Ve n = 150

OAsIs Study MCL Phase 1 R/R MCL Ibr + Obinutuz + Ve n = 33

AIM Study Phase 2 TN & R/R MCL Ibr + Ve n = 24

FCR – fludarabine, cyclophosphamide, rituximab. Ibr – ibrutinib, ritux- rituximab. BR – bendamustine, rituximab. Obinutuz – obinutuzumab. Ve -Venteoclax

The Combination of Imbruvica and Venclexta Rapidly Achieves CR in Patients with R/R MCL: *Preliminary Results of the Phase 2 AIM Study*

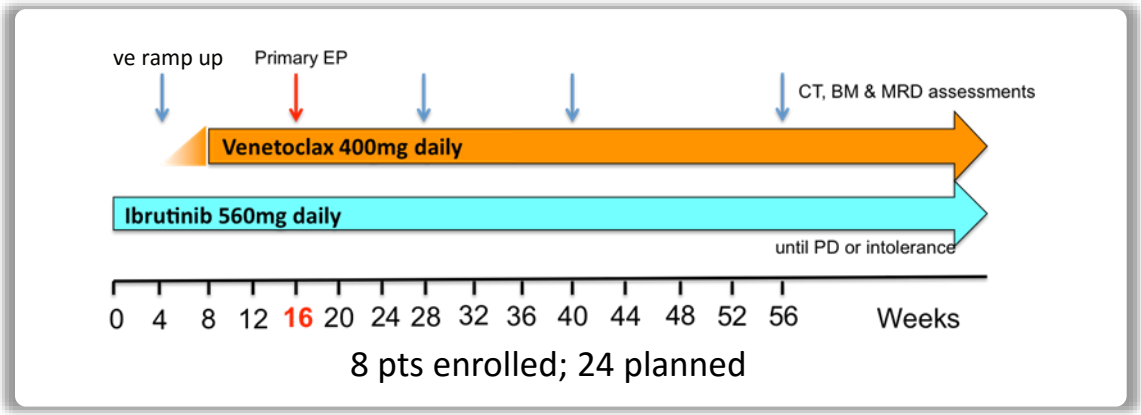
Objective: to Determine Complete Response Rate

Patients

- Median age: 72 y (53-77); median prior Tx: 2 (1-7); high MIPI score: 63%

Safety

- Full Venclexta dose (400 mg) reached in all 4 pts who entered ramp-up with no TLS
- Most common AEs (all Gr 1-2): nausea (n=4), diarrhea (2), oral candidiasis (2)



8 pts enrolled; 24 planned

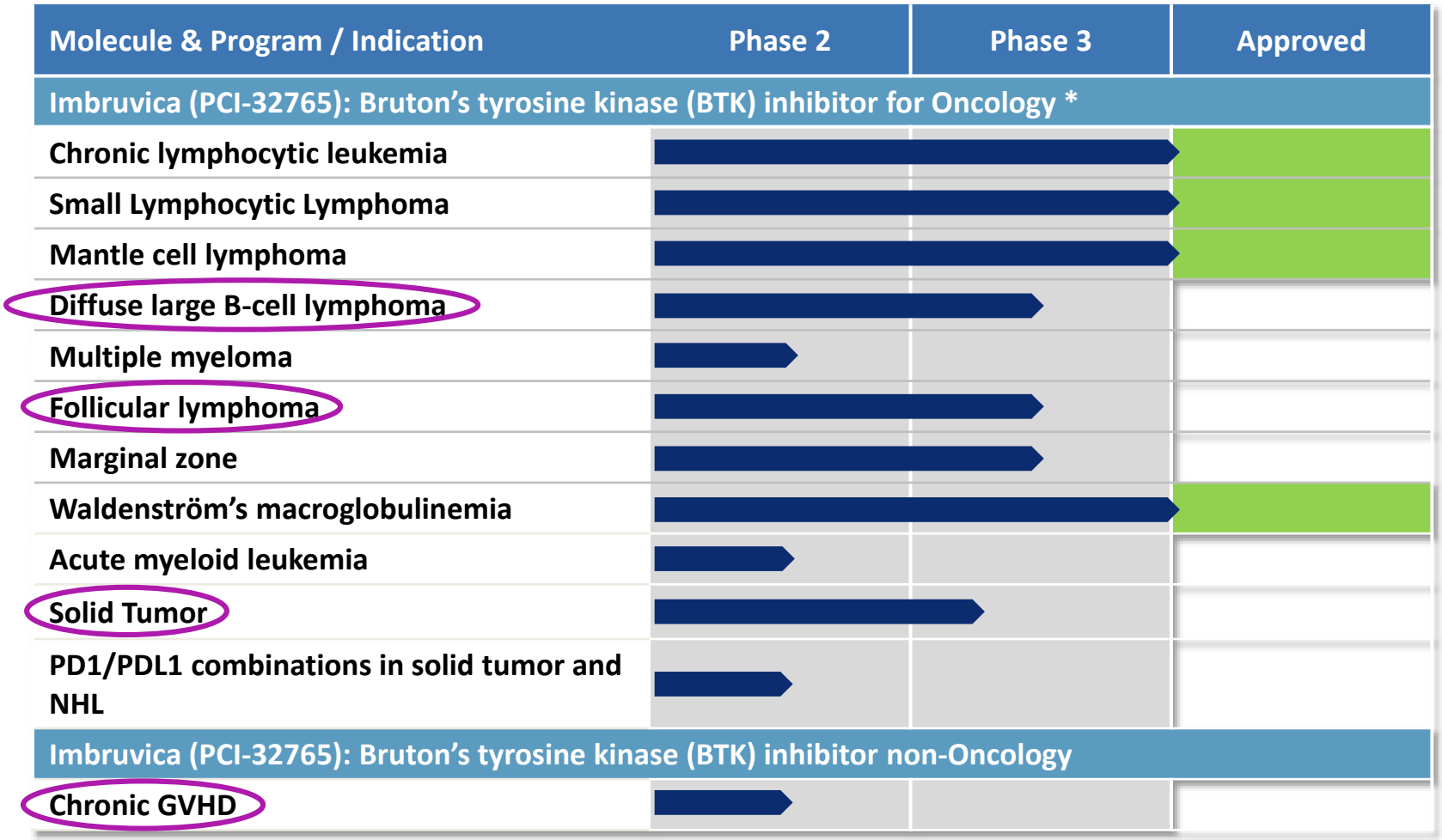
Efficacy

- Response after 4-week ibr induction (n=5 evaluable): 2 PR, 2 SD, 1 PD
- Response after 4 mo (n=3 evaluable): 2 CR , 1 PR
  - CR: normalization of PET ± endoscopy, and complete clearance of previous marrow involvement, including flow cytometry at >10^{-4} sensitivity

Early experience with Imbruvica + Venclexta shows no unexpected safety signals with promising efficacy

**ASCO abstract 7519, Tam 2016*

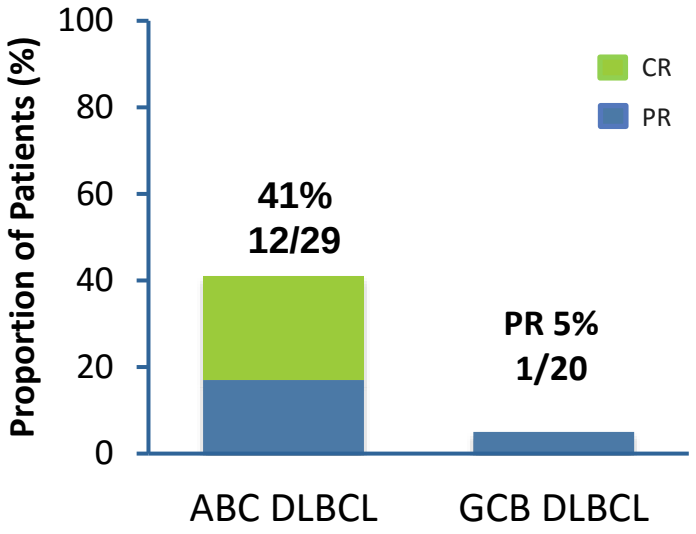
Imbruvica Has Broad Potential Beyond CLL and MCL



**Janssen Biotech: global partnership*

Imbruvica Is Clinically Active in non-Germinal Center B-cell Subtype DLBCL and Can Be Combined with R-CHOP

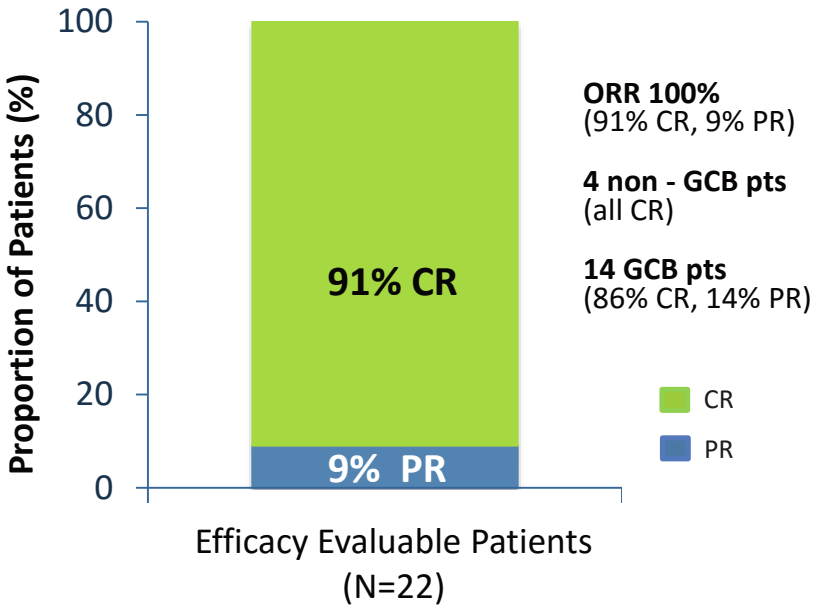
Single Agent Imbruvica



Overall response and depth of response was significantly better with single-agent ibrutinib in patients with ABC subtype compared to GCB subtype.

de Vos et al. 2013.

Imbruvica + R-CHOP in Treatment-Naïve DLBCL Patients

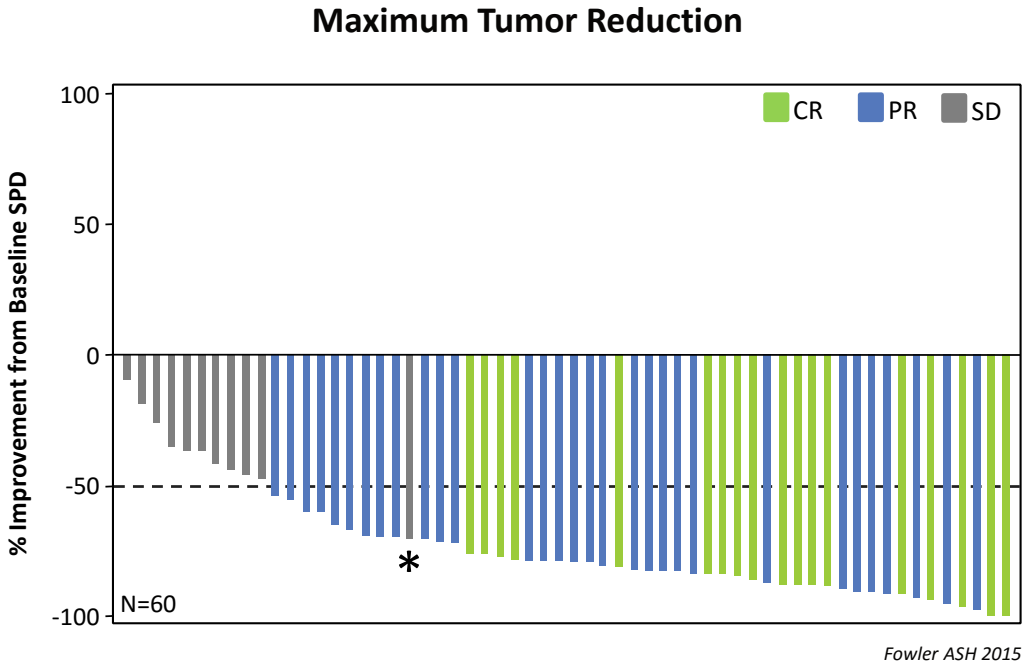


Younes et al. ASH 2013.

Ongoing Phase 3 study, PHOENIX, evaluating Imbruvica in combination with R-CHOP for the first-line treatment of Non-GCB DLBCL in >800 patients

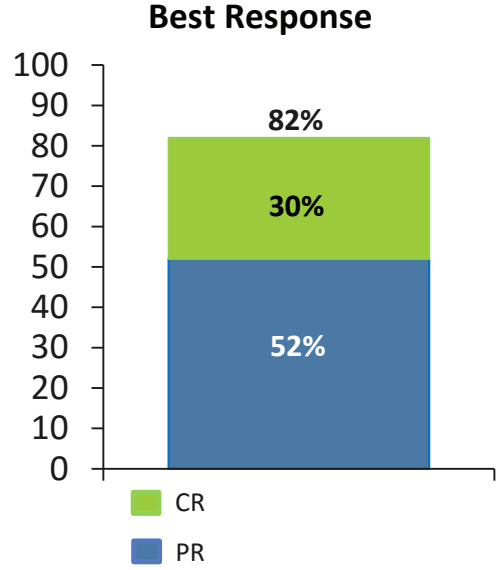
ABC – activated B-cell. GCB – germinal center B-cell. R-CHOP – rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone.

High Activity of Imbruvica + rituximab for the First-line Treatment of Follicular Lymphoma



*Response recorded in database is SD; unresolved query

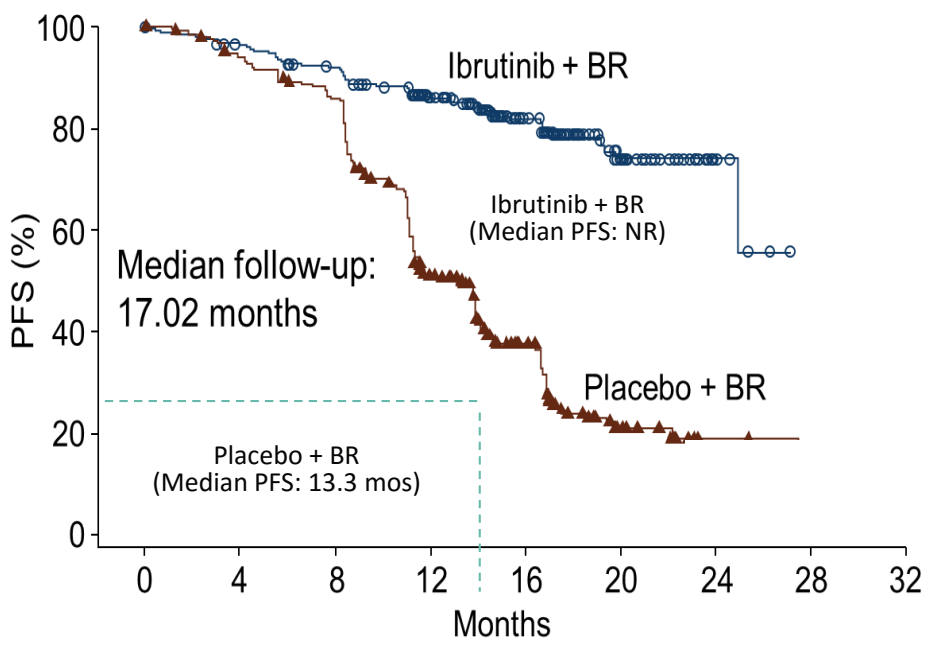
Abbreviations: CR, complete response; PR, partial response; SD, stable disease; SPD, sum of the products of the greatest perpendicular diameters



- ORR 82% in all treated patients (49 of 60)
- Median duration of Imbruvica treatment: 12.55 months

Ongoing pivotal studies in indolent lymphoma to read out 2016–2018

Imbruvica Significantly Enhances the Activity of Chemoimmunotherapy – the Objective of Several Phase 3 Studies



HR: 0.203 (95% CI, 0.15 – 0.28) ***P* < 0.0001**

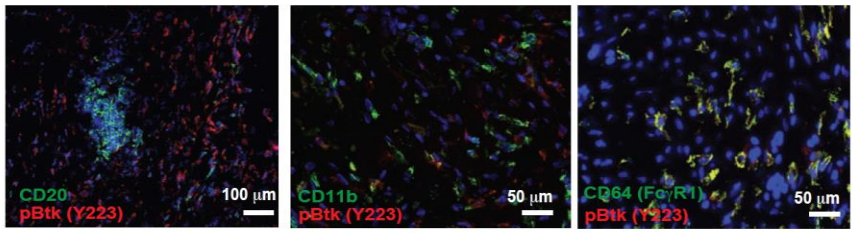
Median follow-up: 17.02 months

Fraser et al, iwCLL, 2015.

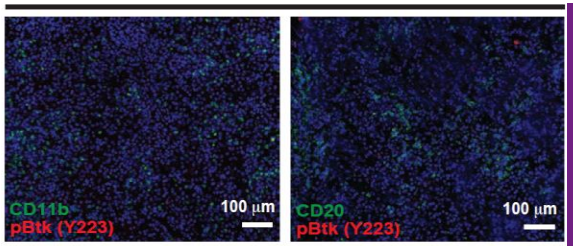
- **HELIOS** the first of three Phase 3 studies in the Imbruvica program Imbruvica-BR
  - Combination data added to USPI and approval of SLL May 2016
- **SELENE**, a fully enrolled Phase 3 study, evaluating Imbruvica+BR vs placebo-BR in **previously treated FL and MZL**
- **SHINE**, a fully enrolled Phase 3 study, assessing Imbruvica+BR vs placebo-BR **as first-line therapy for MCL**

Ongoing Investigation in Solid Tumors

Human Pancreatic Adenocarcinoma



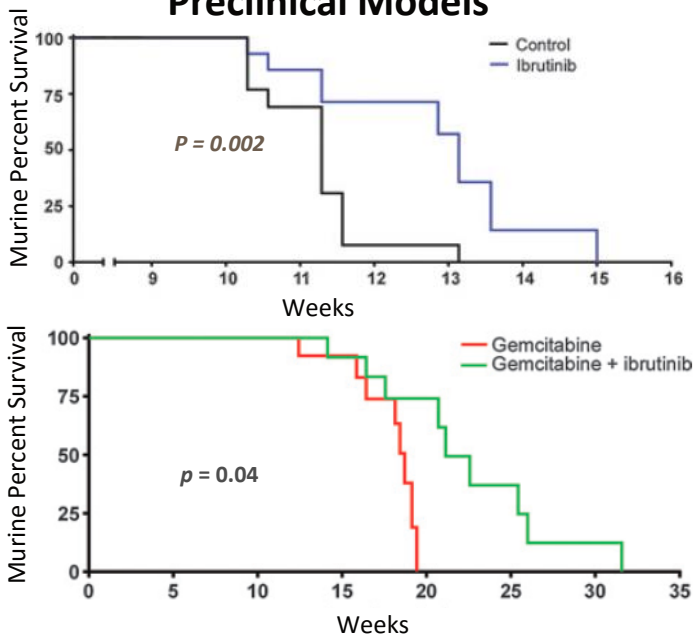
Human Spleen



Prominent phospho-BTK in CD20$^+$, CD11b$^+$ and CD64$^+$ (FcγR1) cells infiltrating human PDAC, but NOT spleen

Gunderson A *et al*. BTK-dependent immune cell crosstalk drives pancreas cancer. *Cancer Discov, 2015*

Imbruvica Prolongs Survival in Preclinical Models

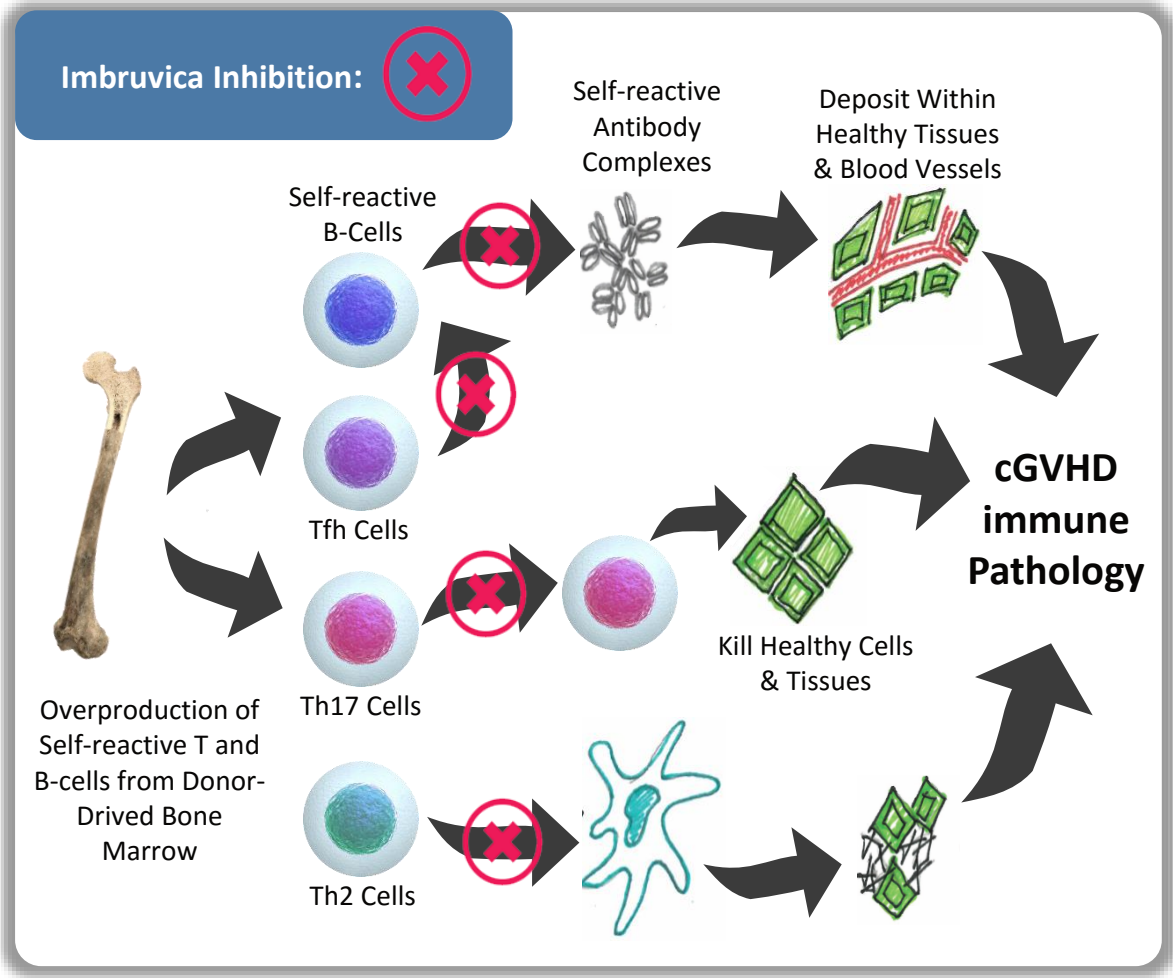


Daniel Massó-Vallés et al. Cancer Res 2015;75:1675-1681

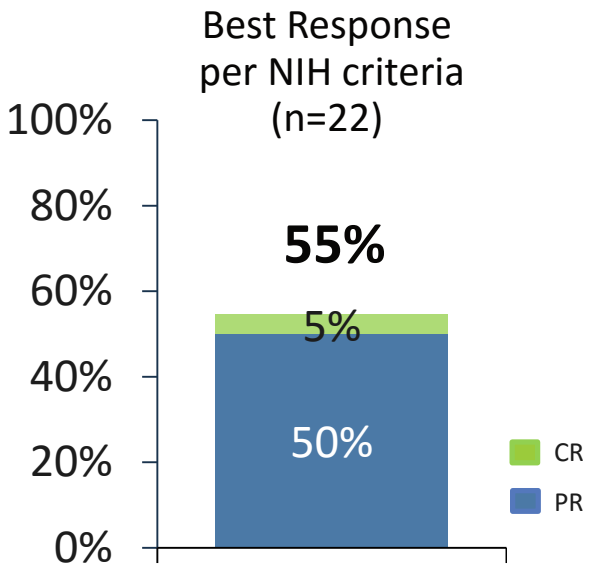
Three ongoing – enrolling company-sponsored clinical trials evaluating Imbruvica in multiple different solid tumors

- Two evaluating Imbruvica in combination with standard of care (chemotherapy or targeted agents)
  - One randomized and one basket study
- One basket study evaluating Imbruvica in combination with checkpoint inhibitor

Imbruvica, Targeting both B and T Cells Combats the Multifactorial Pathology of cGVHD Leading to Responses in High-Risk Patients



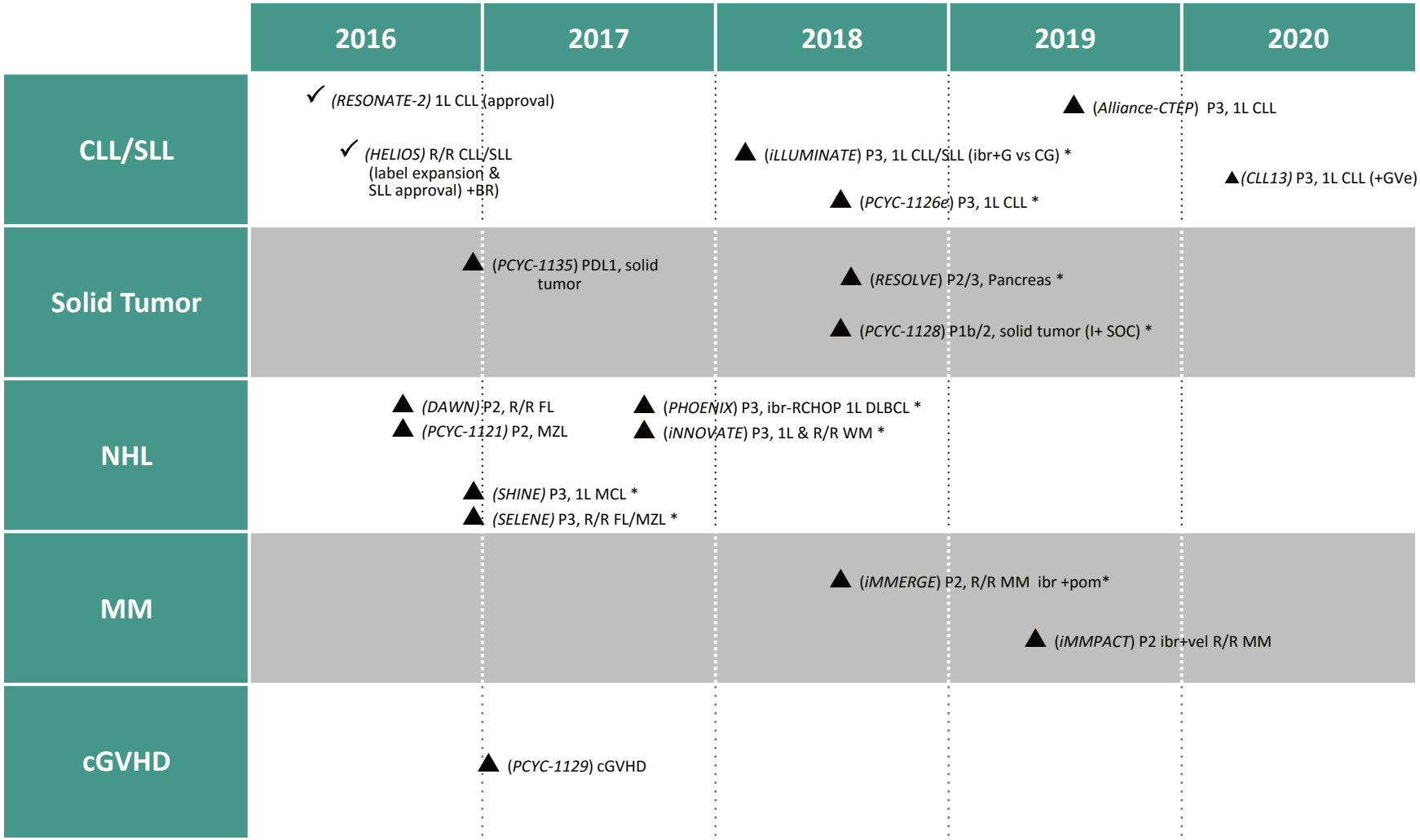
Clinical Data of Imbruvica in high-risk cGVHD



Miklos et. al European Society for Blood and Marrow Transplantation 2016

cGVHD is a common complication of stem cell transplant with substantial morbidity – where there are no approved therapies representing a significant unmet medical need

Imbruvica: Upcoming Milestones



* Approximate dates. Timing for some studies will be based on event rates and interim analysis triggers

R=Rituxan; G=Gazyva; BR=bendamustine/Rituxan; CG=chlorambucil/Gazyva; GI=Gazyva/Imbruvica; RCHOP=Rituxan, cyclcophosphamide, doxorubicin, vincristine, prednisone; Vel=velcade; Dex=dexamethasone; pom=pomalidomide

abbvie

Venclexta (venetoclax)

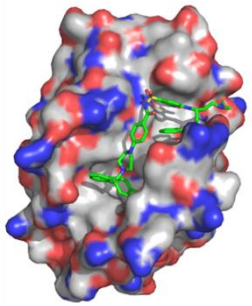
Gary Gordon, M.D., Ph.D.

AbbVie Has Pioneered the Field of BCL-2 Inhibition

NATURE · VOL 381 · 23 MAY 1996

X-ray and NMR structure of human Bcl-x_L, an inhibitor of programmed cell death

Steven W. Muchmore*, Michael Sattler†, Heng Liang†, Robert P. Meadows‡, John E. Harlan†, Ho Sup Yoon†, David Nettesheim†, Brian S. Chang§, Craig B. Thompson§, Sui-Lam Wong||¶, Shi-Chung Ng|| & Stephen W. Fesik†



nature medicine

VOLUME 19 | NUMBER 2 | FEBRUARY 2013

ABT-199, a potent and selective BCL-2 inhibitor, achieves antitumor activity while sparing platelets

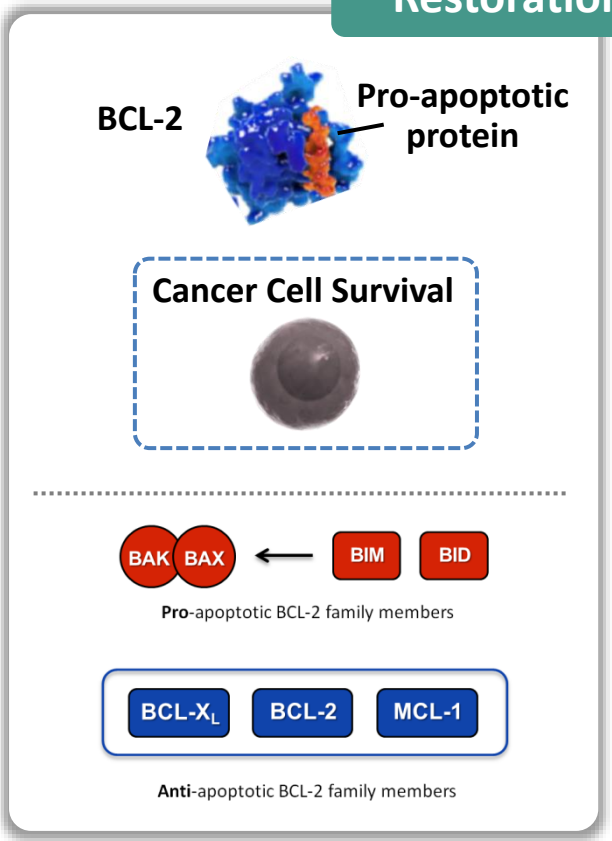
Andrew J Souers[1], Joel D Leverson[1], Erwin R Boghaert[1], Scott L Ackler[1], Nathaniel D Catron[1], Jun Chen[1], Brian D Dayton[1], Hong Ding[1], Sari H Enschede[1], Wayne J Fairbrother[2], David C S Huang[3,4], Sarah G Hymowitz[2], Sha Jin[1], Seong Lin Khaw[3,4], Peter J Kovar[1], Lloyd T Lam[1], Jackie Lee[2], Heather L Maecker[2], Kennan C Marsh[1], Kylie D Mason[3–5], Michael J Mitten[1], Paul M Nimmer[1], Anatol Oleksijew[1], Chang H Park[1], Cheol-Min Park[1,7], Darren C Phillips[1], Andrew W Roberts[3–5], Deepak Sampath[2], John F Seymour[4,6], Morey L Smith[1], Gerard M Sullivan[1], Stephen K Tahir[1], Chris Tse[1], Michael D Wendt[1], Yu Xiao[1], John C Xue[1], Haichao Zhang[1], Rod A Humerickhouse[1], Saul H Rosenberg[1] & Steven W Elmore[1]

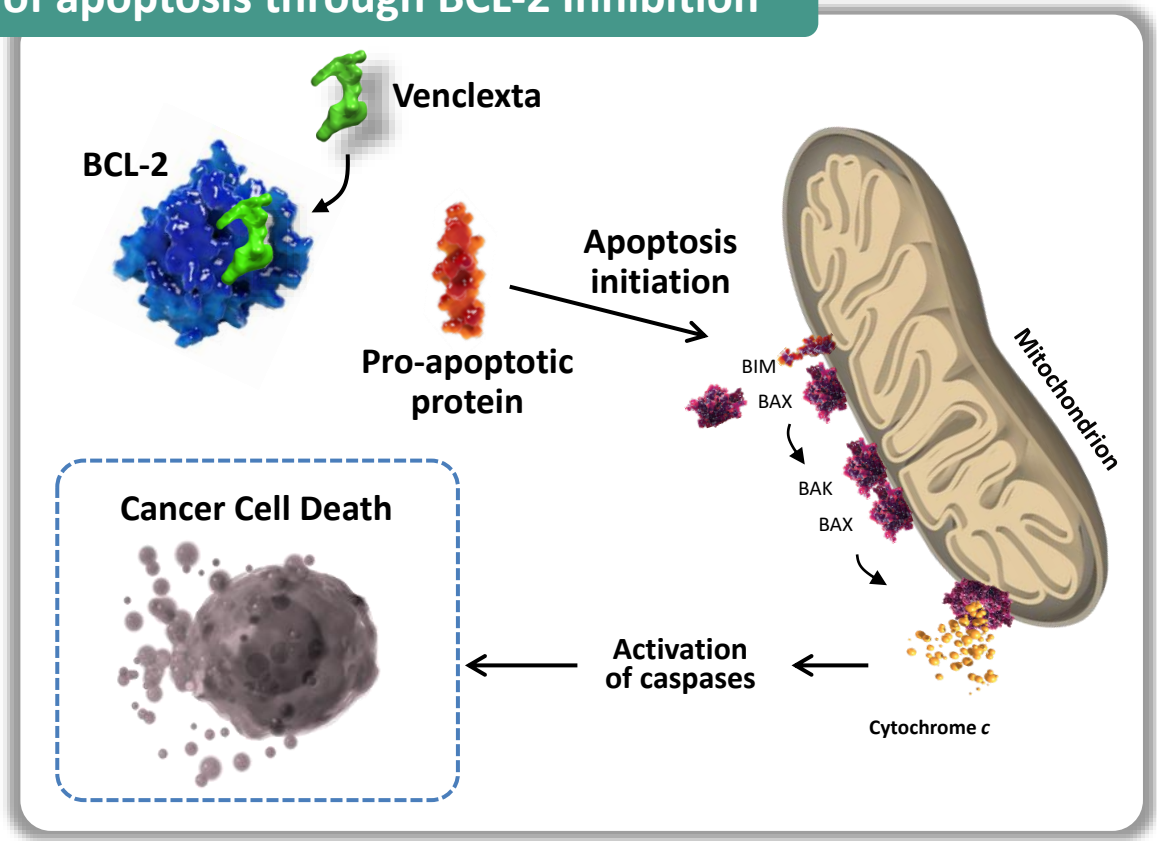
Venclexta Mechanism of Action

- Ability to evade apoptosis (programmed cell death) is a hallmark of cancer
- Increased production of BCL-2 proteins is a key mechanism for preventing the apoptotic process from occurring
- Venclexta binds selectively to BCL-2 proteins initiating a cascade of events leading to rapid cell death

Venclexta Is a BCL-2 Selective Inhibitor

Restoration of apoptosis through BCL-2 Inhibition





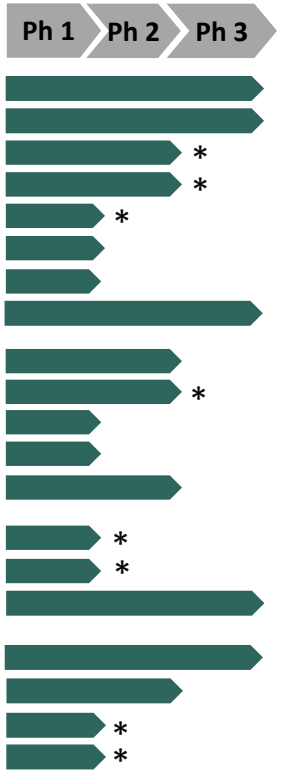
BCL-2 overexpression allows cancer cells to evade apoptosis by sequestering pro-apoptotic proteins.

Venclexta binds selectively to BCL-2, freeing pro-apoptotic proteins that initiate programmed cell death (apoptosis).

Venclexta Has Significant Potential Across a Range of Hematologic Malignancies With High Unmet Need

VENCLEXTA™
venetoclax tablets

	Combination (study name)	Indication
CLL	*+Rituxan (MURANO)*	r/r CLL
	+Gazyva (CLL14)	CLL
	monotherapy	r/r CLL 17p
	monotherapy	r/r CLL after BCRi
	+Rituxan	r/r CLL & SLL
	+BR	r/r CLL & CLL
	+Gazyva	r/r CLL & CLL
	+Gazyva/Imbruvica (CLL13) [(a)]	1L CLL
NHL	*+Rituxan vs BR (CONTRALTO)*	r/r FL
	+R-CHOP vs R-CHOP (CAVALLI)	1L DLBCL
	+BR	r/r NHL
	monotherapy	r/r CLL & r/r NHL
	+Gazyva/polatuzumab	DLBCL & FL
MM	*monotherapy*	r/r MM
	+bortezomib/dex	r/r MM
	+bortezomib/dex [(a)]	r/r MM
AML	*+dec / +aza* [(a)]	AML
	monotherapy	AML
	+dec / +aza	AML
	+Ara-C	AML

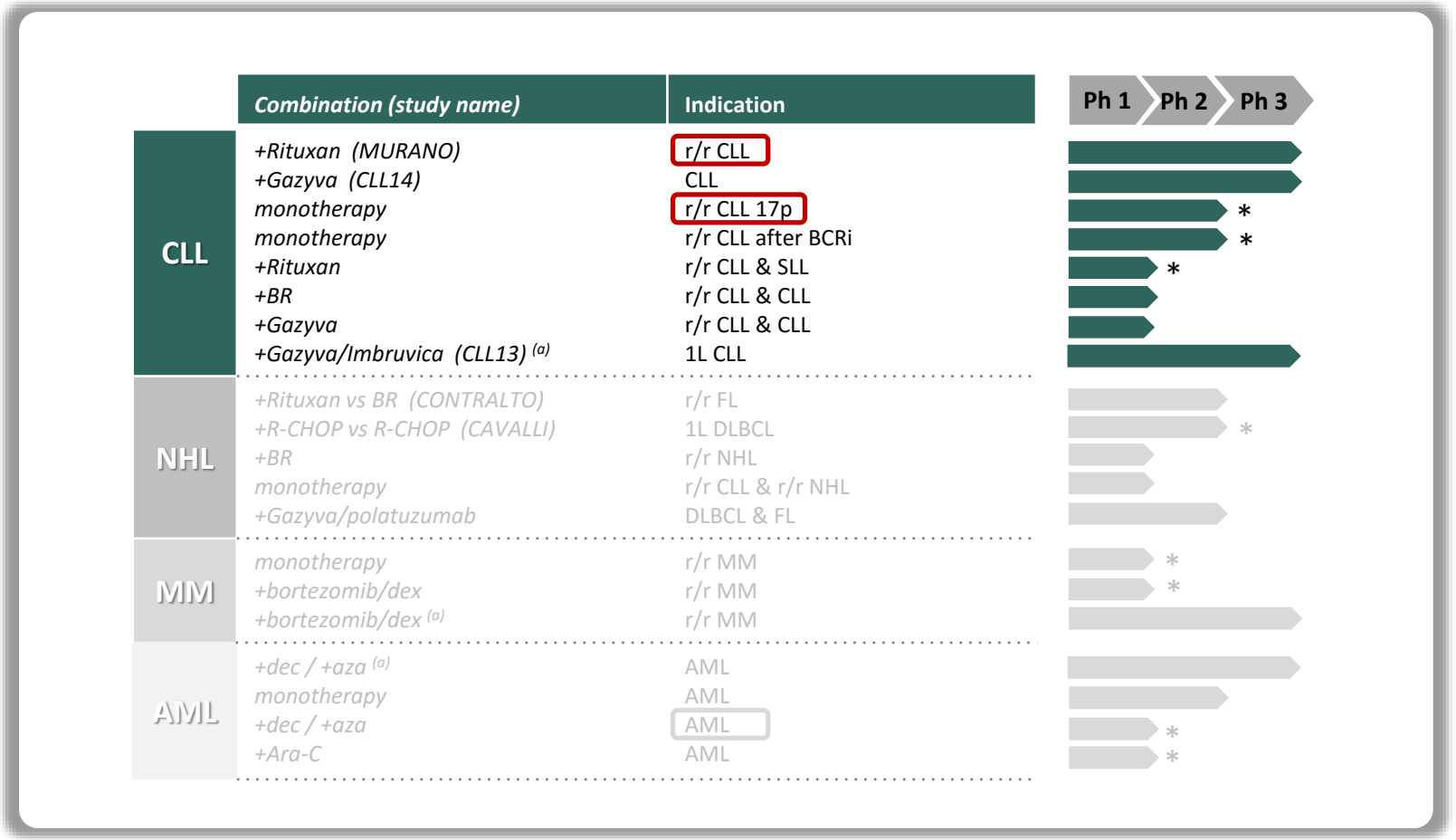


(a) Starting H2:2016.

* Data to be presented at ASCO.

Supported by three breakthrough therapy designations

Venclexta Has Significant Potential Across a Range of Hematologic Malignancies With High Unmet Need



(a) Starting H2:2016.

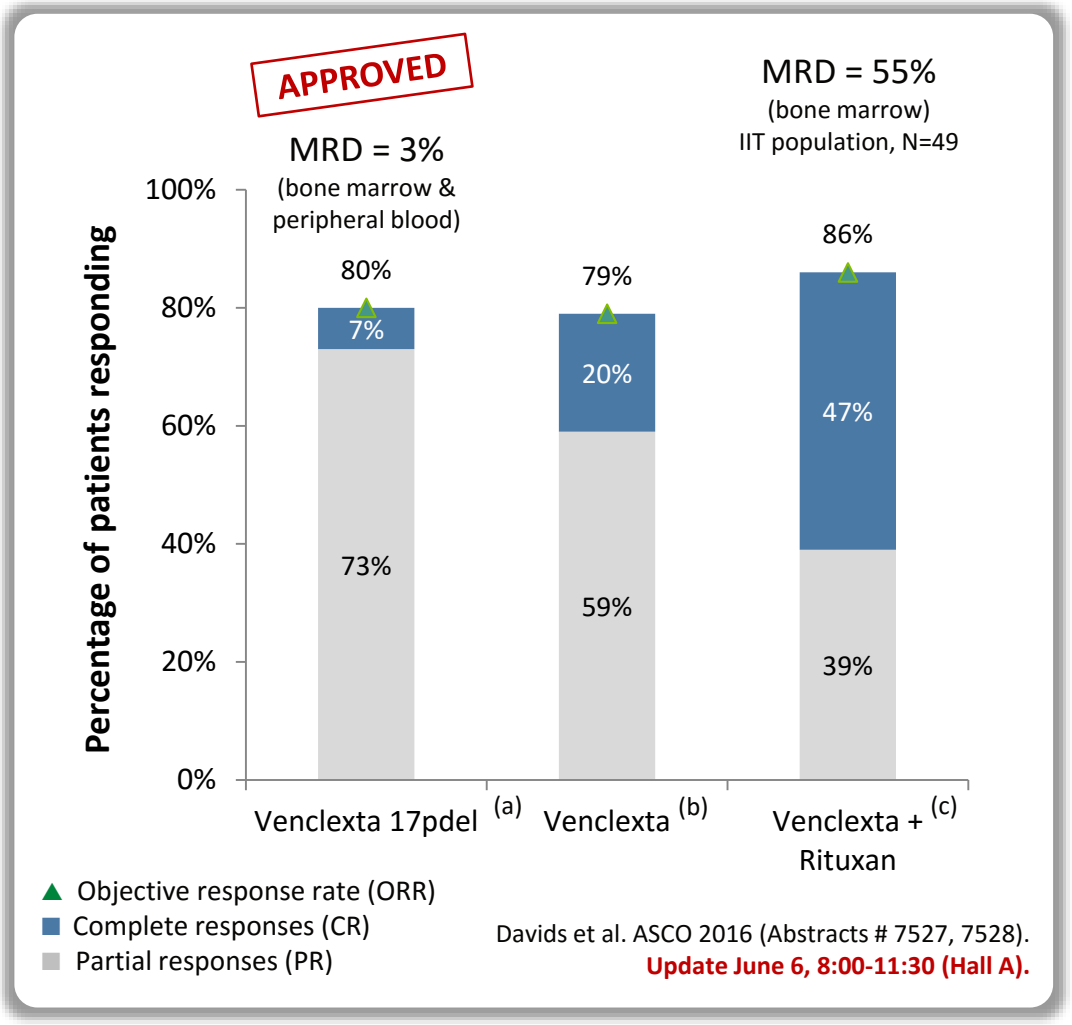
Supported by three breakthrough therapy designations

Venclexta: Approved for R/R CLL with 17p Deletion

- FDA approved for r/r 17p deletion CLL
- Active in broader CLL population
- Next anticipated indication: combination with rituximab
- Minimal residual disease (MRD) negativity – no detectable CLL cells in the patients' bone marrow

« Next step: Phase 3 in 1L CLL »

RESPONSE RATES IN RELAPSED CLL



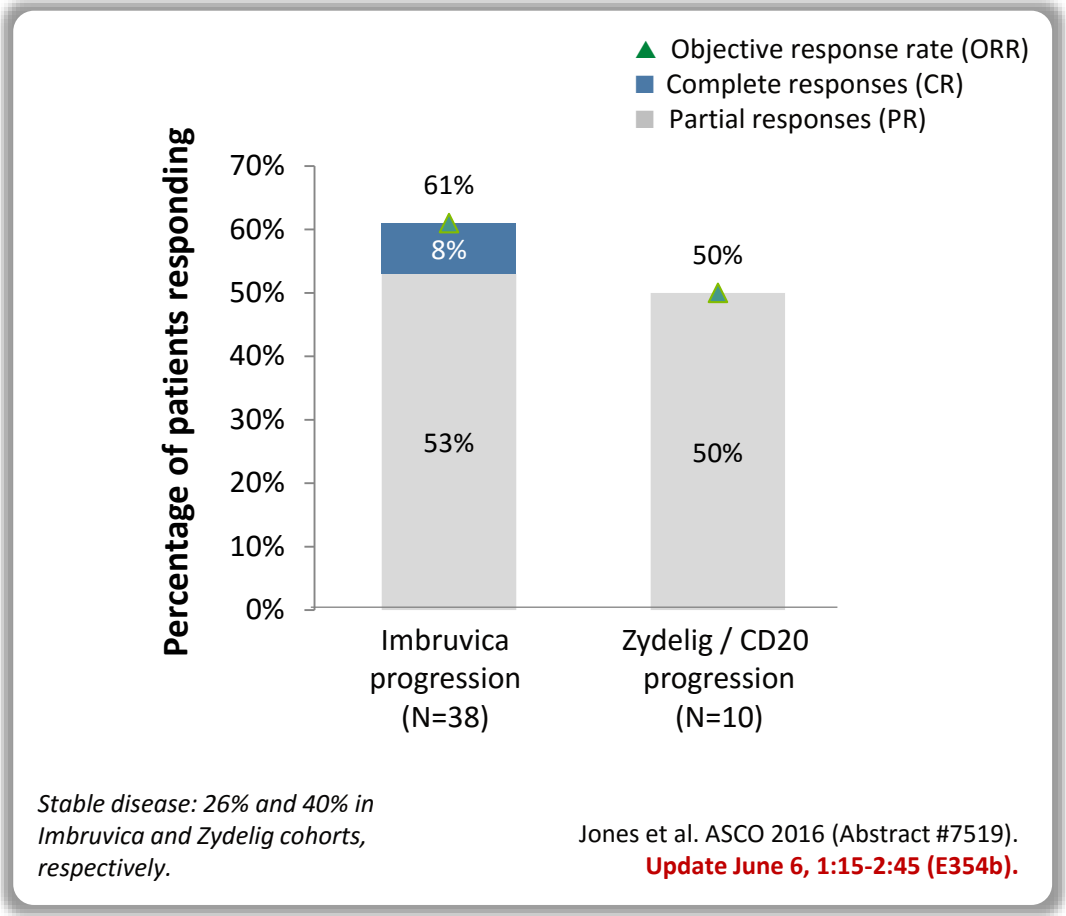
(a) Venclexta package insert. (b) Roberts et al, NEJM 2016. (c) Ma et al. ASH 2015.

Venclexta Monotherapy in CLL Patients Who Progress on BCRi Regimens is Highly Effective

BCRi – inhibitor of B-cell receptor signaling pathway.

- Progression can be rapid when B receptor pathway inhibitors fail
- Treatment options are limited and prognosis is poor
- Alternatives are required to meet this unmet need

RESPONSES AT 24 WEEKS ON VENCLEXTA AFTER BCRi



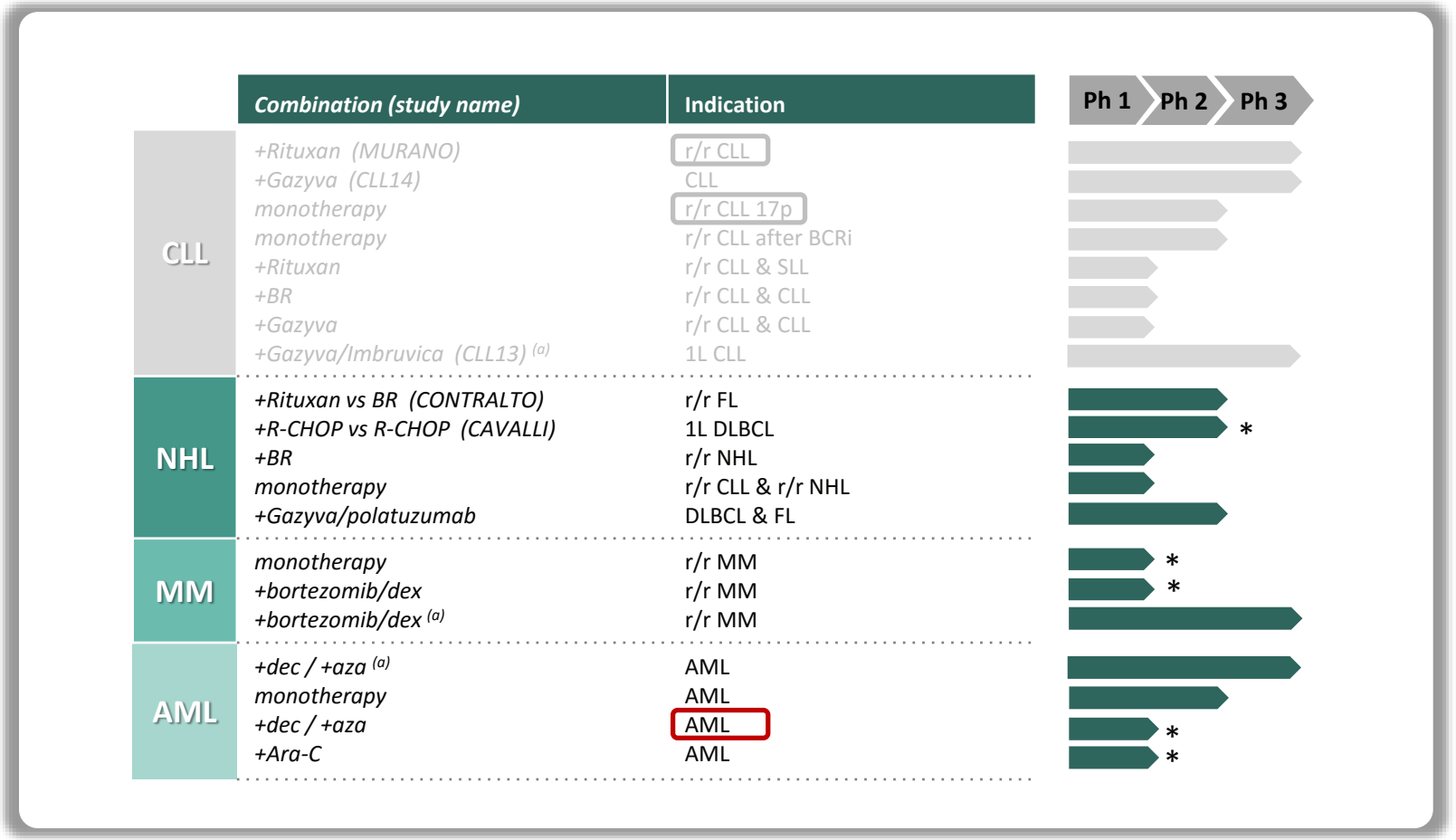
Stable disease: 26% and 40% in Imbruvica and Zydelig cohorts, respectively.

Jones et al. ASCO 2016 (Abstract #7519).
Update June 6, 1:15-2:45 (E354b).

O'Brien et al. ASCO 2016 (Abstract #7520)

« Next step: Phase 2 readout in 2017 »

Venclexta Has Significant Potential Across a Range of Hematologic Malignancies with High Unmet Need

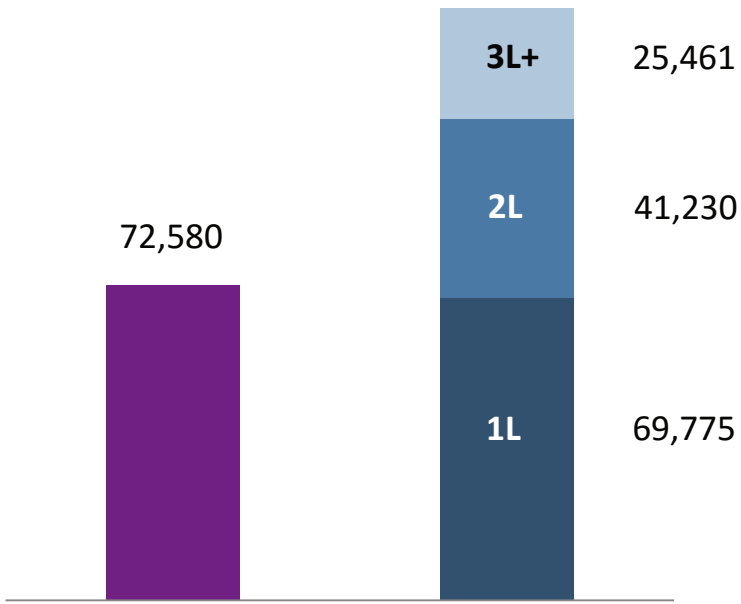


(a) Starting H2:2016.

Supported by three breakthrough therapy designations

Non-Hodgkin Lymphoma

U.S. Epidemiology



- 20,150 deaths annually -

Sources: American Cancer Society, SEER, Kantar Health.

Disease

- Median age at diagnosis: 66
- Multiple subtypes: aggressive (DLBCL, MCL) and indolent (FL, CLL/SLL)
- DLBCL 50% cure; FL median PFS 70 months

Standard of Care

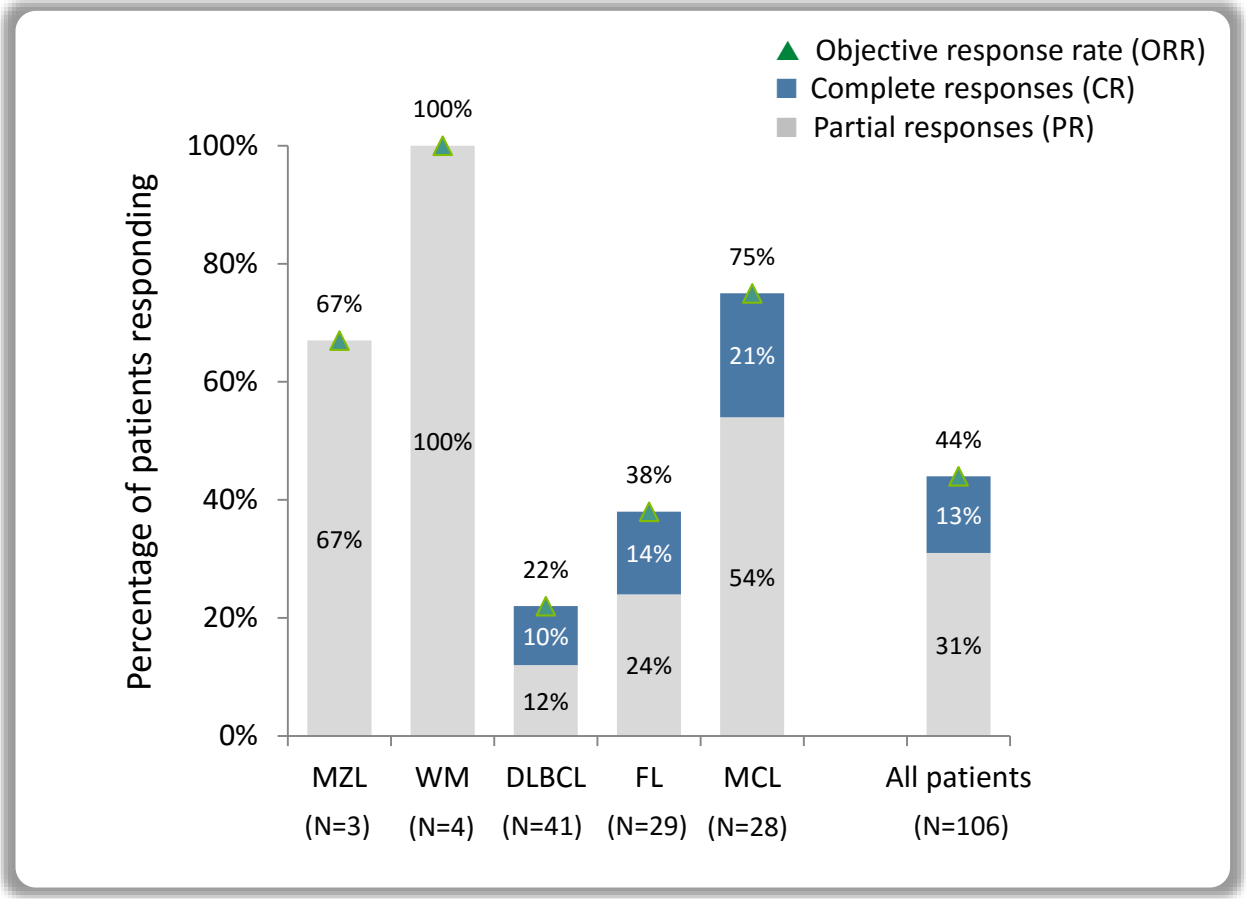
- R-CHOP, BR
- Rituxan
- Imbruvica (MCL)

Unmet Needs

- Curative treatment (FL)
- More efficacious therapies for relapsed/refractory aggressive disease (DLBCL)

Venclexta Monotherapy Has Demonstrated Clear Activity in R/R NHL

OBJECTIVE RESPONSES

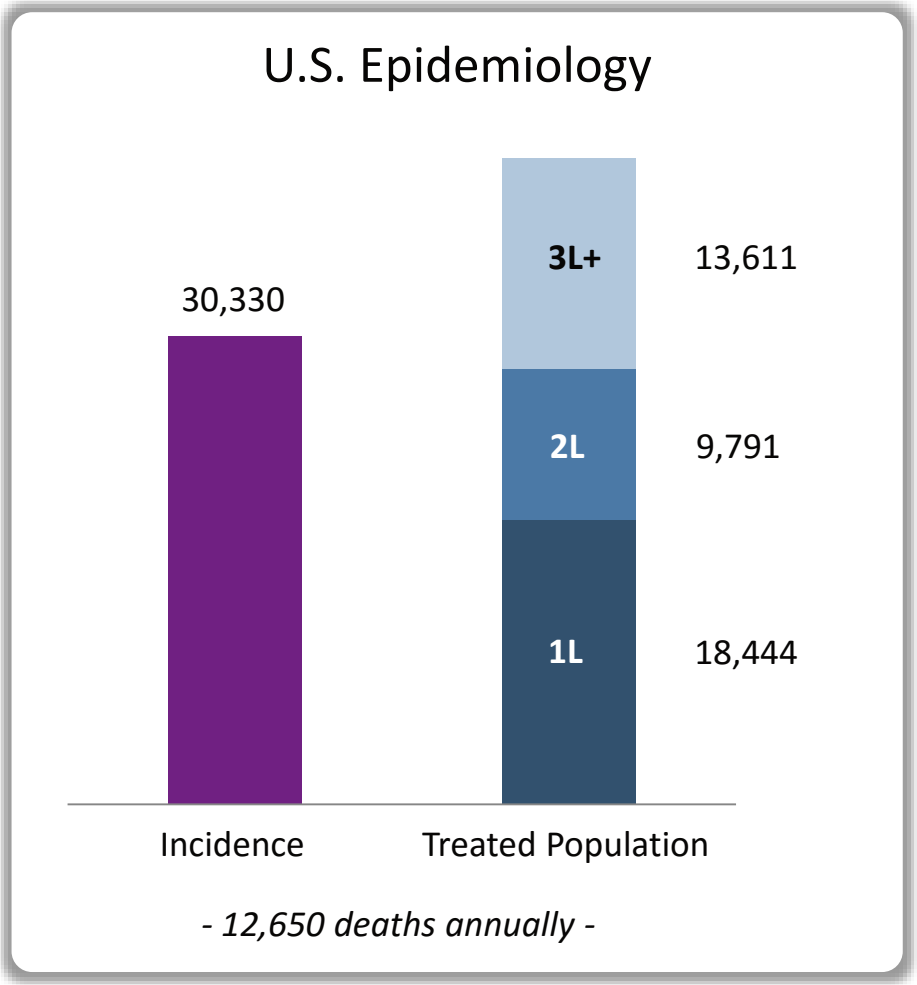


Gerecitano et al. ASH 2015.

« Next step: Phase 2 readouts (1L DLBCL, *CAVALLI and r/r FL, *CONTRALTO*) in 2017 »**

* Zelenz et al. ASCO 2016 (Abstract #7566). **Update June 6, 8:00-11:30 (Hall A).**

Multiple Myeloma



Disease

- Median age at diagnosis: 69
- Five-year survival: 48%

Standard of Care

- Velcade/Revlimid/Dex
- Pomalyst, Kyprolis
- New agents:
  Empliciti, Darzalex, Ninlaro

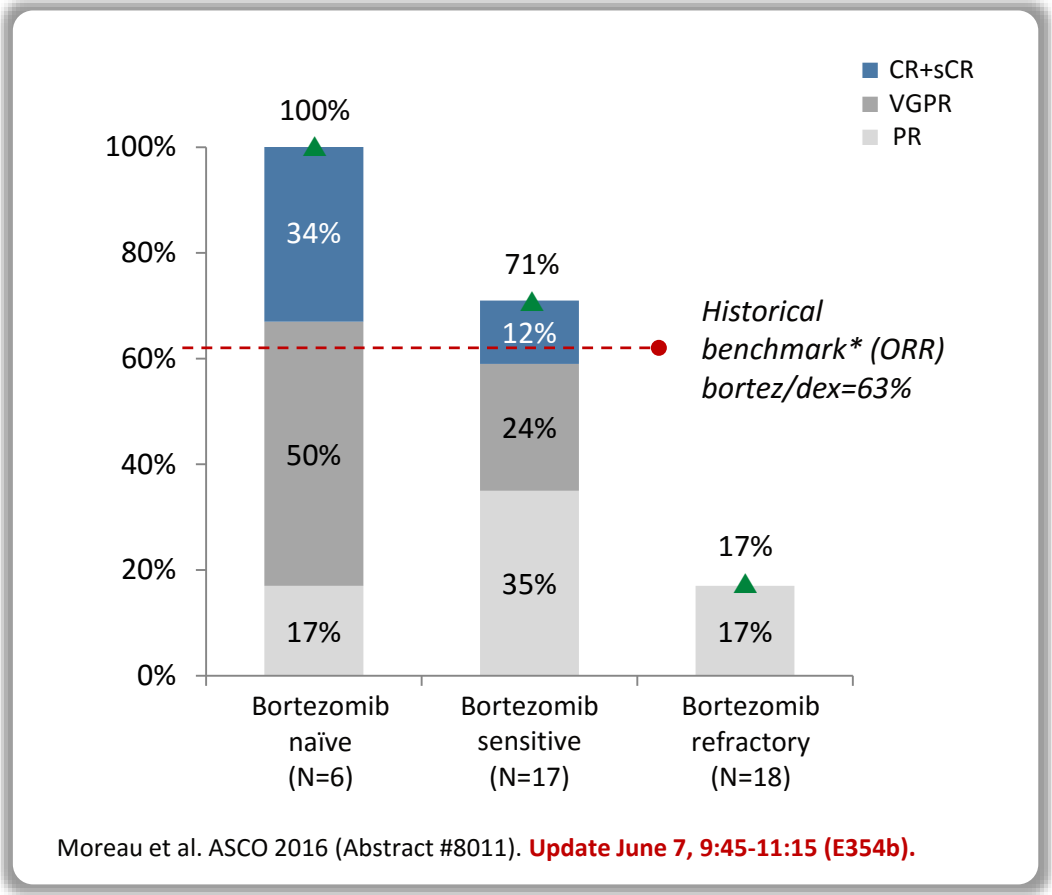
Unmet Needs

- Curative treatment
- Therapies for relapse/refractory patients

Sources: American Cancer Society, SEER, Kantar Health.

Venclexta Plus Bortezomib-dexamethasone Is Active in MM

Strong mechanistic rationale for combination of Venclexta with the proteasome inhibitor bortezomib, which is a cornerstone therapy in multiple myeloma



Moreau et al. ASCO 2016 (Abstract #8011). **Update June 7, 9:45-11:15 (E354b).**

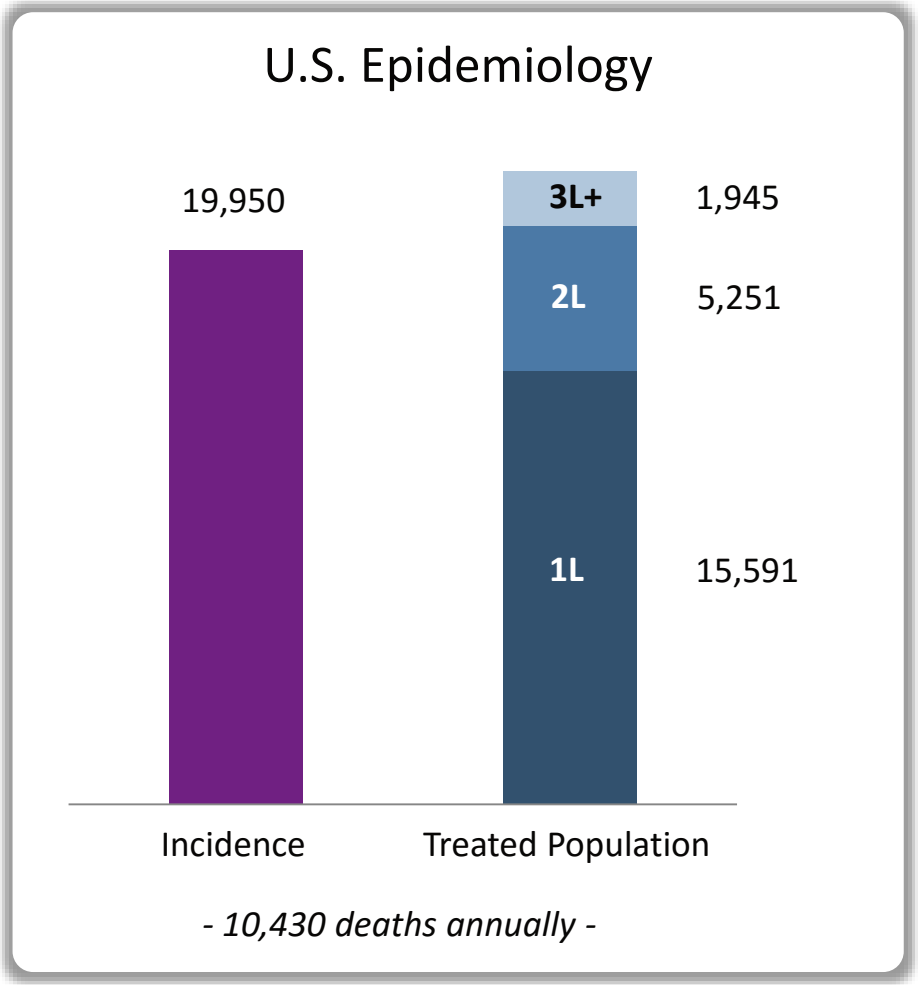
- Overall response rates in r/r MM are superior to historical Velcade data and encouraging compared to novel regimens
- Deep responses (VGPR or CR) in half of these patients
- >80% response rates in patients who received one to three prior lines of therapy

CR=complete response; sCR=stringent complete response; VGPR=very good partial response; PR=partial response; bortez/dex=bortezomib, dexamethasone.

« Next step: Phase 3 trial start (r/r MM) in H2:16 »

* Bortezomib naïve, sensitive, 1-3 prior treatments (ENDEAVOR trial. Dimepoulos et al. Lancet Oncol 2016)

Acute Myeloid Leukemia



Sources: American Cancer Society, SEER, Kantar Health.

Disease

- Median age at diagnosis: 67
- Five-year survival: 27% (<5% in pts 65+ yrs.)
- No improvements in treatment in 25 yrs.

Standard of Care

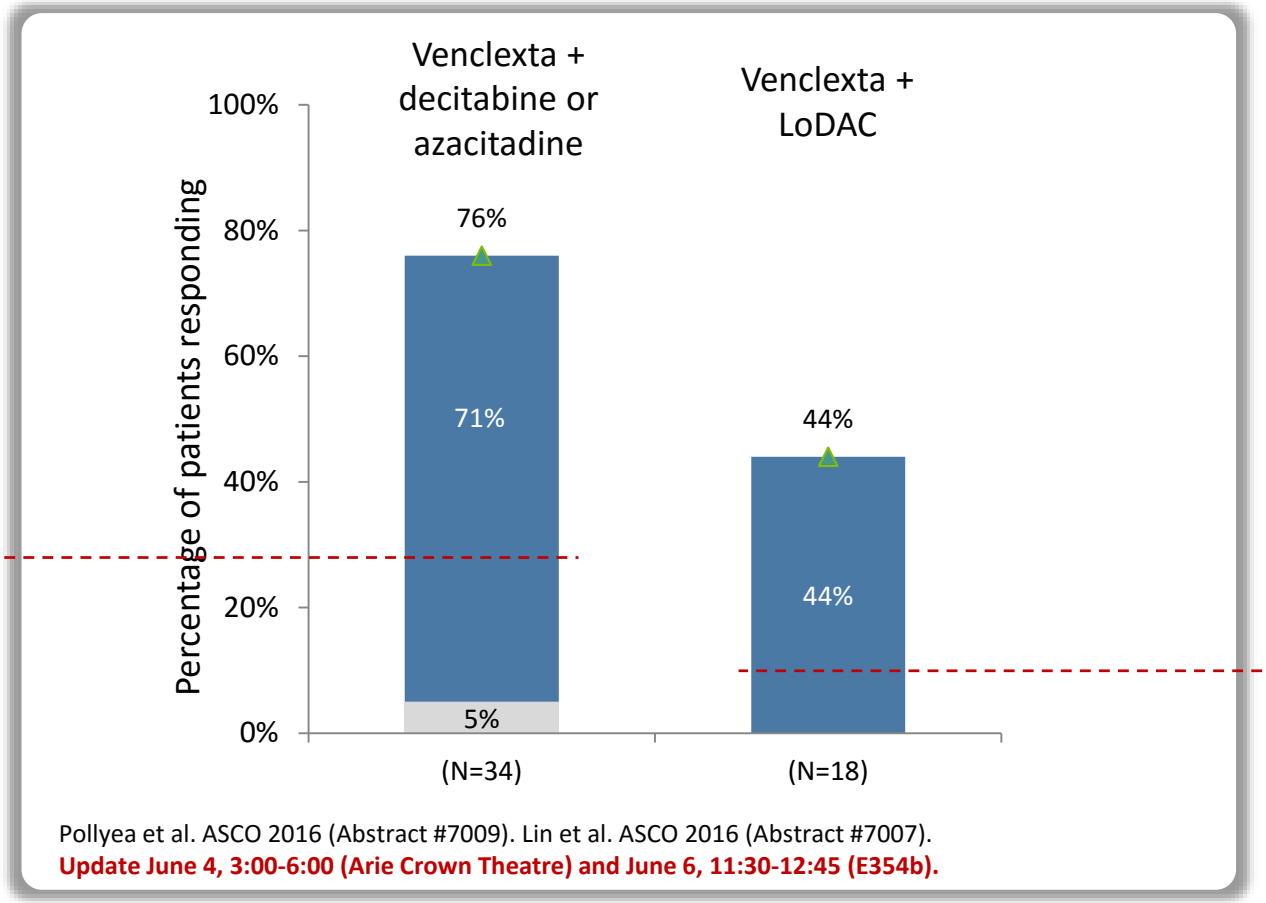
- Younger patients, high-dose intensive chemo (cytarabine/anthracycline)
- Patients with co-morbidities (low-dose cytarabine, hypomethylators)
- Stem-cell transplant

Unmet Needs

- Stem-cell transplant only curative therapy
- Improved options for patients unable to tolerate intensive therapy
- Improved survival for relapsed/refractory setting

Venclexta Has Demonstrated Significant Activity in AML and Is Supported by FDA Breakthrough Therapy Designation

OBJECTIVE RESPONSES



Historical benchmarks (CR+CRi)
azacitidne = 28%
decitabine = 26%

Dombret et al. Blood 2015.
Kantarjian et al. JCO 2012.

Historical benchmark (CR+CRi)
LoDAC = 11%

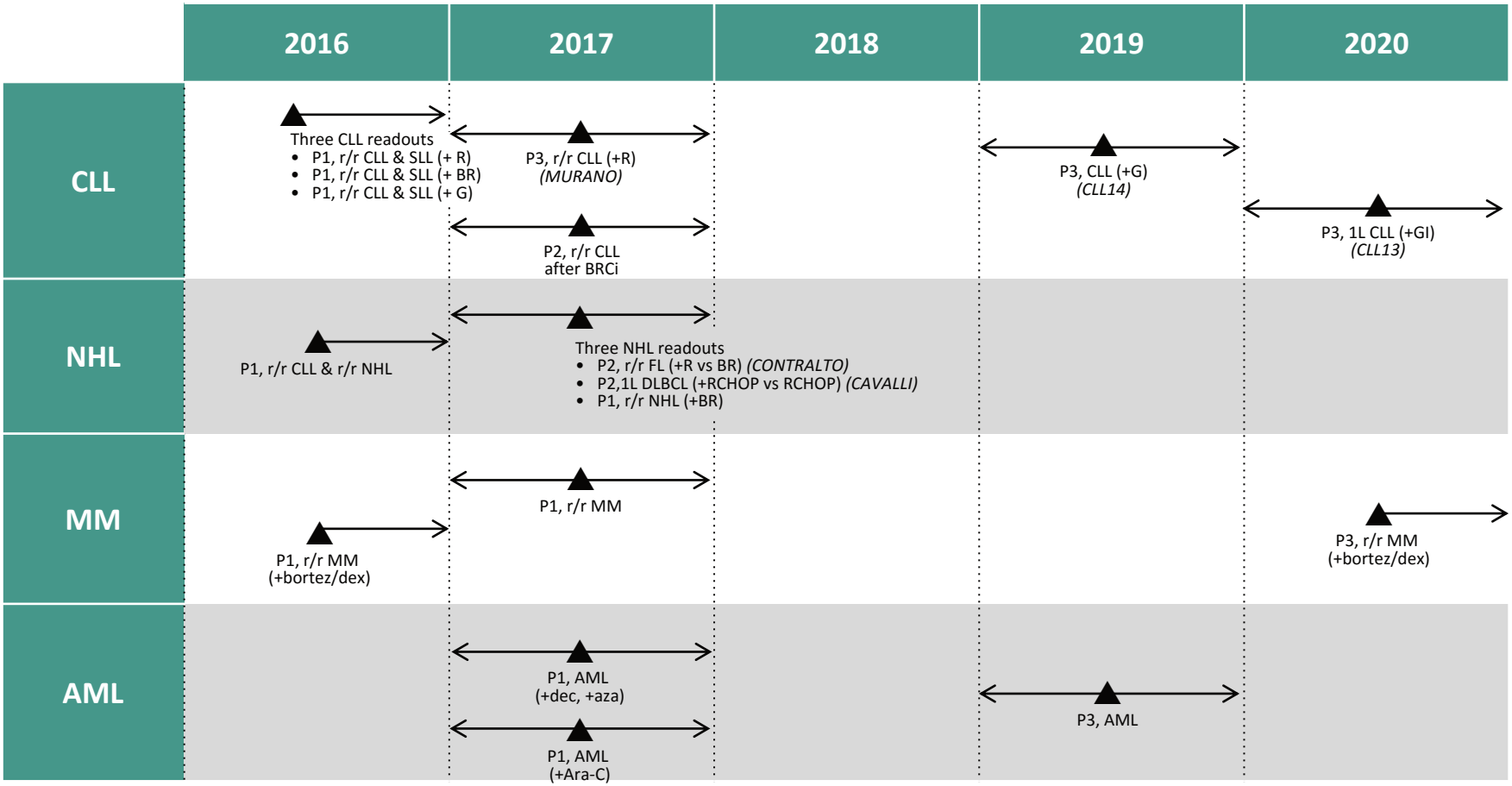
Kantarjian et al. JCO 2012.

Pollyea et al. ASCO 2016 (Abstract #7009). Lin et al. ASCO 2016 (Abstract #7007).
Update June 4, 3:00-6:00 (Arie Crown Theatre) and June 6, 11:30-12:45 (E354b).

CR = complete remission. CRi = complete remission with incomplete blood count recovery.

« Next step: Phase 3 trial start in H2:2016 »

Venclexta: Upcoming Milestones



* Approximate dates. Timing for some studies will be based on event rates and interim analysis triggers

R=Rituxan; G=Gazyva; BR=bendamustine/Rituxan; GI=Gazyva/Imbruvica; RCHOP=Rituxan, cyclcophosphamide, doxorubicin, vincristine, prednisone; Bortez=bortezomib; Dex=dexamethasone; Dec=decitabine; Aza=azacitidine; Ara-C=cytarabine.

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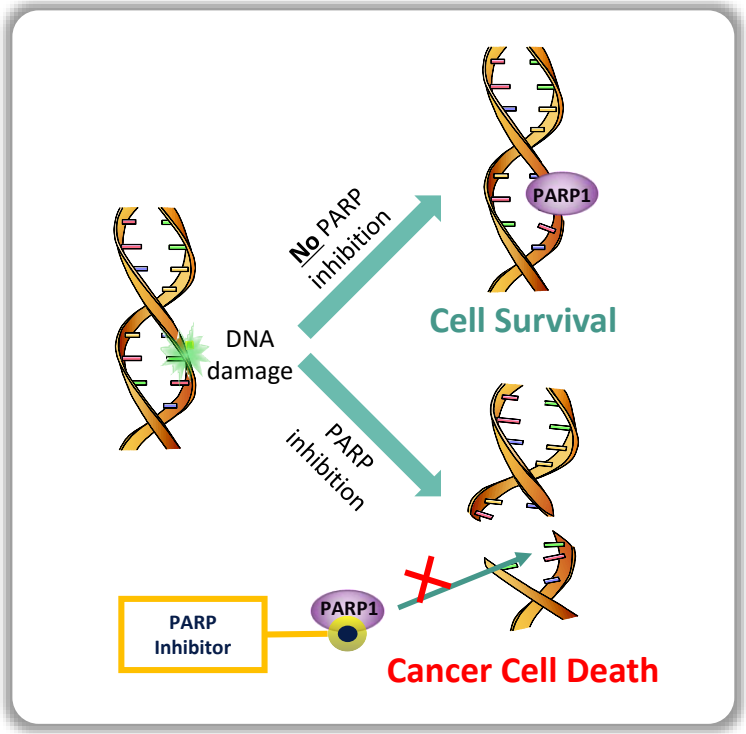
Veliparib and ABT-414

Veliparib Activity in Phase 2 Trials Provides Evidence for: 1) Monotherapy Efficacy; and 2) Synergy with Chemotherapy

Veliparib inhibits PARPs 1 and 2 which are critical nuclear enzymes for DNA damage repair

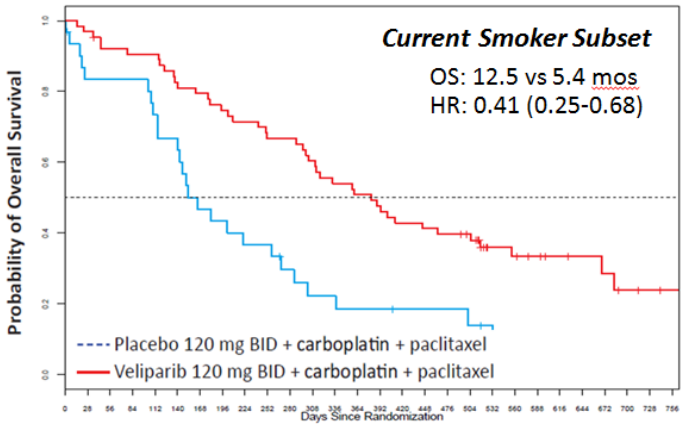


1 **Veliparib has demonstrated single-agent activity in BRCA-deficient tumors**

Population (study)	N	ORR (%)
Recurrent ovarian cancer (GOG 0280)	50	26
Recurrent ovarian cancer (CTEP 8282)	39	40
Recurrent ovarian cancer (VeliBRCA)	32	65 [(a)]

(a) RECIST or GCIG CA125 criteria.

2 **Overall survival benefit in a pre-specified population of smokers in a randomized trial (n = 95)**



Veliparib Has Built a Foundational Strategy Across BRCA and non-BRCA Tumors in Combination with Standard Chemotherapy

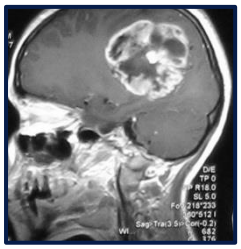
Hypothesis	Pivotal Phase 3 Trials Underway	Follow-on Indications
Genetic Defects + DNA-Damaging Chemotherapy Inherited defects in BRCA1/2, impair DNA repair	1-3L BRCA Breast (BROCADE3) 1L Ovarian (VELIA)	Tumors with HRD phenotype e.g., Fanconi anemia related, prostate, pancreas
DNA-Damaging Chemotherapy (non-BRCA) Reliance on PARP-mediated DNA repair (NER/TLS)	1L NSCLC SQ (VELA) 1L NSCLC NonSQ (VESTA) TNBC Neo-adjuvant (BRIGHTNESS)	Indications where platinums or topoisomerase inhibitors are used as standard therapies

« Readouts anticipated between 2017–2019 »

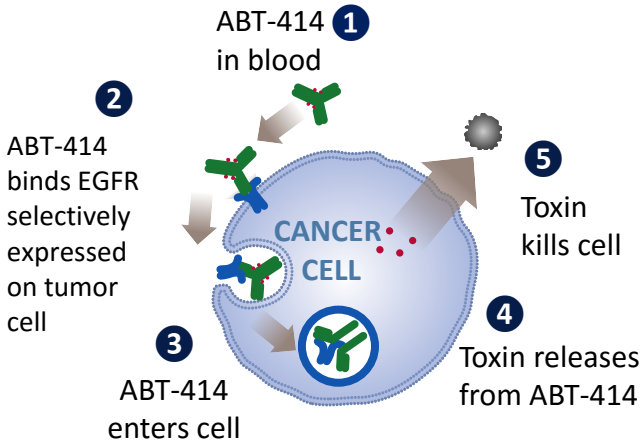
ABT-414 Is an Antibody-Drug Conjugate (ADC) Which Targets Epidermal Growth Factor Receptor (EGFR)

Glioblastoma (GBM) kills more than 95% of those diagnosed

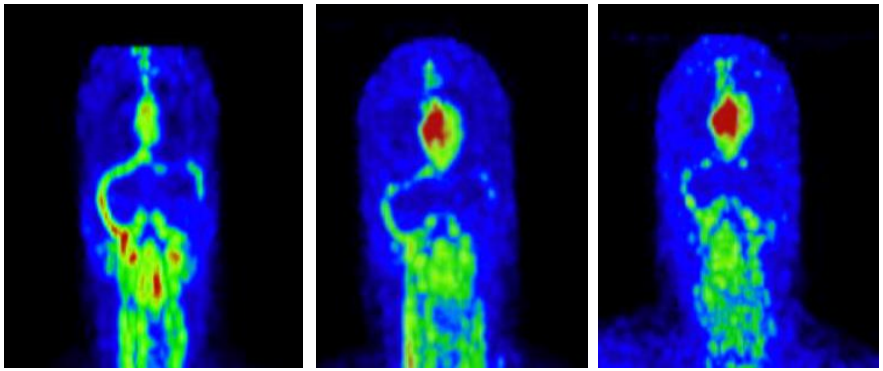
- Most common primary brain tumor in adults (peak age 55–65 yr)
- Grows rapidly and infiltrates tissue
- Chemotherapy has marginal benefit
  - Median survival of ~14 months
  - 5-year survival rate of <5%
- Worldwide incidence ~28,000



- ABT-414 targets unique epitope exposed upon EGFR activation
- Activation occurs when either EGFR is amplified or has vIII mutation
- Selective binding to tumors confirmed in first-in-human and imaging studies
- No typical EGFR inhibitor skin rash



Zirconium ImmunoPET in a patient with GBM

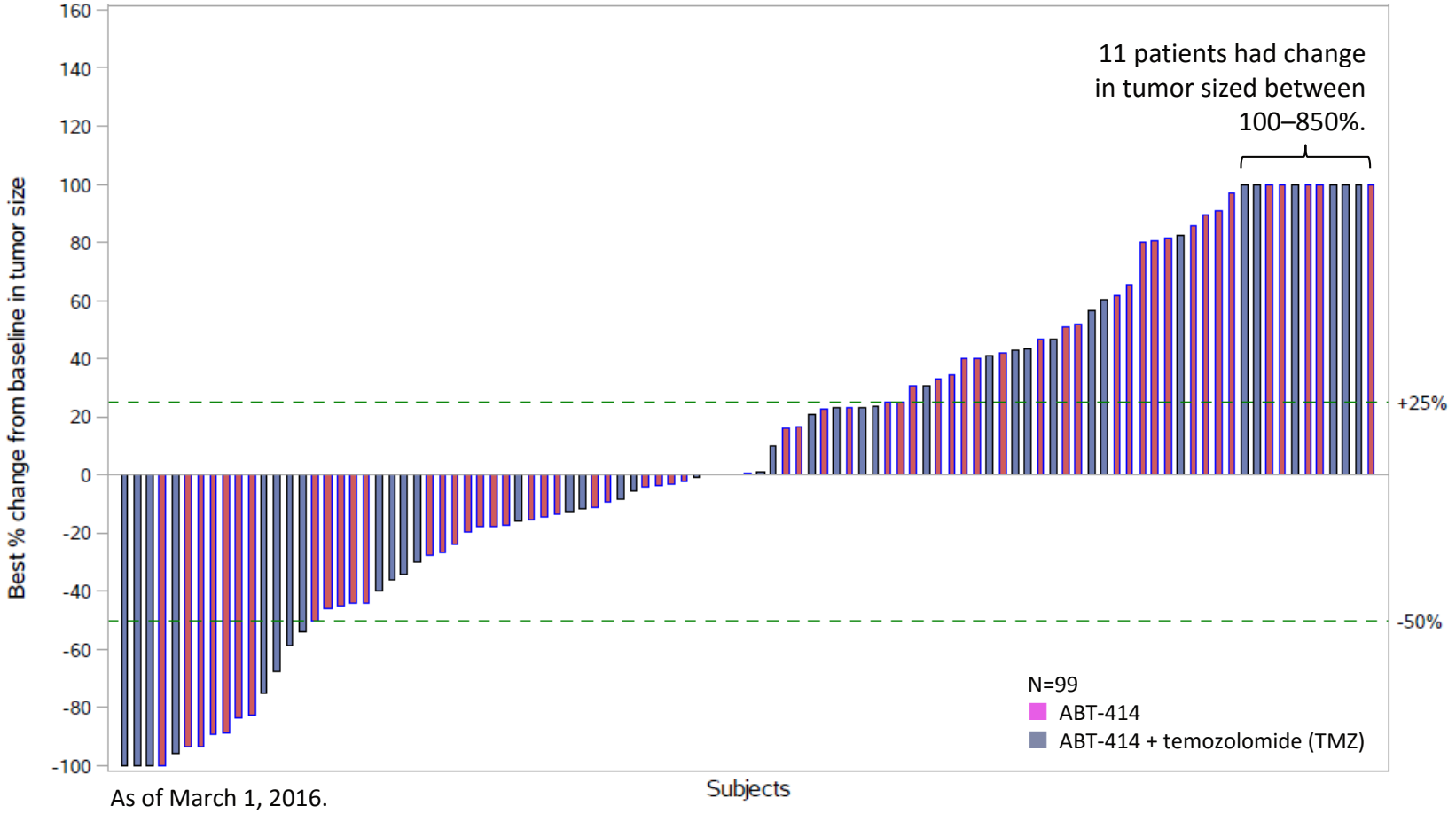


4h **72h** **120h**

ABT-414 Has Encouraging Efficacy in Refractory GBM

Best percent change from baseline in tumor size (target lesion)

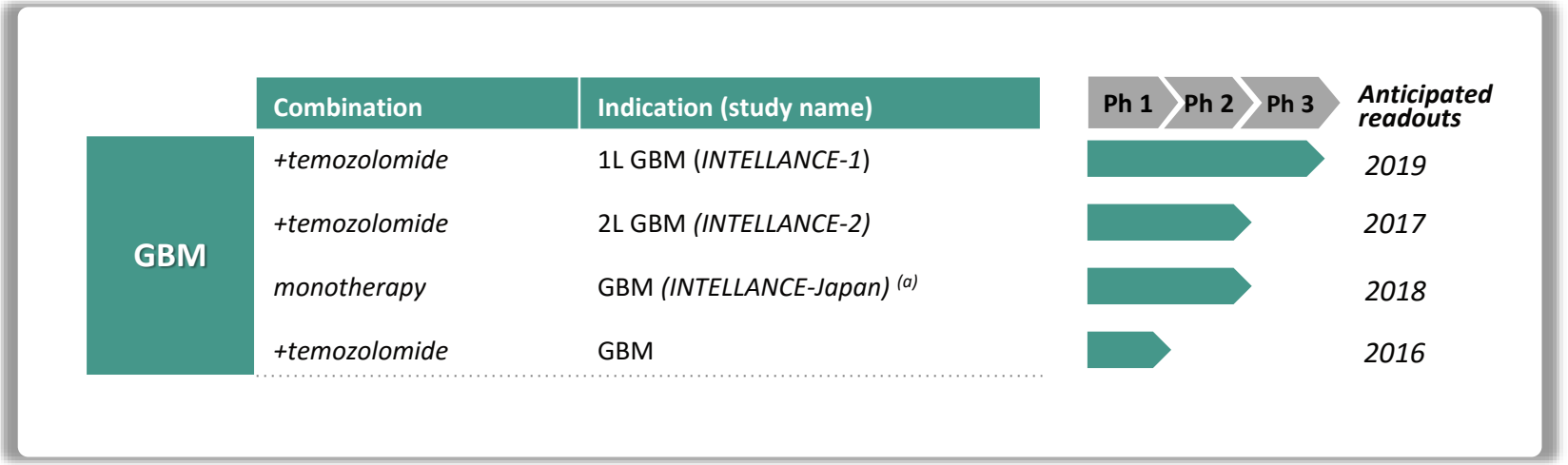
– monotherapy and combination with TMZ in recurrent GBM and EGFR amplified positive –



As of March 1, 2016.

AbbVie Has Launched an Aggressive Program in GBM for ABT-414

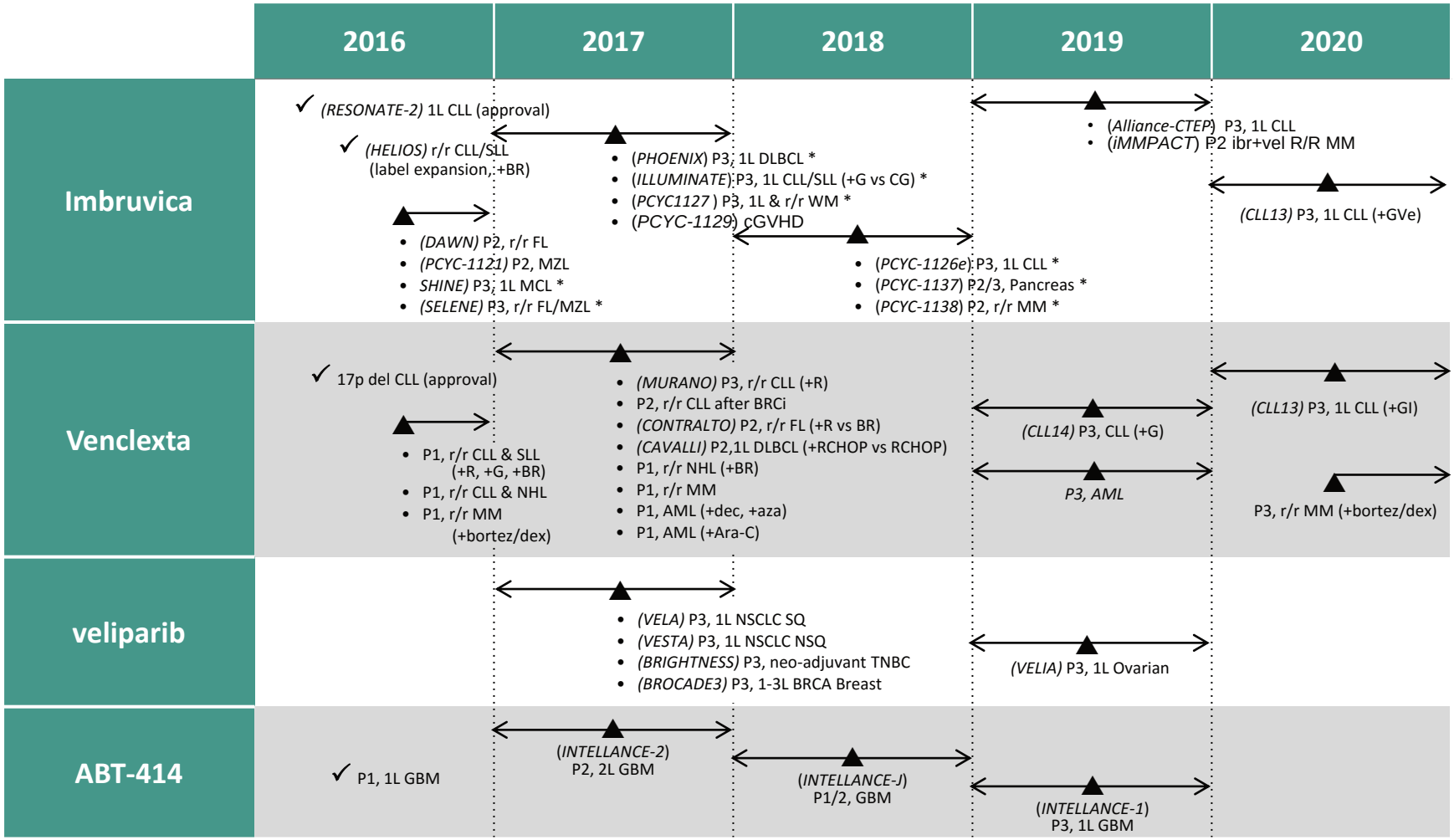
- Since the first patient with GBM was treated with ABT-414 (2013), ABT-414 has advanced to international, randomized trials
- ABT-414 is now being studied in over 30 countries in both recurrent and front-line settings
- Collaborations with recognized, academic cooperative groups (EORTC, RTOG)
- Biomarker work will refine the population most likely to benefit (e.g., EGFR amp+)



(a) Phase I/II.

EORTC – European Organization for Research and Treatment of Cancer. RTOG – Radiation Therapy Oncology Group.

We Expect Our Oncology Pipeline To Show Significant Advancement Over the Next Two to Three Years



R=Rituxan; G=Gazyva; BR=bendamustine/Rituxan; CG=chlorambucil/Gazyva; GI=Gazyva/Imbruvica; RCHOP=Rituxan, cyclcophosphamide, doxorubicin, vincristine, prednisone; Bortez=bortezomib; Dex=dexamethasone; Dec=decitabine; Aza=azacitidine; Ara-C=cytarabine.

* Interim data

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Innovative Medicines in Oncology

Better and Safer Therapies for Cancer Patients

Thomas Hudson, M.D.

Background

"In the U.S., one in two men and one in three women will get cancer in their lifetime; one out of four Americans will die from cancer."

- American Cancer Society

In his State of the Union Address, President Obama invited Vice President Joe Biden to champion and spearhead a national effort – a "**moonshot**" in the fight against cancer.

"I know that we can help solidify a genuine global commitment to end cancer as we know it today — and inspire a new generation of scientists to pursue new discoveries and the bounds of human endeavor."

- U.S. Vice President Joe Biden

Experience in Genomics and Cancer Research

Human Genome Project

OICR
Ontario Institute for Cancer Research

p3G

1990 1995 2000 2003 2004 2005 2007 2013

International HapMap Project

Global Alliance for Genomics & Health

International Cancer Genome Consortium

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The International Cancer Genome Consortium

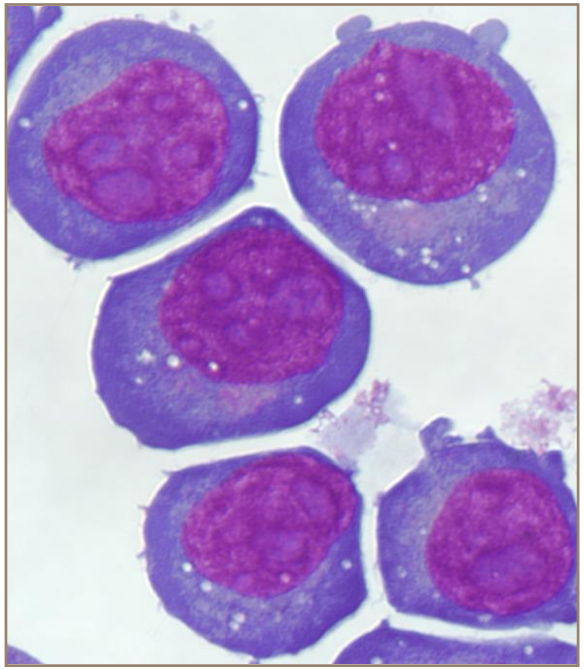
A Moonshot Launched in 2007 by the Global Cancer Research Community

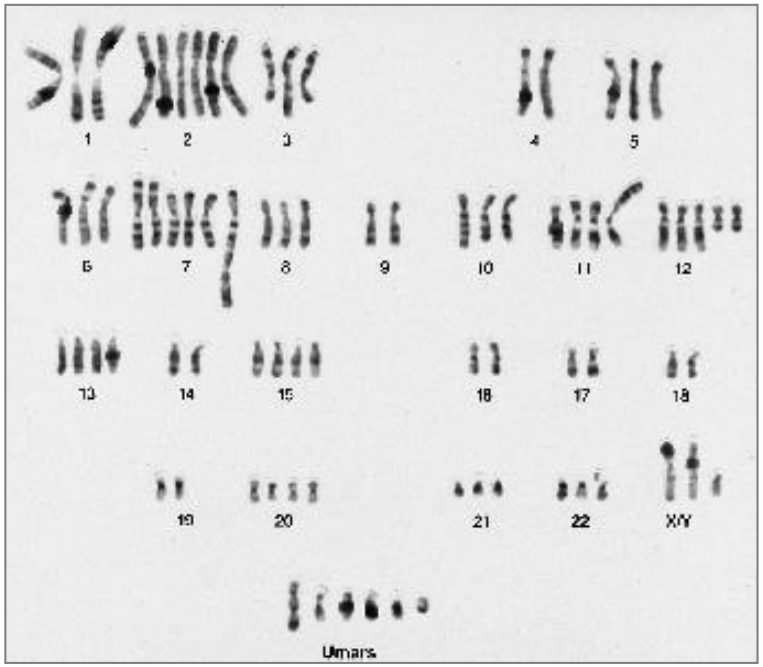
Thomas Hudson, M.D.

Chair, ICGC Executive and International Scientific Steering Committees

International Cancer Genome Consortium

Cancer Is a Disease of the Genome

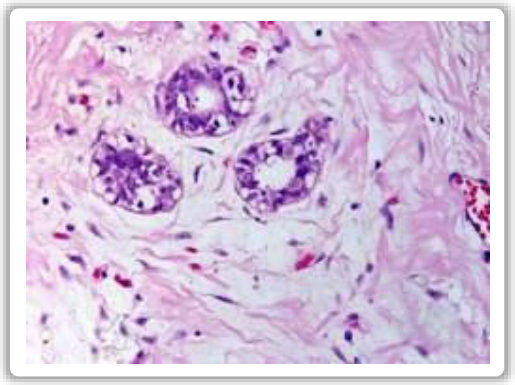




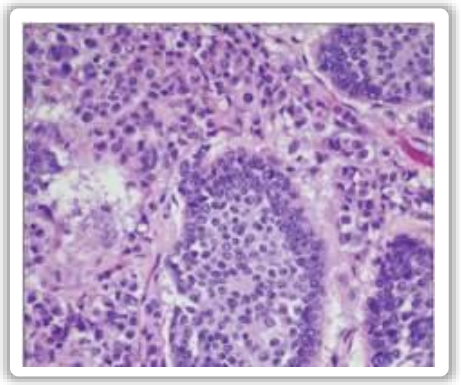
- **Every tumor is different**
- **Every cancer patient is different**

Goals of the International Cancer Genome Consortium (ICGC)

- Collect ~500 tumor/normal pairs from each of 50 different major cancer types
- Comprehensive genome analysis of 25,000 cancer genomes, transcriptomes and methylomes
- Make the data available to the research community and public



...GATTATTCCAGGTAT...



...GATTATTGCAGGTAT...

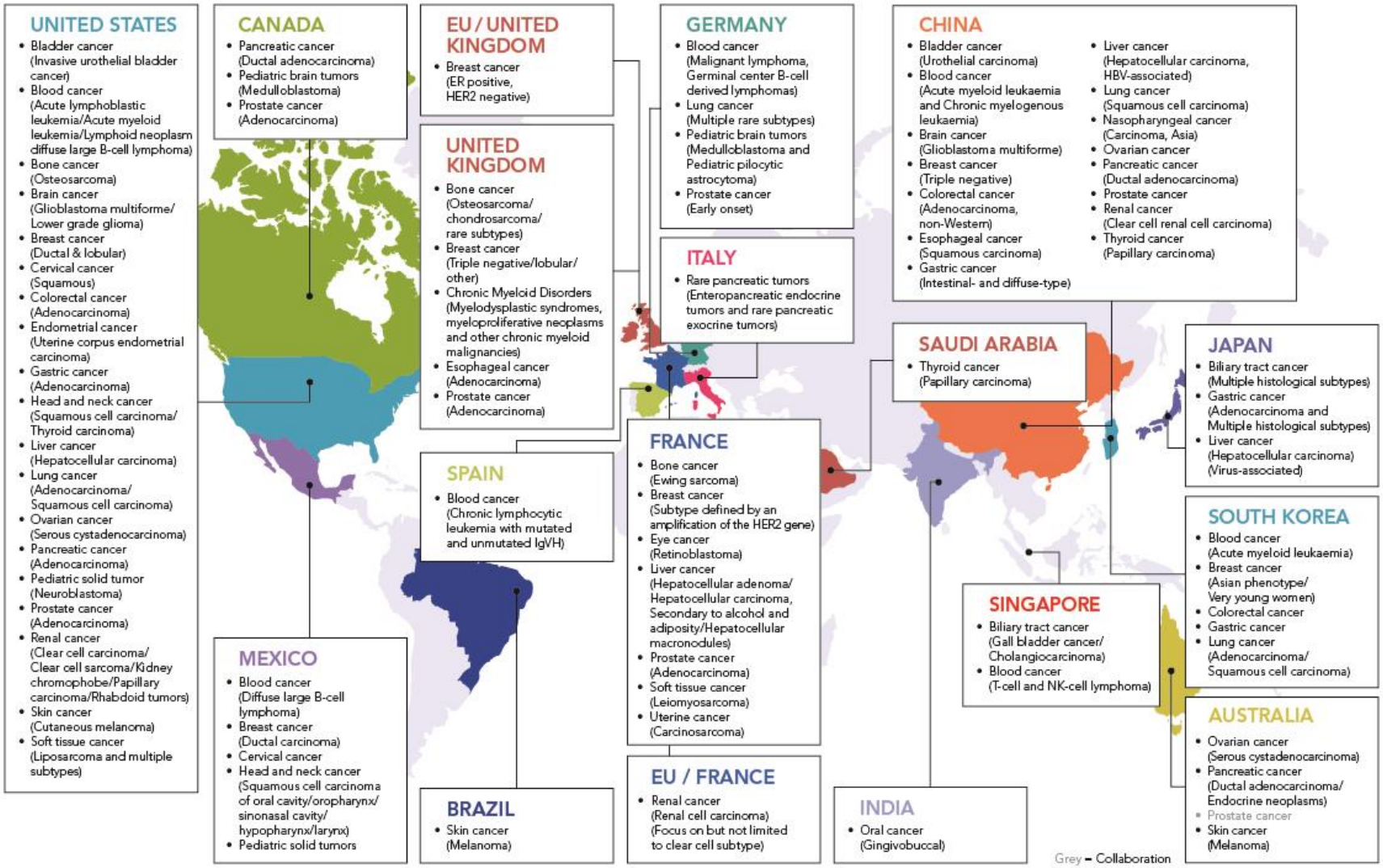
Identify genome changes

...GATTATT**G**CAGGTAT...

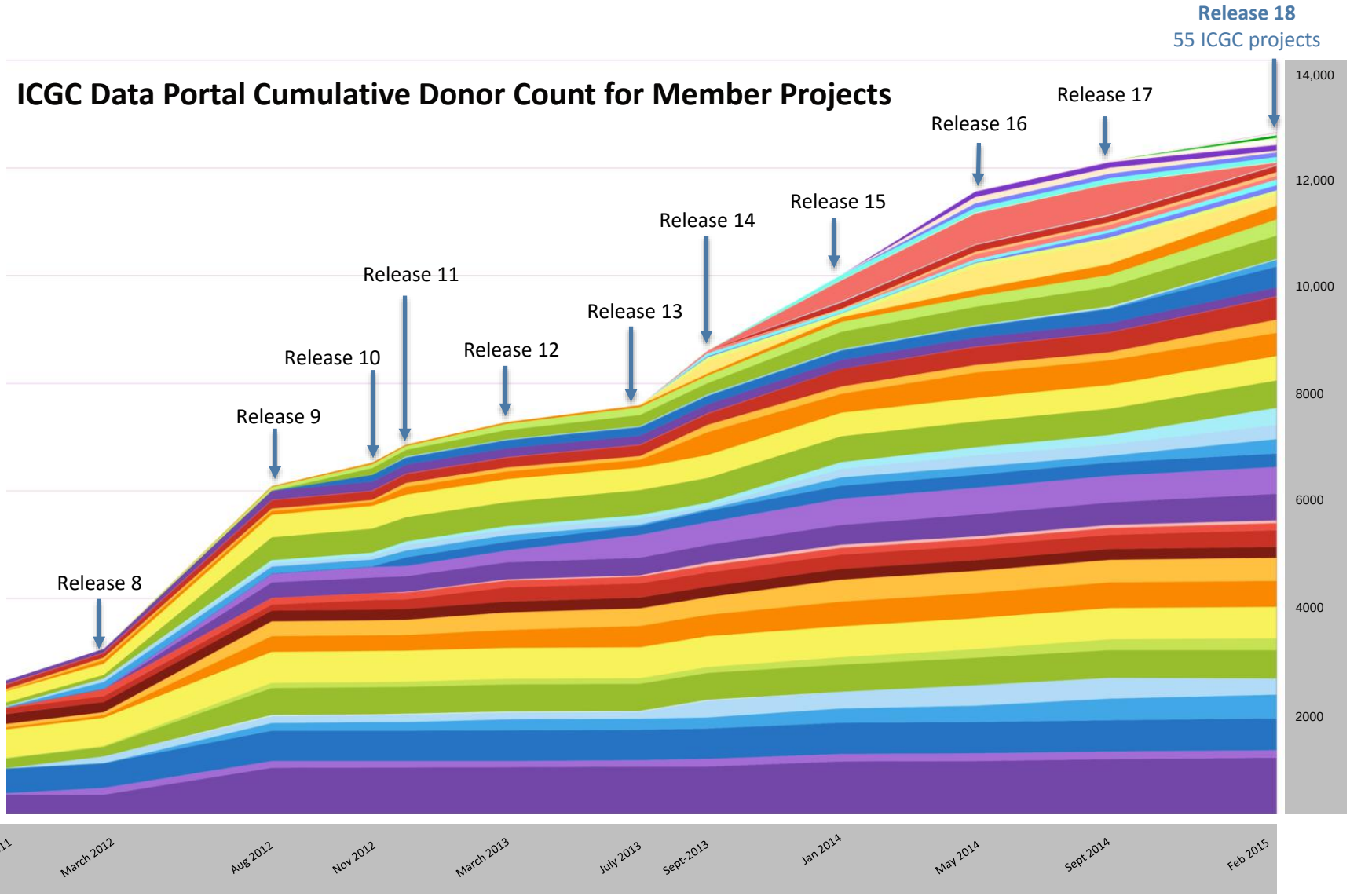
In 2007 – ICGC Was a Moonshot!

- The study of cancer genomes offered the potential to identify hundreds of new targets for better diagnoses and drug development
- No cancer genome had been sequenced
- Sequencing 25,000 cancer genomes was deemed an ambitious goal!
- Next generation technologies were on the horizon
- The spectrum of cancers across the world varies greatly
- The founders of ICGC realized the importance of **coordination, standardization and need for uniform quality measures** to enable the **merging of datasets and increasing power** to detect new cancer biomarkers and targets

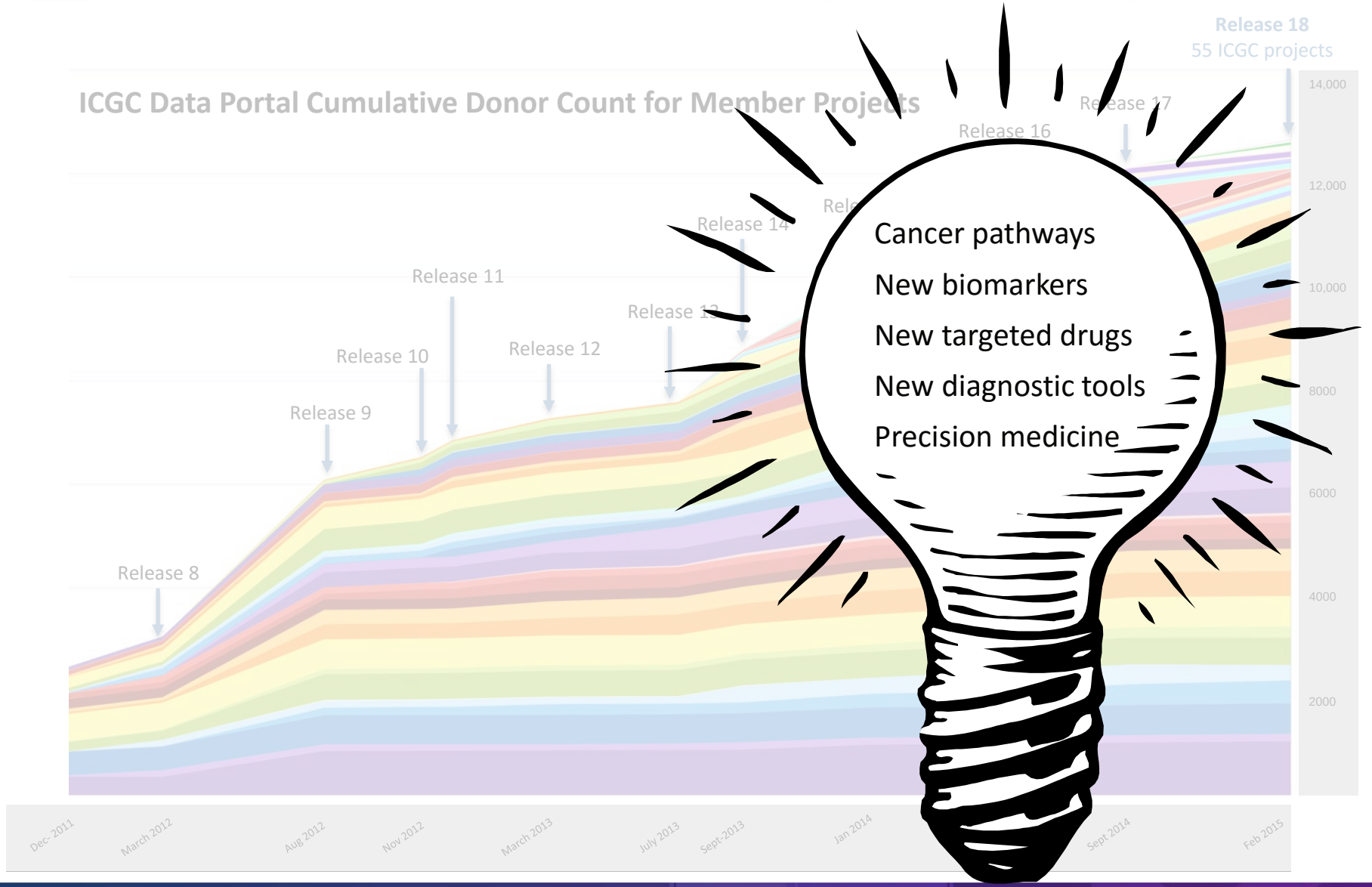
88 ICGC Projects as of April 2016



Growth of ICGC datasets



Growth of ICGC datasets



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Downstream Impact of ICGC

International Cancer Genome Consortium

ICGC Led to a Flood of Discoveries

Vol 464|15 April 2010|doi:10.1038/nature08987 nature

805 citations

PERSPECTIVES

International network of cancer genome projects

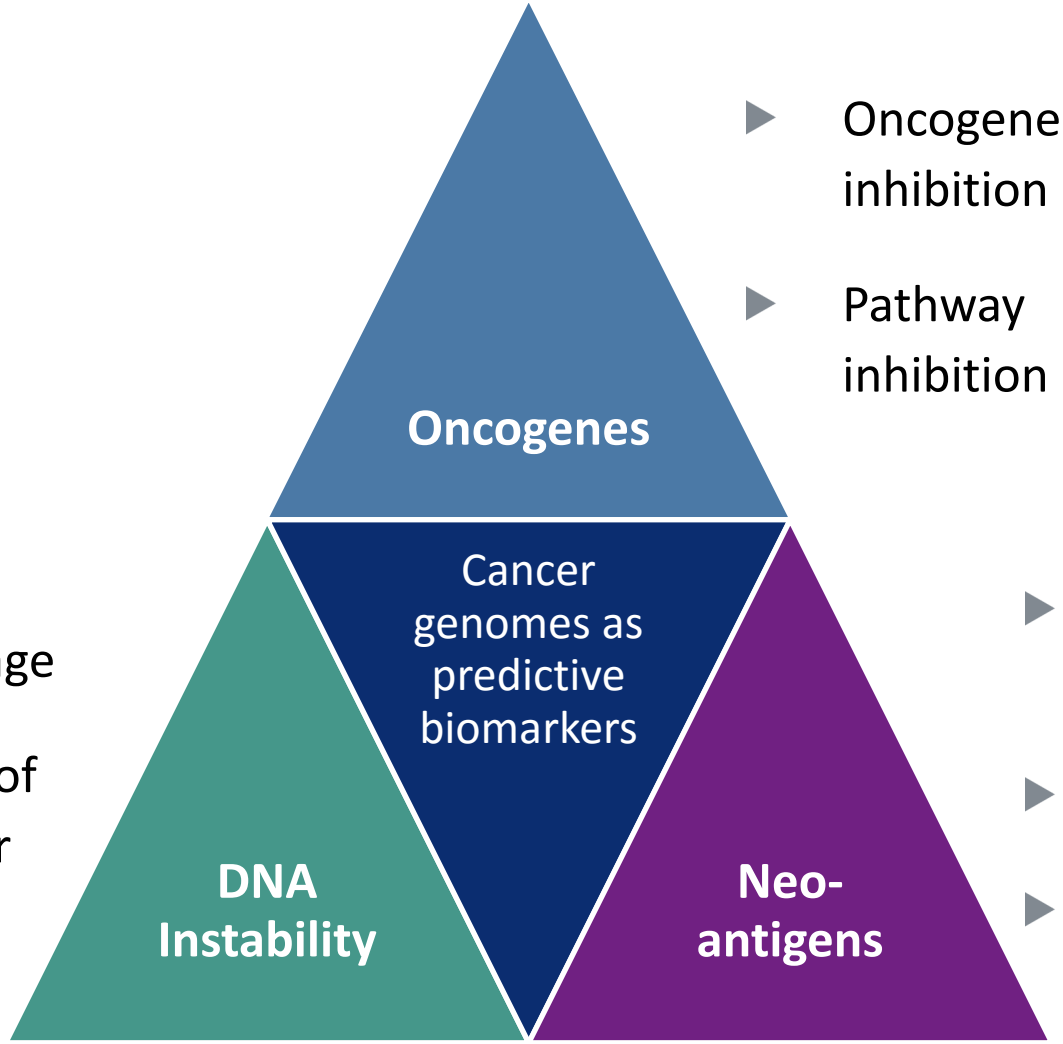
Nature 464, 993-998 (15 April 2010)

The International Cancer Genome Consortium*

The International Cancer Genome Consortium (ICGC) was launched to coordinate large-scale cancer genome studies in tumours from 50 different cancer types and/or subtypes that are of clinical and societal importance across the globe. Systematic studies of more than 25,000 cancer genomes at the genomic, epigenomic and transcriptomic levels will reveal the repertoire of oncogenic mutations, uncover traces of the mutagenic influences, define clinically relevant subtypes for prognosis and therapeutic management, and enable the development of new cancer therapies.

Seminal publications reporting new cancer genes and pathways in Nature, Nature Genetics, Science, Cell, etc.

Cancer Genomes Have Become Informative Biomarkers of Drug Response



- Oncogene inhibition
- Pathway inhibition

- DNA damage
- Inhibition of DNA repair

- Immuno-modulation
- CAR T cells
- Cancer vaccines

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The Ontario Institute for Cancer Research

A Translational Research Institute Launched by the Government of Ontario

Thomas Hudson, M.D.

President and Scientific Director, OICR

OICR
Ontario Institute
for Cancer Research

OICR: An Academic Biotech

The **Ontario Institute for Cancer Research (OICR)** is a translational research institute headquartered in downtown Toronto's Discovery District, with an Ontario-wide mandate and global reach

Ontario investments since 2006: **$750 M**

Other sources (federal, charities, private sector): **$540 M**

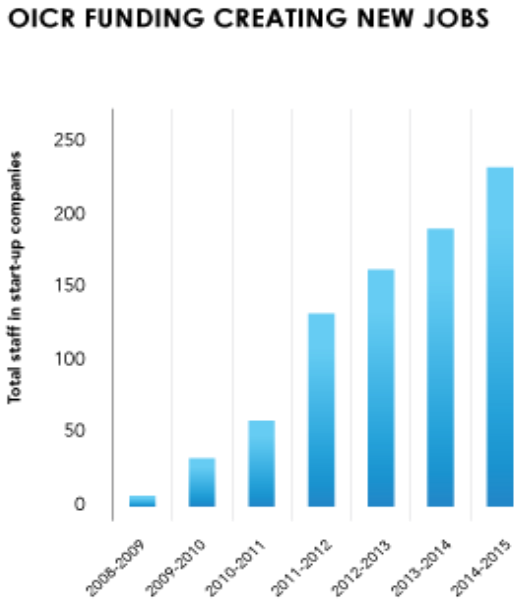
OICR: An Academic Biotech

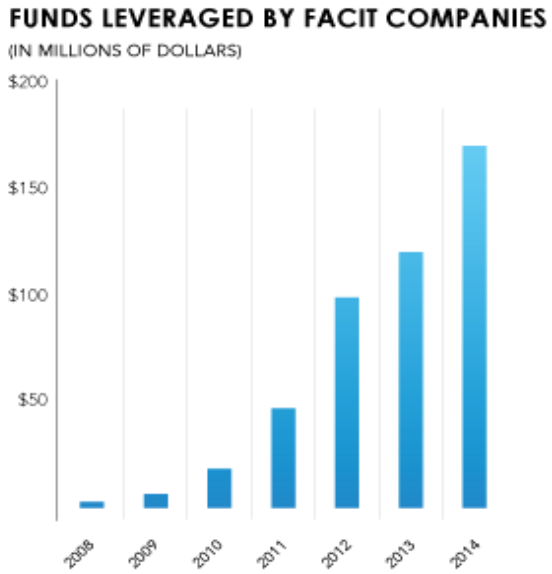
Mission: Partner with the Ontario oncology community to accelerate the development and implementation of clinically important knowledge, products, services and policies to improve cancer prevention, detection, diagnosis and treatment and enable patients in Ontario and worldwide to live longer and better lives.

Translational Research Priorities

Research areas build on Ontario strengths: Small molecules, biologics, stem cells, imaging, genomics, informatics and bio-computing, pathology, clinical trials and health outcomes.

The OICR Story So Far





#1 of 103

for research excellence and impact in Canada

These are size-independent indicators from SCImago institutions rankings 2014

425

colon cancer deaths/year potentially averted due to improved participation in colon cancer screening

1,700

investigators, clinician scientists, research staff and trainees supported by OICR research across Ontario

32

outstanding scientists/ clinician researchers have been attracted to Ontario

OICR Pipeline

Breast cancer

Biomarkers to avoid over-treatment of early disease

Biomarkers for customizing treatment of invasive breast cancer so that patients receive safe and effective therapy

Prostate cancer

Better imaging technique for minimizing over-treatment of early disease

Biomarkers to personalize treatment for intermediate disease so that patients receive safe and effective therapy

Pancreatic cancer

Molecular or radiomic biomarkers predictive of patient outcome, treatment response and drug sensitivity

Lymphoma

New drug for disease subtype resistant to current therapy

Leukemia

Stem cell biomarkers to personalize therapy and develop new drugs

Multiple cancers

Novel therapeutic approaches

- Immunotherapy
- Radiopharmaceuticals
- Therapeutic ultrasound
- Nanoparticles for drug delivery

Software, databases for personalized medicine

Legend

April 2015 → April 2017

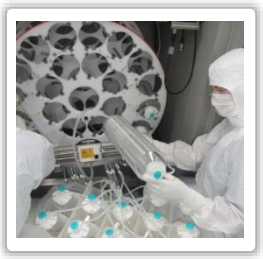
Maraba: “Onco-vaccine” Strategy

Dr. John Bell

OICR Program Director, Immuno- and Bio-therapies (ORBiT)

Senior Scientist, Cancer Therapeutics, Ottawa Hospital Research Institute

Professor, Departments of Medicine and Biochemistry, Microbiology and Immunology, University of Ottawa



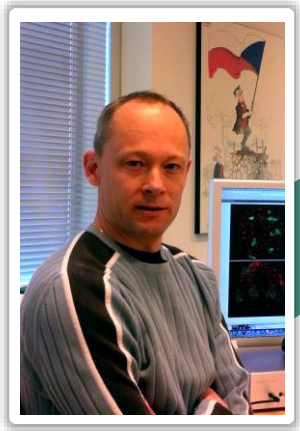
Innovative concept of associating tumour vaccine (MAGE-A3) and oncolytic virus (Maraba)

OICR Catalyzed the Development of a Novel Experimental Approach

Dr. Brian Lichty

Prime: Boost

2009-12



Dr. David Stojdl

Maraba Virus

2009-12

POC

- Assay development
- Manufacturing
- Toxicology (NHP)
- Regulatory (CTA)
- Clinical operations

2012-2014

Phase 1/2 Trial

2015-16

Constant interactions between translation teams and basic/science discovery teams

Looking Forward to New Opportunities at AbbVie

Build on experience with ICGC, OICR and moonshots

- Inspire individuals and groups to think **BIG!**
- Stimulate creative thinking and risk taking
- Intensify the interactions between discovery teams and clinician researchers to accelerate translation and make new discoveries
- Capitalize on new technologies and new biology

What will be my priorities?

- Continue to grow the existing AbbVie Pipeline
- Build critical mass in immuno-oncology
  - Unlock the potential of different types of immune cells
  - Explore interactions between cancer genome signatures and immune response

Bring long-term benefits to individuals and society

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IMMUNOLOGY

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Immunology

Shao-Lee Lin, M.D., Ph.D.
Development

Lisa Olson, Ph.D.
Discovery

AbbVie Immunology: A Promise that Extends into the Future

Currently being used to treat more than **975,000 patients** in **13 indications** worldwide.

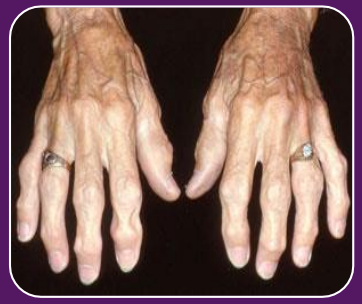
PIPELINE

20 new molecules being evaluated across **14 disease states.**

195 active immunology studies in **more than 50 countries.**

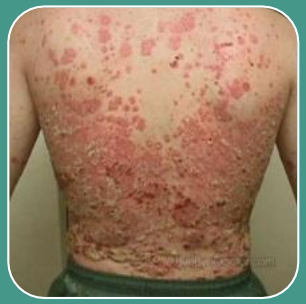
Focused on Redefining the Standard of Care in our Core Areas

Rheumatology



Achieve deep response and remission

Dermatology



Achieve full clearance with durable response

Oral agent

Gastroenterology

Improve remission rates and achieve mucosal healing

ABT-494 and Risankizumab: Poised to Make a Remarkable Impact

Rheumatology

JAK
Phase 3 in RA

IL-23
Phase 2 in PsA

ABT-494 has potential for best efficacy, particularly in the most difficult to treat RA patients

Dermatology

IL-23
Phase 3 in Psoriasis

Risankizumab has potential for best efficacy and most convenient dosing in psoriasis

Gastroenterology

JAK
Phase 2 in Crohn's

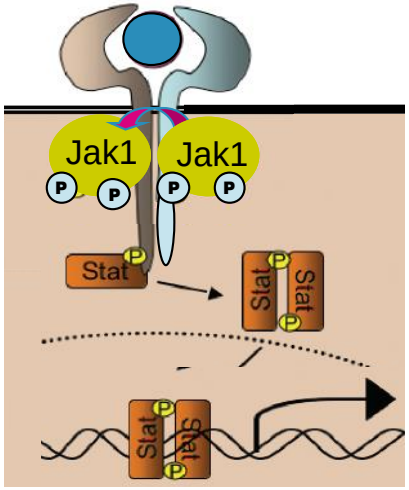
IL-23
Phase 2 in Crohn's

ABT-494 and risankizumab both have potential in IBD

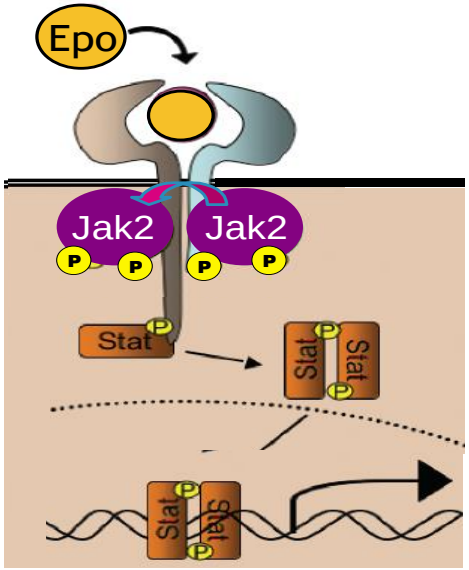
Leveraging our Strength in Immunology for ABT-494

JAK-1 Selectivity Offers Potential for Higher Efficacy, While Limiting Pan-JAK Side Effects

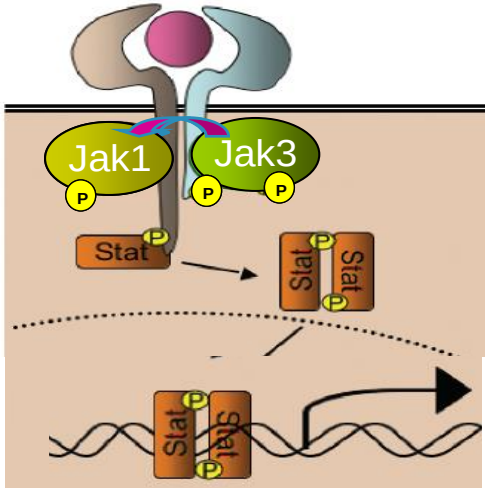
JAK1 inhibition blocks signaling driving rheumatoid arthritis disease process



JAK2 inhibition leads to anemia



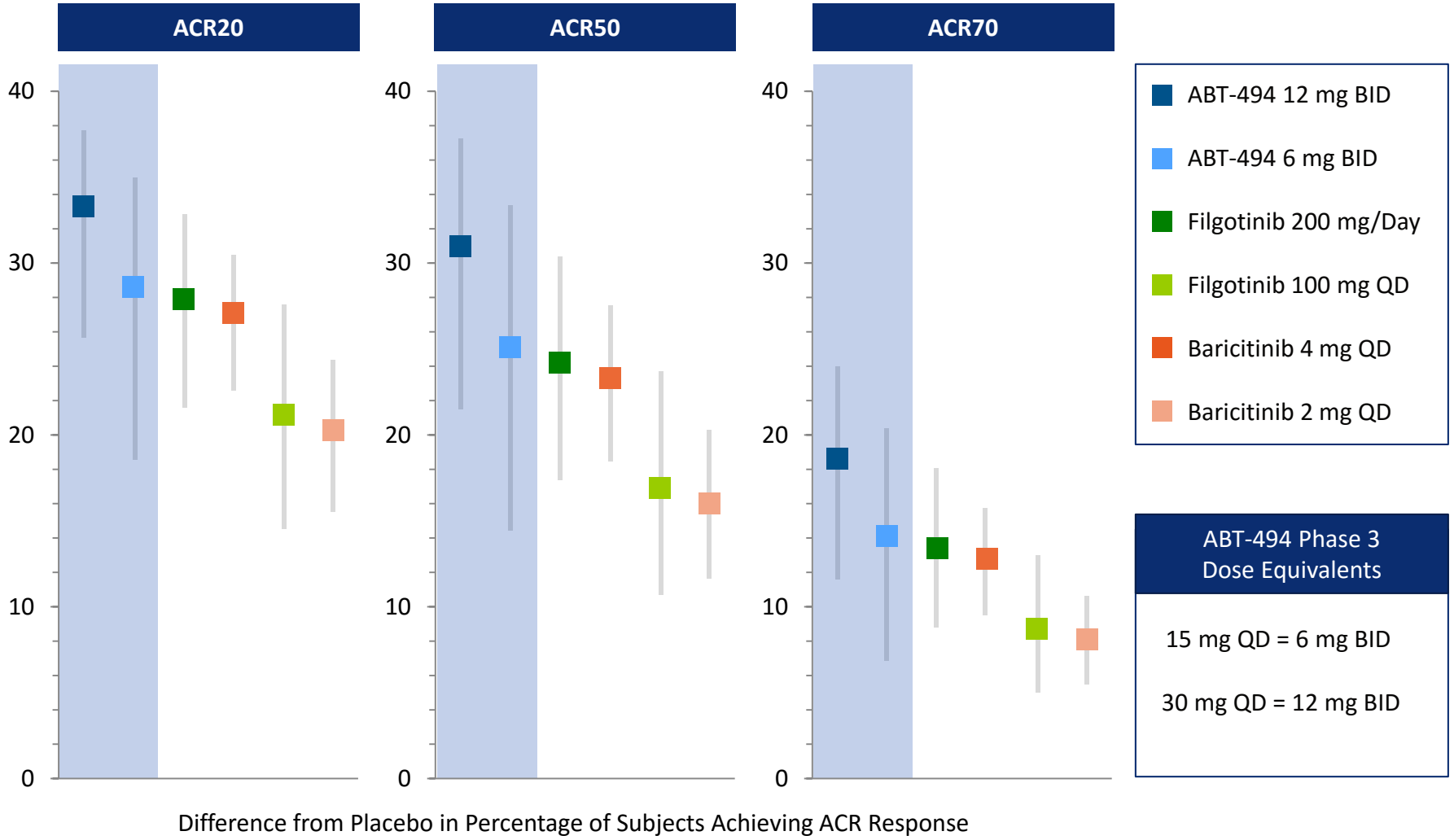
JAK3 inhibition affects cells that monitor for tumors and infections



Molecule	JAK1 Potency	JAK1/JAK2 Selectivity	JAK1/JAK3 Selectivity
ABT-494	8.5 nM IC50	74 X	19 X

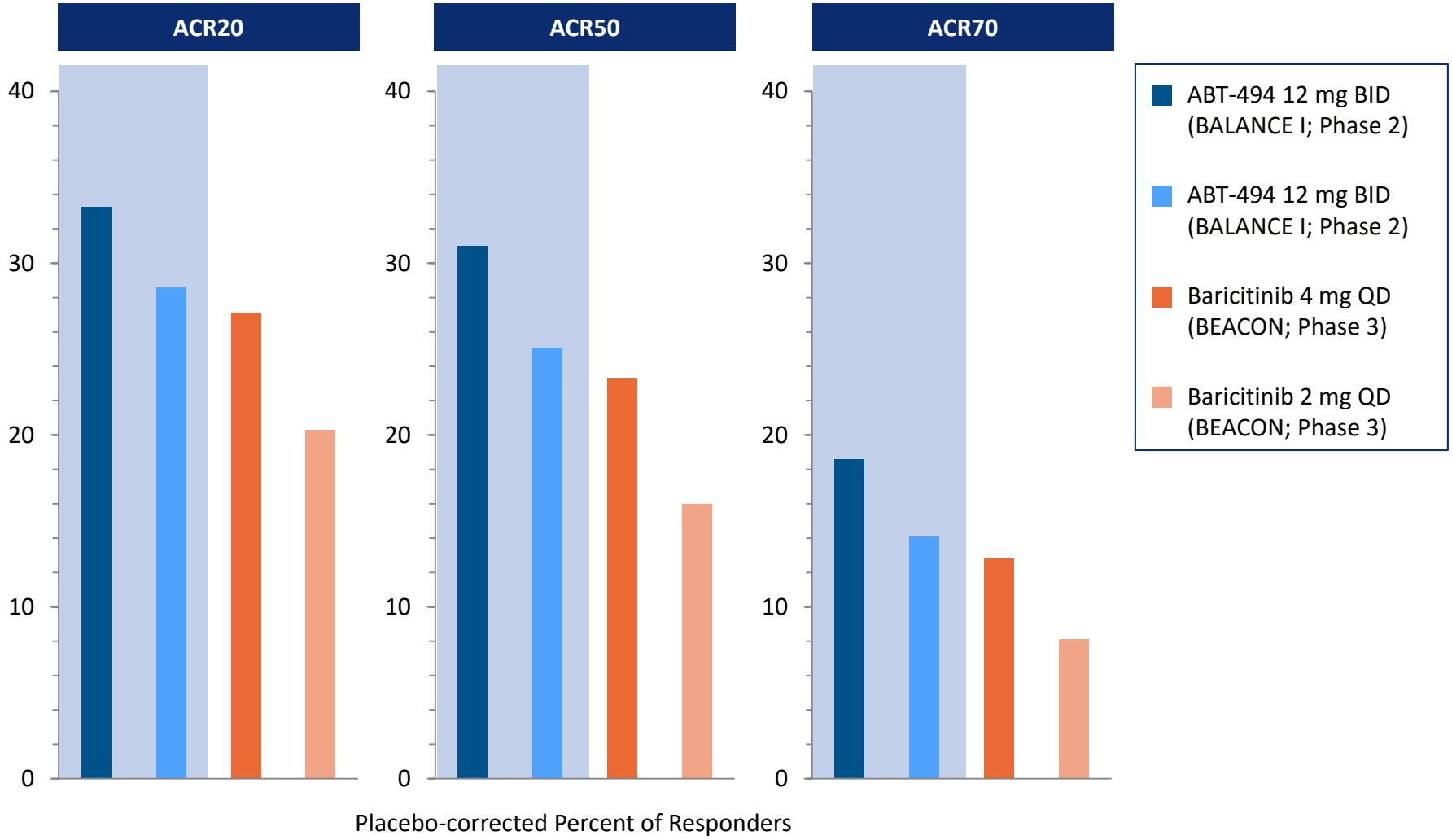
Potential for Best-in-Class Efficacy Among JAK1 Selective Agents

Efficacy of ABT-494 relative to other JAK1 inhibitors based on model-based meta analysis



*Meta analysis across all clinical trials in RA to date for these agents

Results from the Most Challenging Population, TNF-inadequate Responders, Are Especially Encouraging



(Data from cross-study comparison)

ABT-494 RA Phase 3 Program is Expected to Deliver a Strong and Comprehensive Label

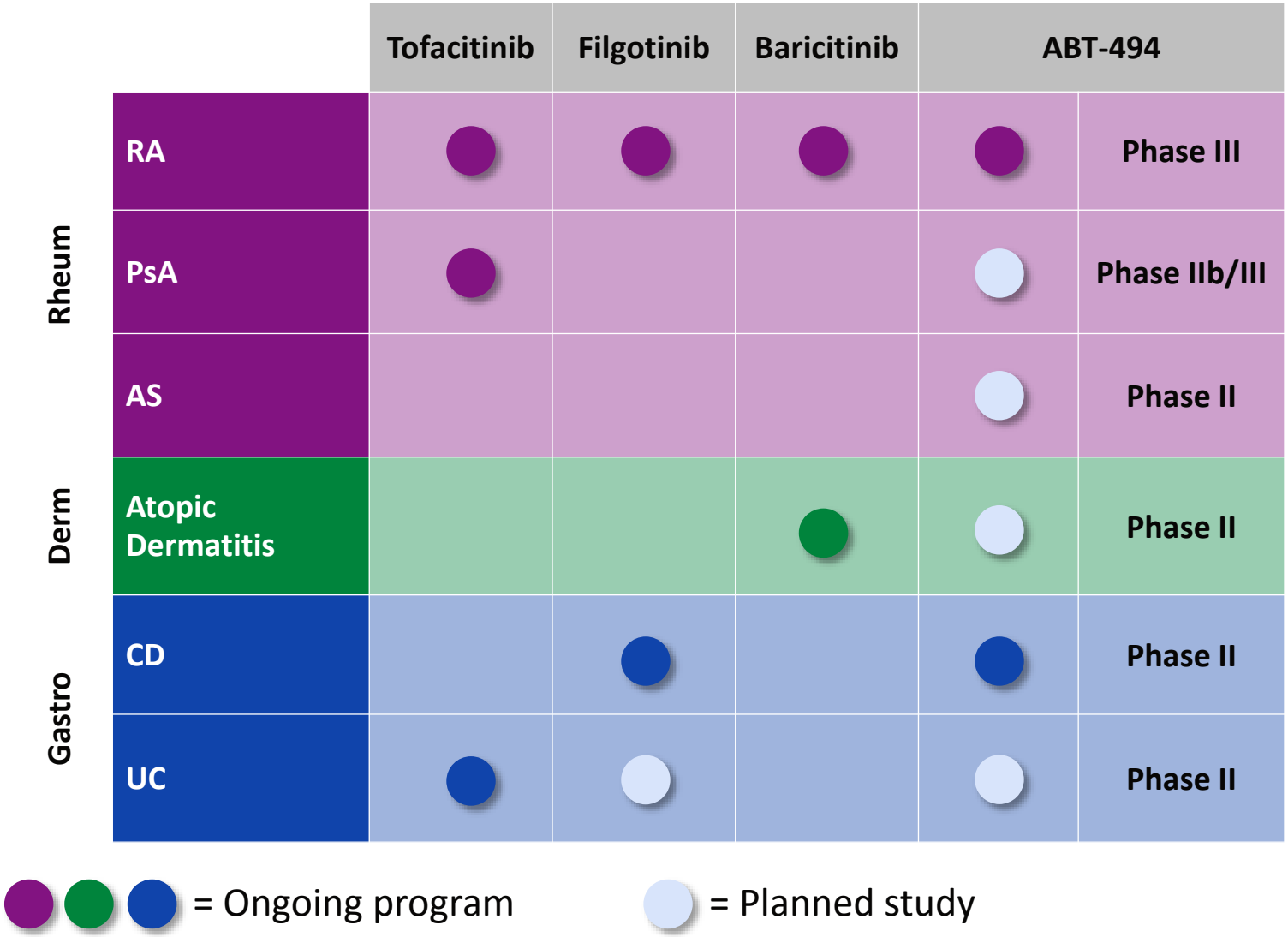
	MTX-naïve	MTX-IR	csDMARD-IR	MTX-IR	Biologic-IR	Biologic-IR
Type of Therapy	Mono	Combo	Combo	Mono	Combo	Combo
Background	–	MTX	csDMARDs	–	csDMARDs	csDMARDs
Active Comparator	MTX	**Adalimumab**	Placebo	MTX	Placebo	**Abatacept**
Duration of Period 1	**48 weeks**	**48 weeks**	12 weeks	14 weeks	24 weeks	12 weeks

Supports use earlier in therapy

Supports use after first biologic failure

Rapid Phase 2-to-Phase 3 transition for RA. Three months from 'go' decision to first subject dosed in Phase 3.

Maximizing the Potential of ABT-494



Leveraging our Strength in Immunology for Risankizumab

immhance

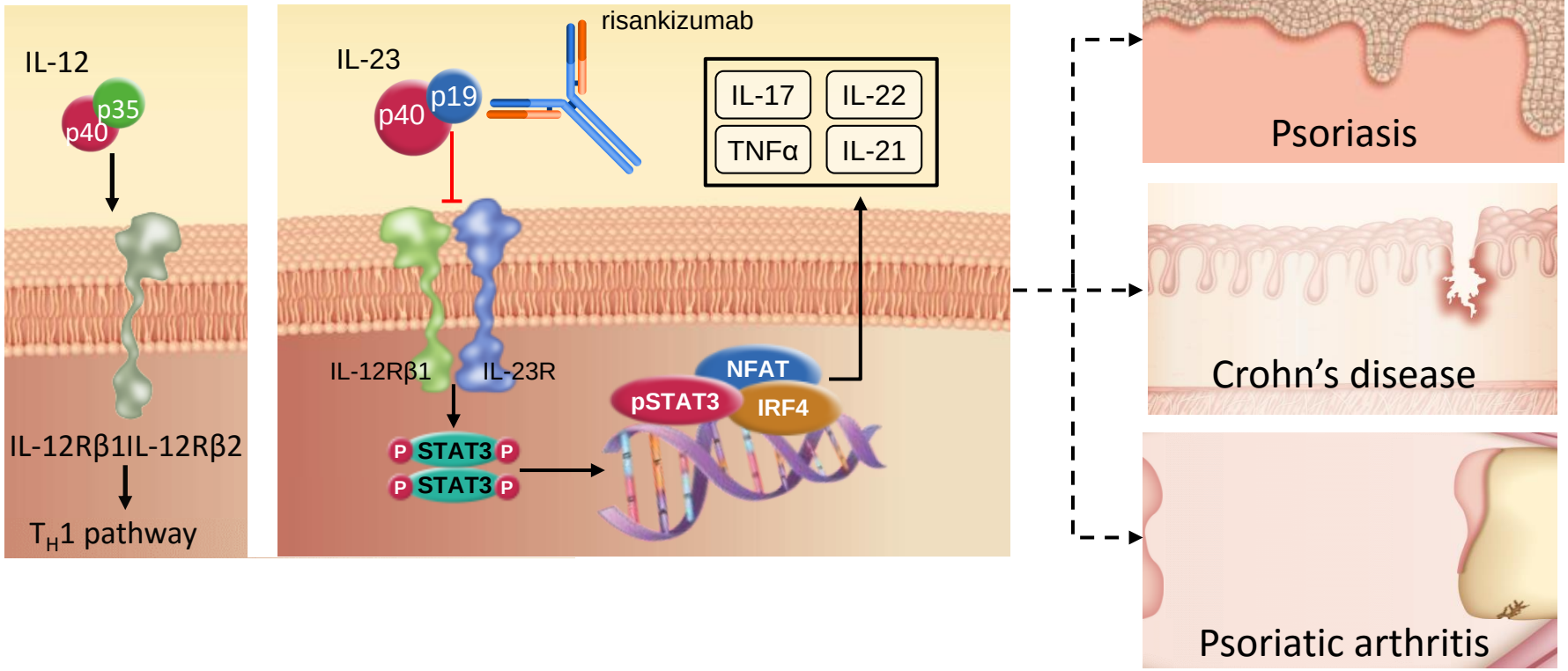
ultimma-1

immvent

ultimma-2

Risankizumab licensed from Boehringer Ingelheim

IL-23 Is Implicated in the Inflammatory Cascade Across Multiple Autoimmune Diseases



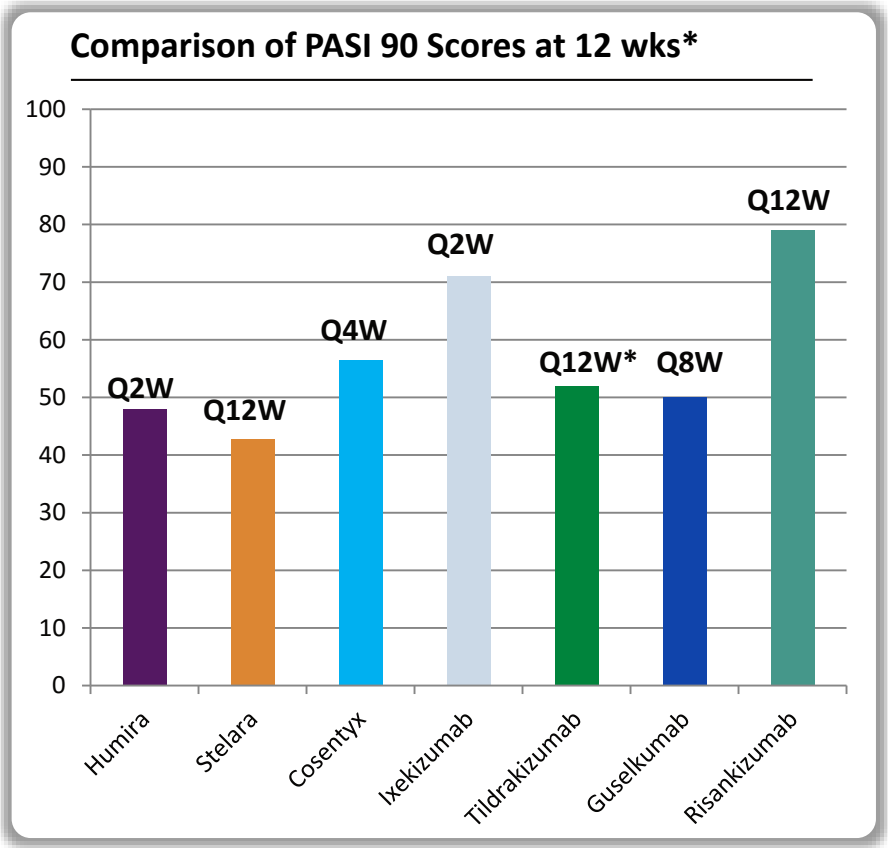
Risankizumab recognizes an epitope on IL-23p19

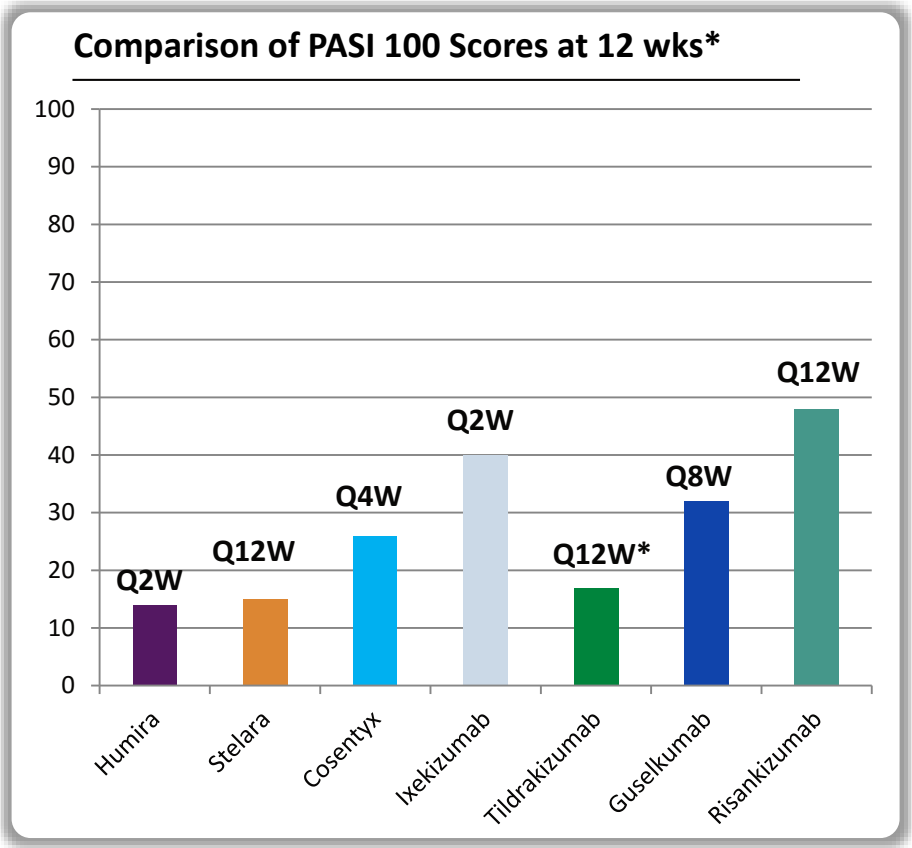
- Inhibits binding of IL-23 to its receptor
- Binding is highly specific for the p19 subunit
- No direct impact on T_H1 pathway

Singh S *et al. mAbs* 2015;7:778
Patel M *et al. Dermatol Ther* 2012;2:16
Sofen H *et al. J Allergy Clin Immunol* 2014;133:1032
Mahtur A *et al. J Immunol* 2007;178:4901
Muranski P & Restifo NP. *Blood* 2013;121:2402

Risankizumab Has Potential to Be a Transformational New Therapy in Psoriasis

- **Expected PASI90 efficacy above anti-IL-12/23, IL-17s and other IL-23s after 12 weeks**
- **Dosing has potential to be the most patient friendly at once every 3 months**
- **Potential for durability above IL-12/23 and IL-17s at one year**

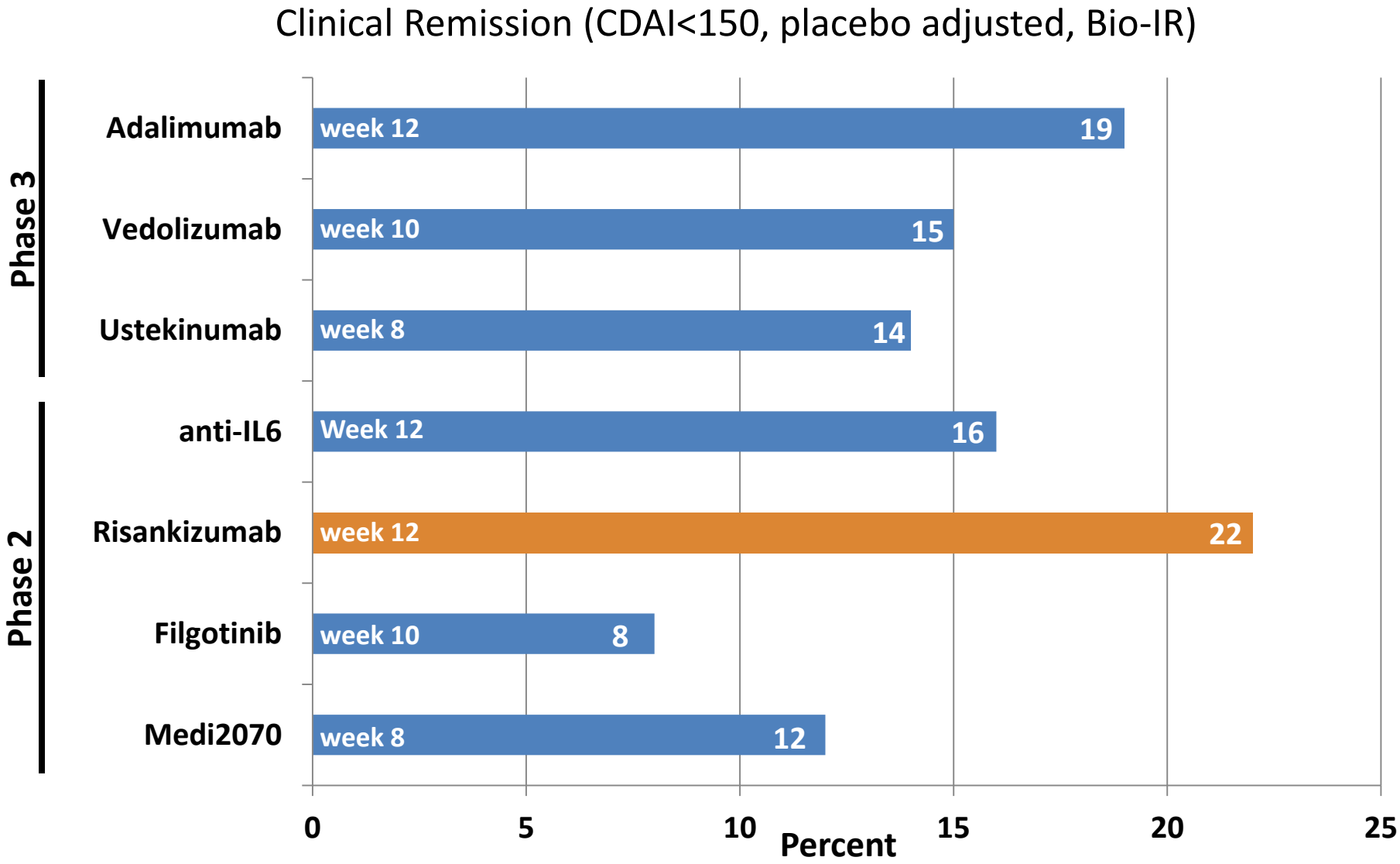




PASI90 and PASI100 data from multiple studies, including: Humira (CHAMPION), Stelara (ave PHOENIX 1+2), Cosentyx (ave ERASURE/ FIXTURE, 300 mg), Ixekizumab (UNCOVER2/3), Tildrakizumab (ClinicalTrials.gov), Guselkumab (NEJM 2015), BI655066 (EADV2015).

*Tildrakizumab data at 16wks

Risankizumab Has Demonstrated Encouraging Phase 2 Data in Crohn's Disease



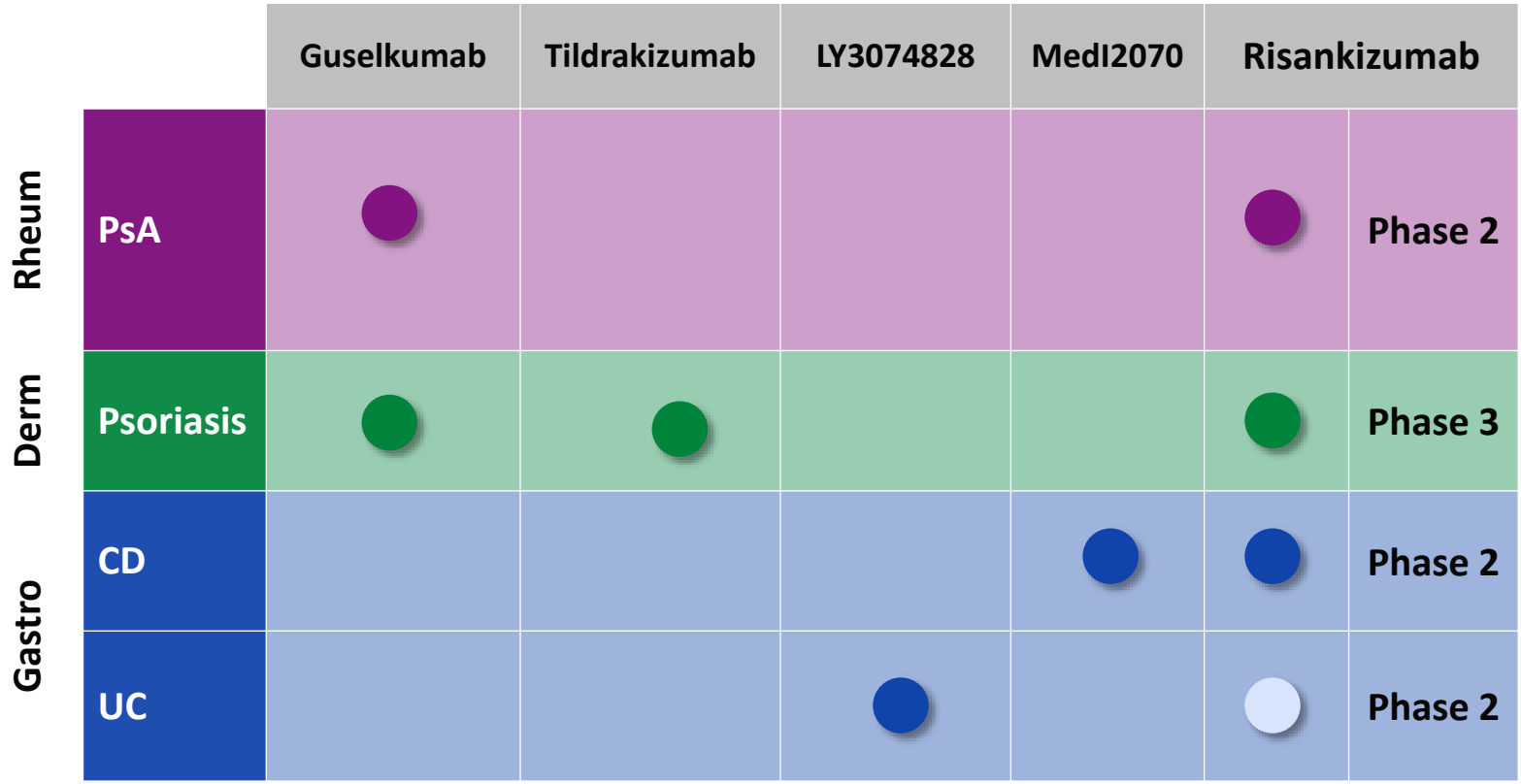
Data from multiple studies, including: Adalimumab: EXTEND, data on file; Vedolizumab: GEMINI 3; Ustekinumab: UNITI-1; anti-IL6: ANDANTE; Risankizumab: DDW 2016; Filgotinib: ECCO 2016; Medi2010: ECCO 2015

Risankizumab Phase 3 Psoriasis Program Includes Two Head-to-Head Studies Versus Stelara

Trial Name	Trial Description	N Primary Endpoint
ultimma-1	Phase 3 head-to-head, placebo-controlled study of the efficacy and safety of Risankizumab compared with **ustekinumab** for moderate-to-severe psoriasis	500 sPGA0/1 @ wk 16 PASI 90 @ wk 16
ultimma-2	Phase 3 head-to-head, placebo-controlled study of the efficacy and safety of Risankizumab compared with **ustekinumab** for moderate-to-severe psoriasis	500 sPGA0/1 @ wk 16 PASI 90 @ wk 16
immhance	Phase 3 placebo-controlled, **withdrawal and retreatment** study of the efficacy and safety of Risankizumab for moderate-to-severe psoriasis	500 sPGA 0/1 @ wk 16 PASI 90 @ wk 16
immvent	Phase 3 Risankizumab Compared to Active Comparator (**adalimumab**) in patients with moderate-to-severe chronic plaque psoriasis	600 sPGA0/1 @ wk 16 PASI 90 @ wk 16
LIMMitless	Open-label extension enrolling subjects from all of the Phase 3 efficacy studies	Phase 3 completers

Source: www.clinicaltrials.gov

Maximizing the Potential of Risankizumab

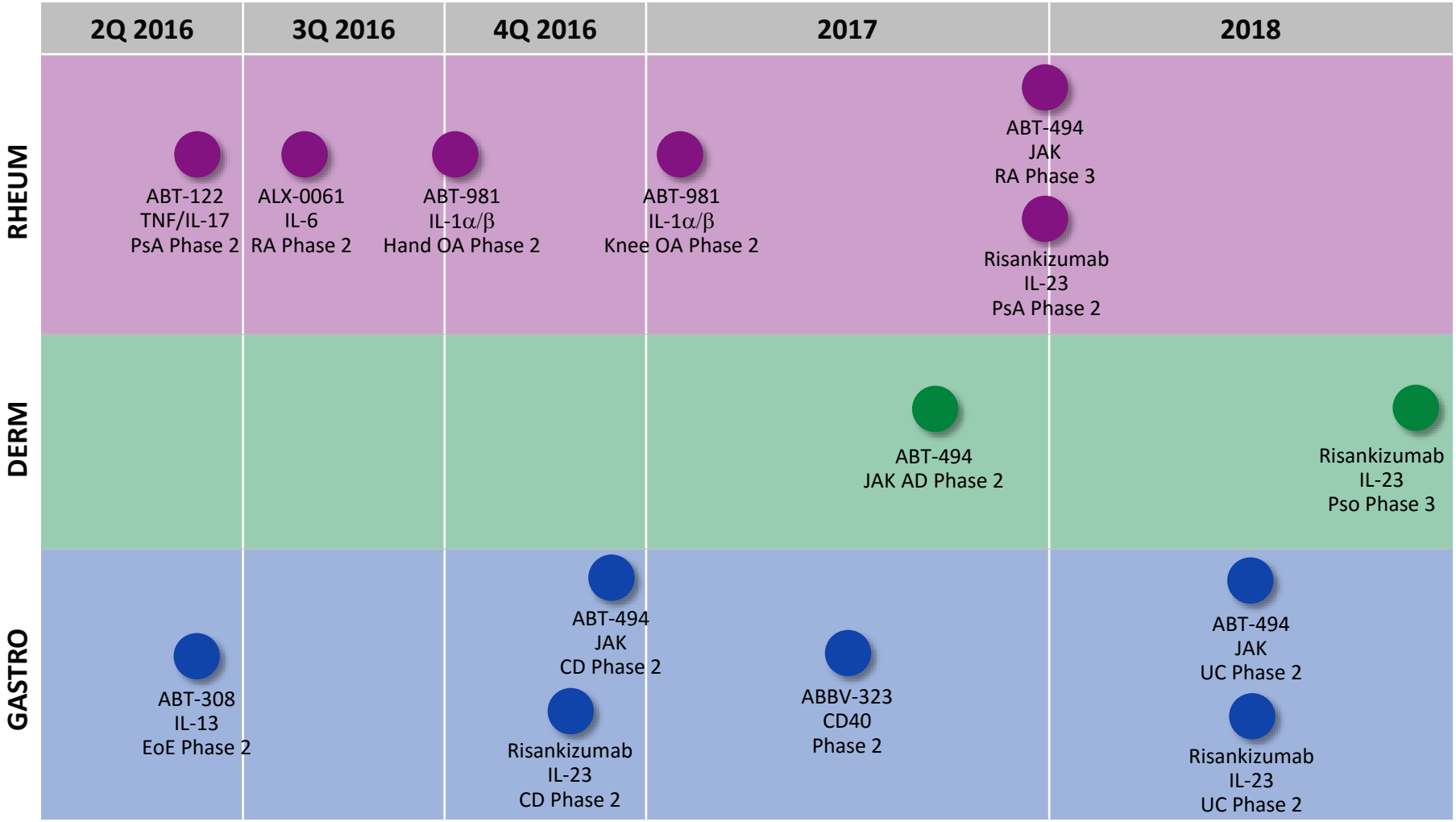


= Ongoing program

= Planned study

AbbVie's Pipeline Anticipated to Provide Sustained Growth for the Franchise

Anticipated News Flow



Our Early Programs Bring New Approaches to Redefining the Standard of Care in our Core Disease Areas

Rheumatology

- JAK Phase 3 in RA
- IL-23 Phase 2 in PsA

Our goal is to achieve deep remission.

- Anti-TNF Steroid ADC
- JAK-BTK Combo

Dermatology

- IL-23 Phase 3 in Psoriasis

Developing an oral agent with high efficacy.

- RORγT

Gastroenterology

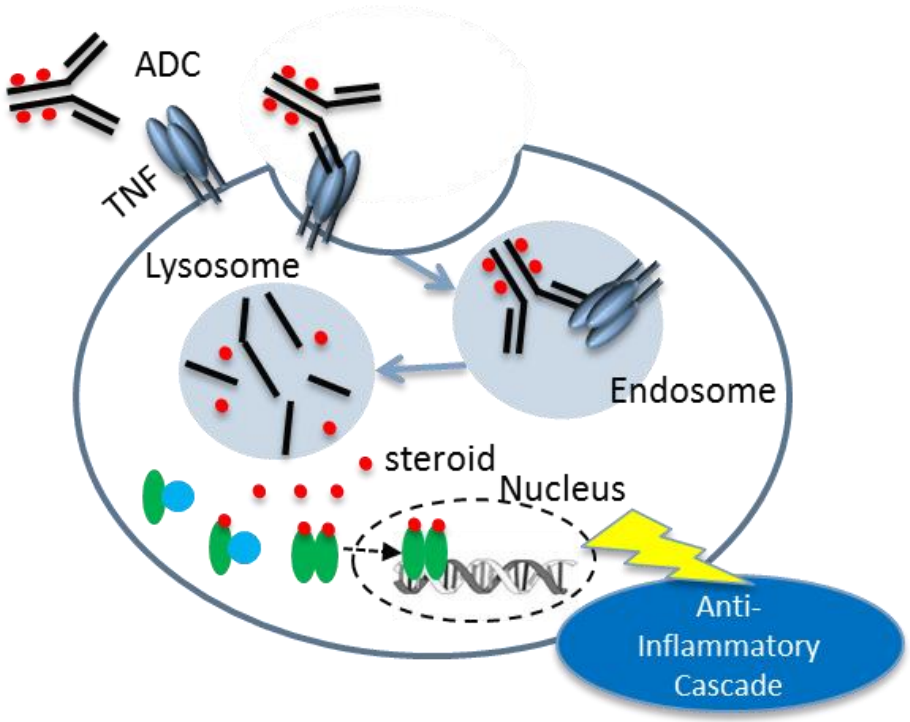
- JAK Phase 2 in Crohn's
- IL-23 Phase 2 in Crohn's

Unmet need in remission and mucosal healing.

- Anti-TNF Steroid ADC

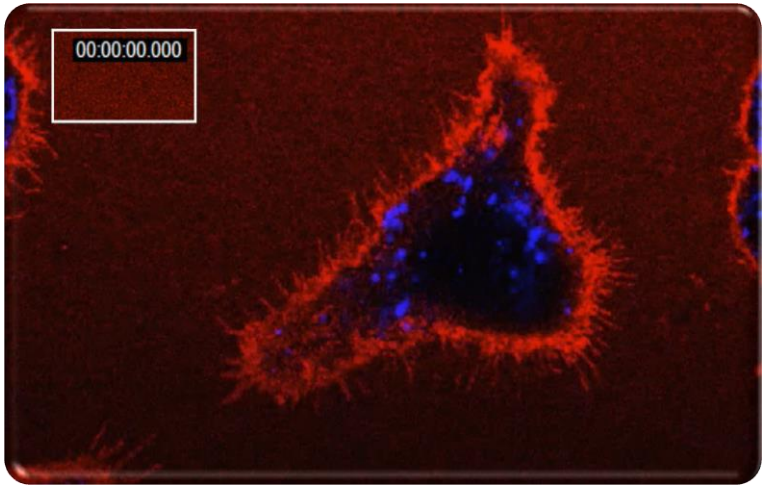
Targeting Complete Remission in RA and IBD
Anti-TNF Steroid ADC Project

Targeted Release of Novel Steroid



Blue = LysoTracker

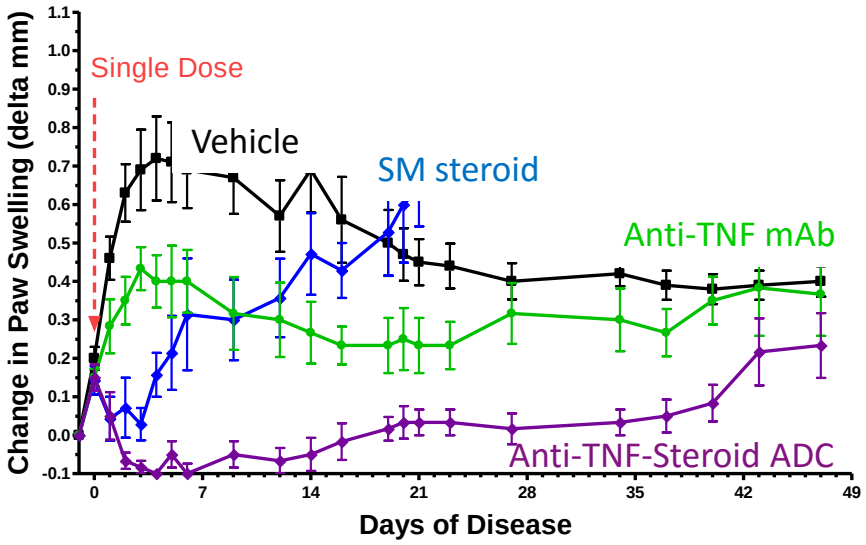
Red = Anti-TNF



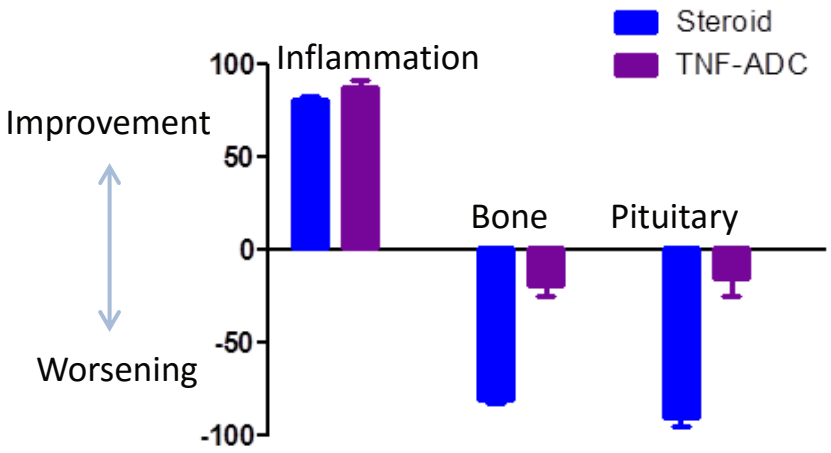
Targeting Complete Remission in RA and IBD

Anti-TNF Steroid ADC Project

Resolution of Disease with a Single Dose in Mouse Arthritis Model



Anti-TNF ADC Demonstrates Comparable Efficacy to High Dose Steroid Without Side Effects



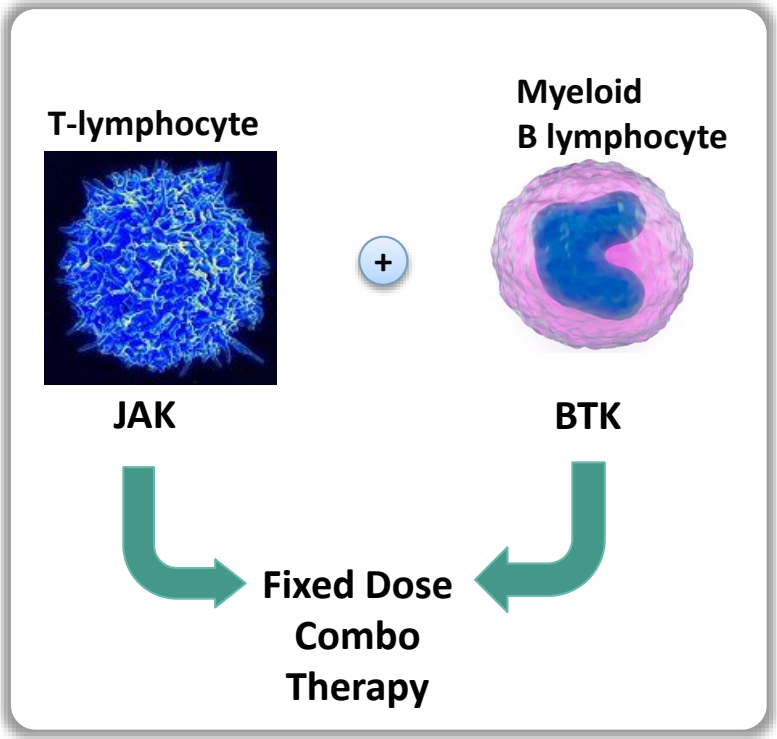
Remarkable efficacy with just a single dose of anti-TNF Steroid ADC

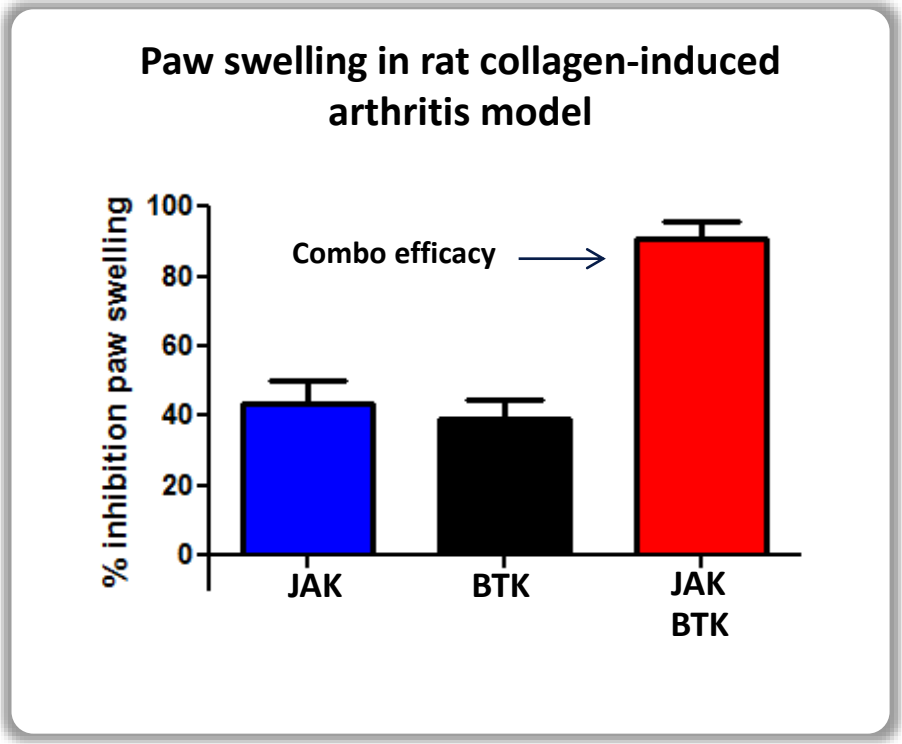
Lack of unwanted steroid side effects

Combination Therapy Is a Well-accepted Practice in Rheumatology

JAK1 / BTK Inhibitor Combination for RA

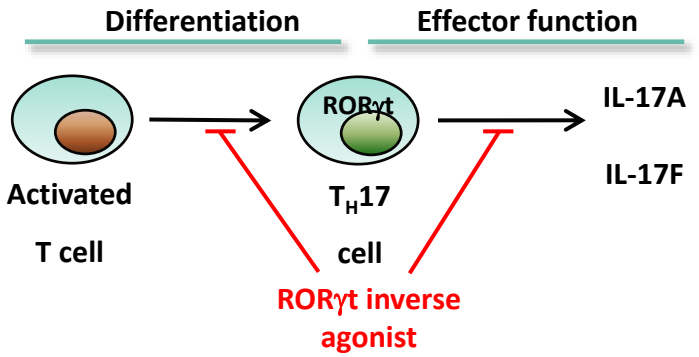
Hypothesis: Combining inhibitors of JAK1 and BTK will confer additive efficacy in autoimmune disease



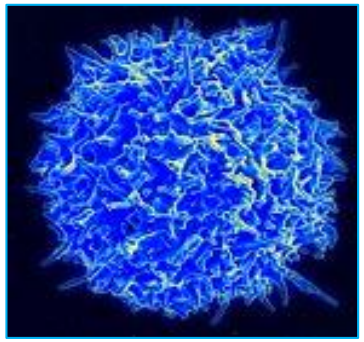


Oral Small Molecule for Moderate-to-Severe Psoriasis
RORγt Inverse Agonists Target the Clinically Validated IL17/IL23 Pathway

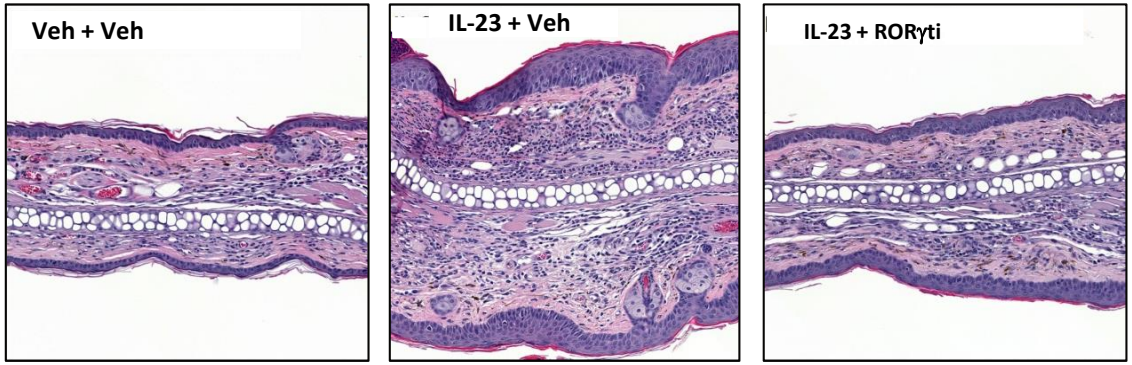
RORγt essential for production of IL-17

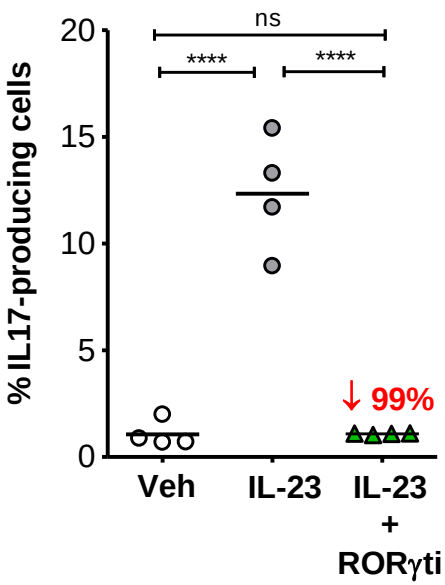


Th-17 lymphocyte



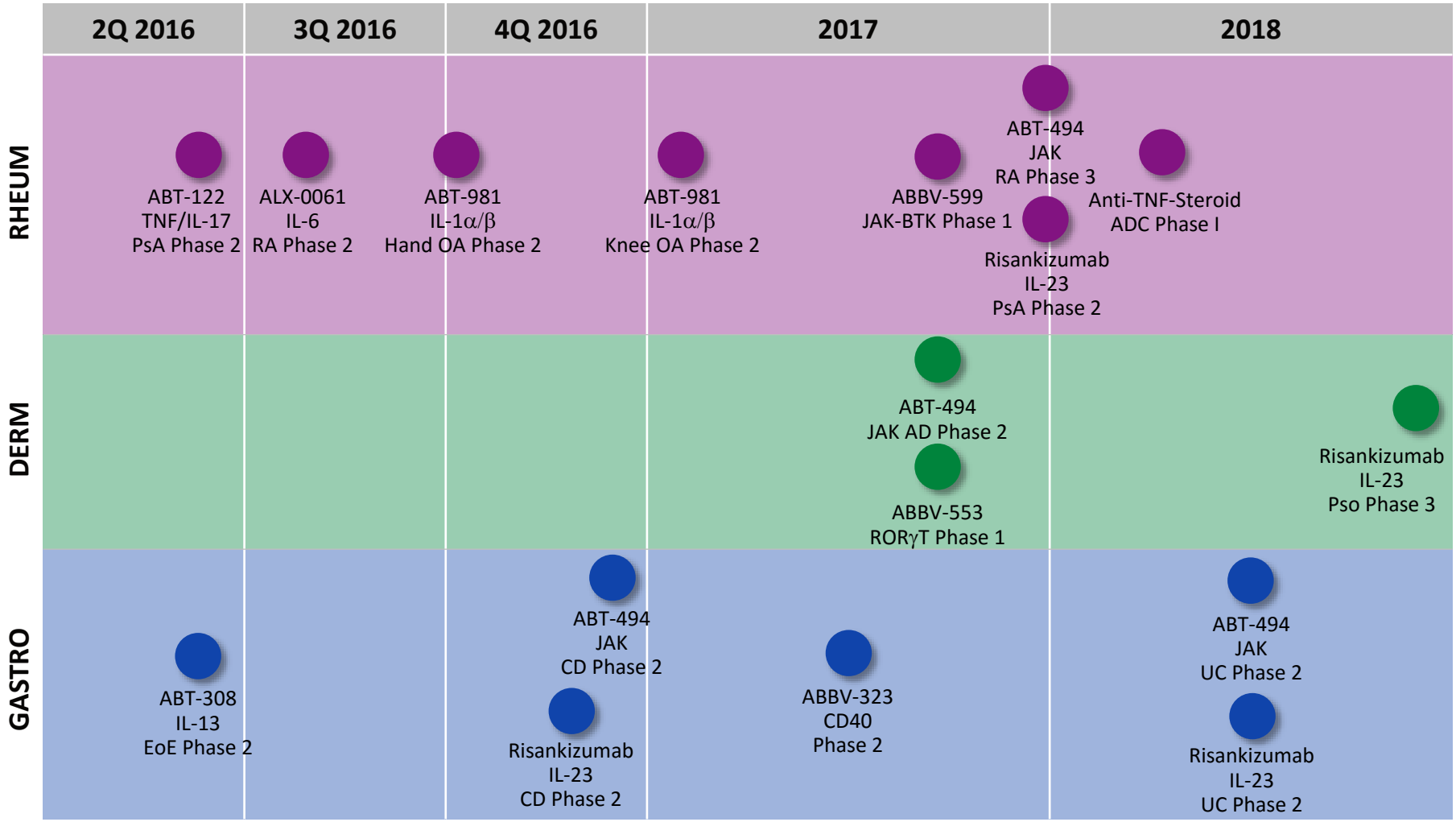
RORγt inhibition significantly decreased inflammation and reduced the frequency of IL17-producing cells





AbbVie's Pipeline Is Positioned for Continued Leadership in Immunology

Anticipated News Flow



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HCV and Elagolix

Shao-Lee Lin, M.D., Ph.D.

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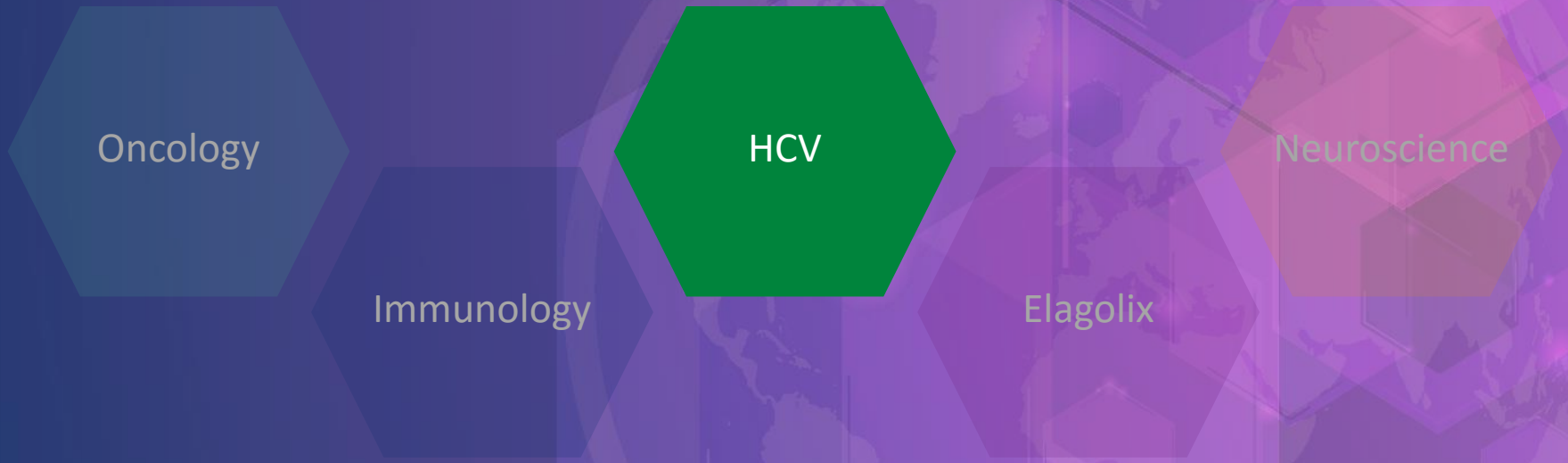
HCV



Advancing the Next Generation of HCV Cure

Current therapies

- >1 million patients cured
- Cure rates >95% for many genotypes

Unmet Need:

- >100 million patients remain*
- Pan-genotypic
- Resistance associated variants
- Difficult to treat populations
- Shorter treatment durations

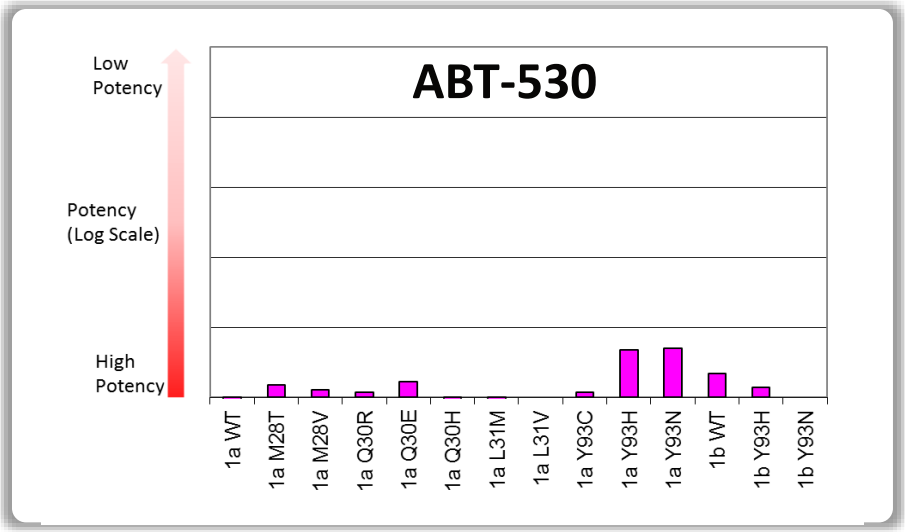
AbbVie's Next Gen:

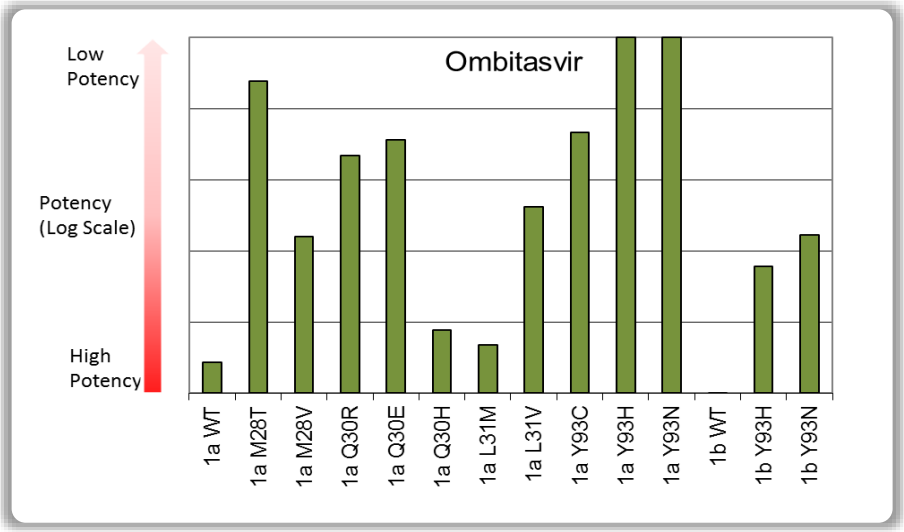
Once-daily oral combo

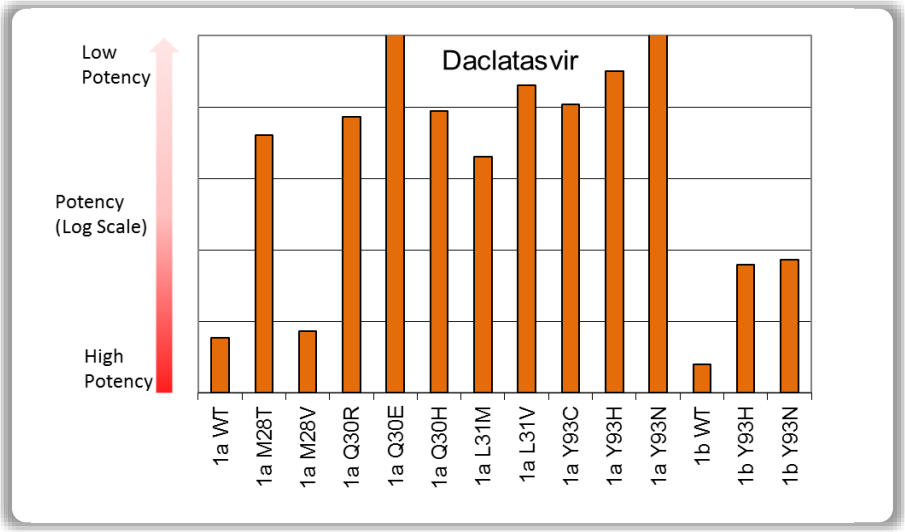
ABT-530
NS5A inhibitor
+
ABT-493
NS3/4a protease inhibitor

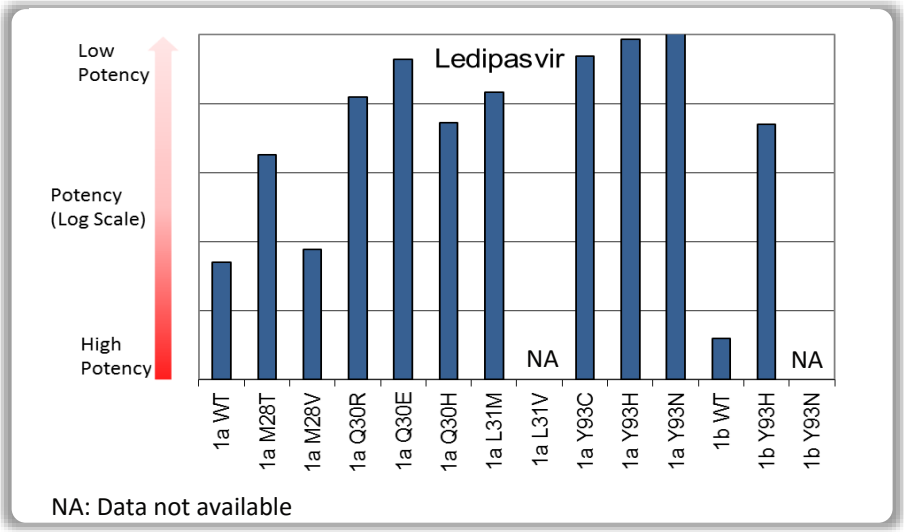
* WHO assessment (many are undiagnosed)

Next Gen Has Potent Activity Against Common Resistance-Associated Variants In-Vitro









NA: Data not available

Source: AbbVie data on file

High Cure Rates Are Achieved in Patients with Baseline Resistance: Phase 2 Data from MAGELLAN-1 study

	ABT-493 300mg + ABT-530 120mg + Ribavirin 800mg	ABT-493 300mg + ABT-530 120mg
SVR_{12}, n (%)	90.1 (20/22)	86.3% (19/22)
Breakthrough	0	1
Relapse	1	0
Other	1*	2**
mITT SVR_{12}, n (%)	95.2% (20/21)	95% (19/20)

* 1 LTFU, ** 1 death from CA after UD RNA at PTW 8 and 1LTFU

Baseline Resistance-Associated Variants
82% patients with RAVs at NS3 and/or NS5A
32% with both NS3 and NS5A RAVs detected
24% with double- or triple-NS5A RAVs

High Cure Rates Across All Patient Populations in Phase 2

	GT/ F stage	Treatment History	Duration (weeks)	SVR_{12} (non-virologic failures excluded)	
SUREVEYOR-1 and MAGELLAN-1	1/ F0-F3	Treatment naïve and experienced	8	**100%**	
		Treatment naïve and experienced	12	**100%**	
		DAA experienced	12	**95%**	First-generation treatment failures
	1/ F4	Treatment naïve and experienced	12	**96%**	
SUREVEYOR-2	2/ F0-F3	Treatment naïve and experienced	12	**100%**	
		Treatment naïve and experienced	8	**100%**	
SUREVEYOR-2	3/ F0-F3	Treatment naïve and experienced	12	**97%**[a]	
		Treatment naïve	8	**100%**	GT3 non-cirrhotic
		Experienced	12	**92%**	
SUREVEYOR-1	3/ F4	Treatment naïve	12	**100%**[b]	GT3 compensated cirrhotic
	4-6/ F0-F3	Treatment naïve and experienced	12	**100%**	

a. SVR12 in TN patients was 100%; b. Screening of GT3 cirrhotic PR-exp. was stopped prematurely (FDA recommendation); only 4 GT3 cirrhotic PR-experienced (not included in the table) were randomized and their duration was extended to 16 weeks, 1 out of these 4 patients relapse.

DAA = Direct Acting Antivirals

High Cure Rates Across All Patient Populations in Phase 2

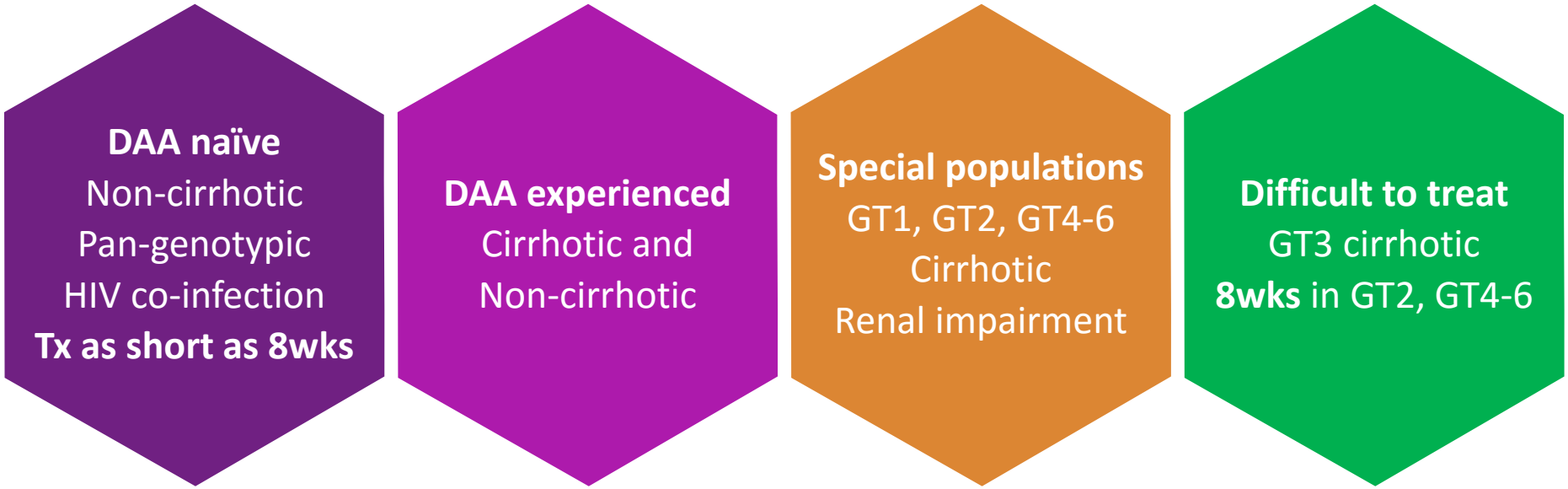
	GT/ F stage	Treatment History	Duration (weeks)	SVR_{12} (non-virologic failures excluded)
SUREVEYOR-1 and MAGELLAN-1	1/ F0-F3	Treatment naïve and experienced	8	**100%**
		Treatment naïve and experienced	12	**100%**
		DAA experienced	12	**95%**
	1/ F4	Treatment naïve and experienced	12	**96%**
SUREVEYOR-2	2/ F0-F3	Treatment naïve and experienced	12	**100%**
		Treatment naïve and experienced	8	**100%**
SUREVEYOR-2	3/ F0-F3	Treatment naïve and experienced	12	**97%**[a]
		Treatment naïve	8	**100%**
		Experienced	12	**92%**
SUREVEYOR-1	3/ F4	Treatment naïve	12	**100%**[b]
	4-6/ F0-F3	Treatment naïve and experienced	12	**100%**

8wk regimen being tested in Phase 3

a. SVR12 in TN patients was 100%; b. Screening of GT3 cirrhotic PR-exp. was stopped prematurely (FDA recommendation); only 4 GT3 cirrhotic PR-experienced (not included in the table) were randomized and their duration was extended to 16 weeks, 1 out of these 4 patients relapse.

DAA = Direct Acting Antivirals

The Next Gen Phase 3 Program Is Designed to Address Residual Unmet Medical Need



Next Gen commercialization expected in 2017

abbvie

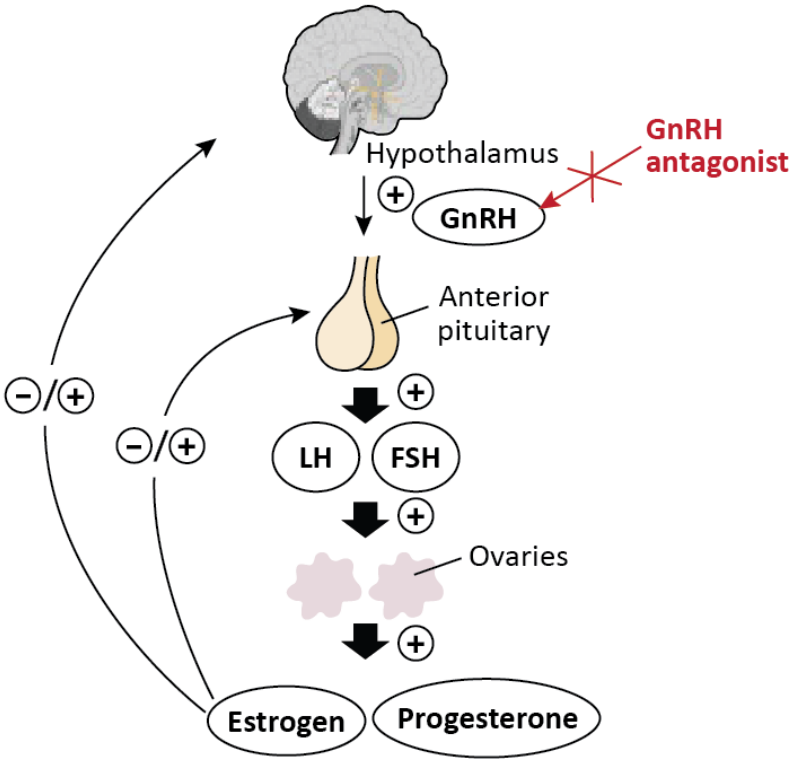
ELAGOLIX

Elagolix Profile

Attributes and Mechanism of Action

- Orally active
- Gonadotropin releasing hormone (GnRH) antagonist
- Dose dependent suppression of estrogen and progesterone
- Rapid onset of action and readily reversible when therapy stopped
- Potential for management of hormonally-mediated conditions, such as endometriosis and uterine fibroids

Female HPG Axis



Elagolix for the Management of Endometriosis

Endometriosis

Abnormal growth of endometrial tissue

- Tissue that lines the uterus grows outside of the uterus
- Tissue is responsive to estrogen

Epidemiology

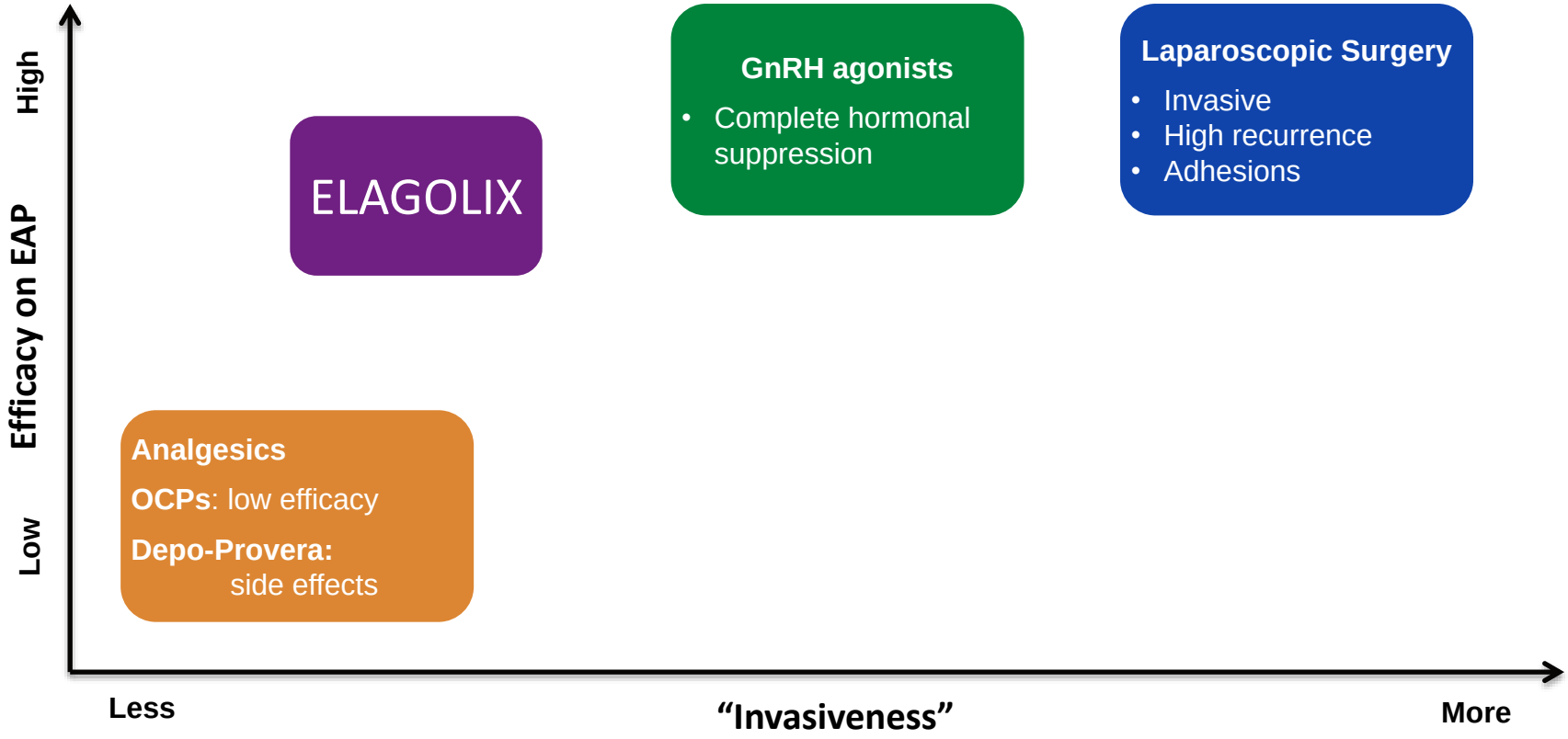
- Endometriosis affects an estimated 176 million women worldwide.[1]

Symptoms:

- **Menstrual pain (Dysmenorrhea)**
- **Chronic non-menstrual pelvic pain**
- Infertility

[1] The World Endometriosis Research Foundation: Facts about Endometriosis.

Elagolix Has the Potential to Improve the Limited Treatment Options for Endometriosis-Associated Pain (EAP)



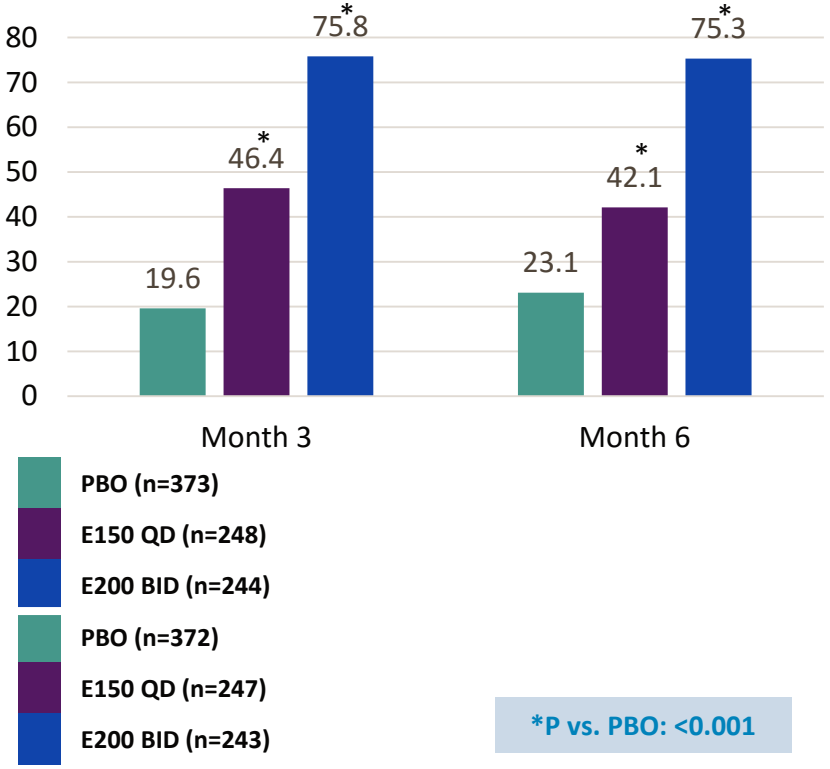
Unmet Need

- Oral agent
- Rapid reversibility
- Significant pain reduction
- Laparoscopy not required to initiate treatment
- Long-term efficacy

Elagolix Endometriosis Phase 3 Pivotal Studies
Change from Baseline in Dysmenorrhea (DYS)

Violet Petal

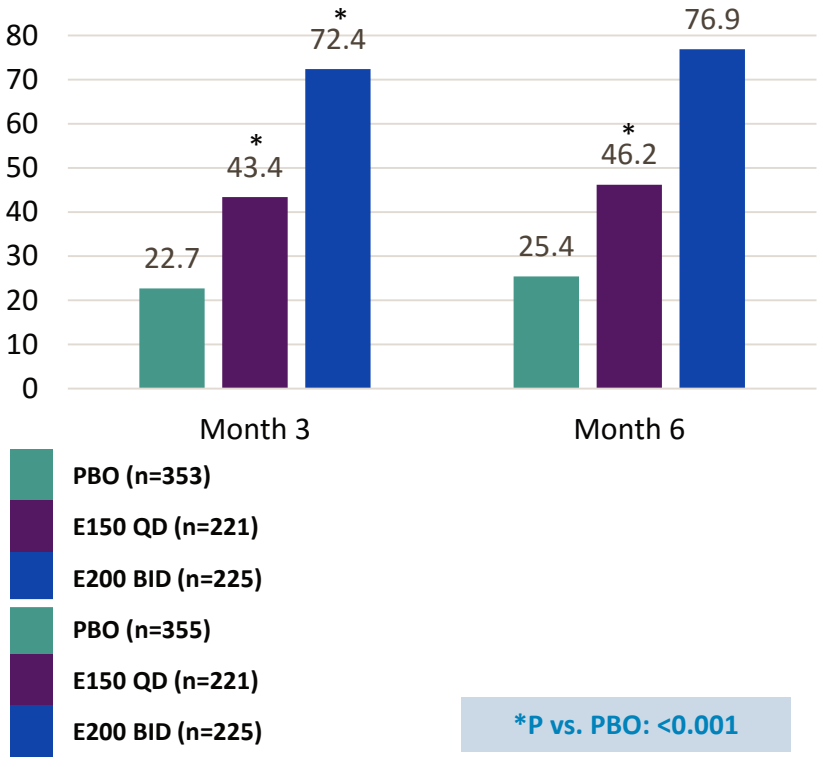
Responder Rates



*P vs. PBO: <0.001

Solstice

Responder Rates



*P vs. PBO: <0.001

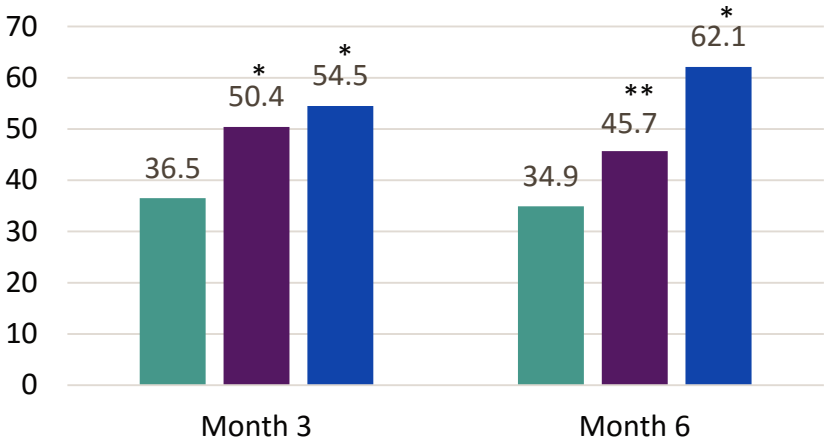
violet petal STUDY

Solstice

Elagolix Endometriosis Phase 3 Pivotal Studies
Change from Baseline in Non-Menstrual Pelvic Pain (NMPP)

Violet Petal

Responder Rates



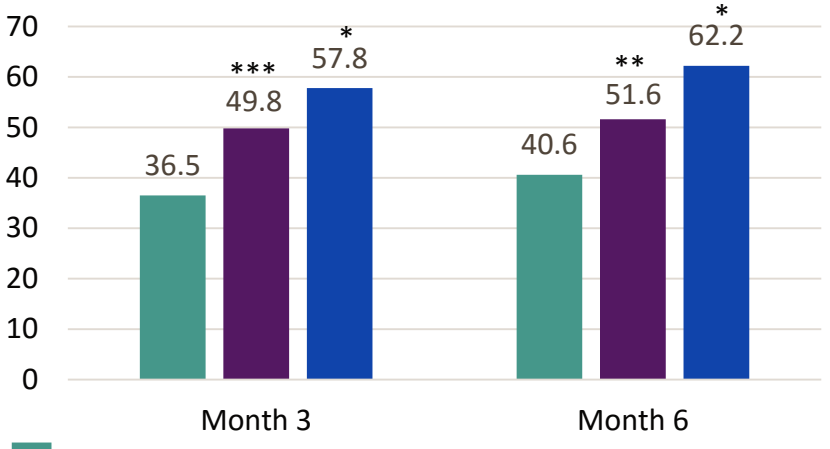
PBO (n=373)
E150 QD (n=248)
E200 BID (n=244)
PBO (n=372)
E150 QD (n=247)
E200 BID (n=243)

*P vs. PBO: <0.001;
**P vs. PBO: <0.01;
***P vs. PBO: 0.003

violet petal STUDY

Solstice

Responder Rates

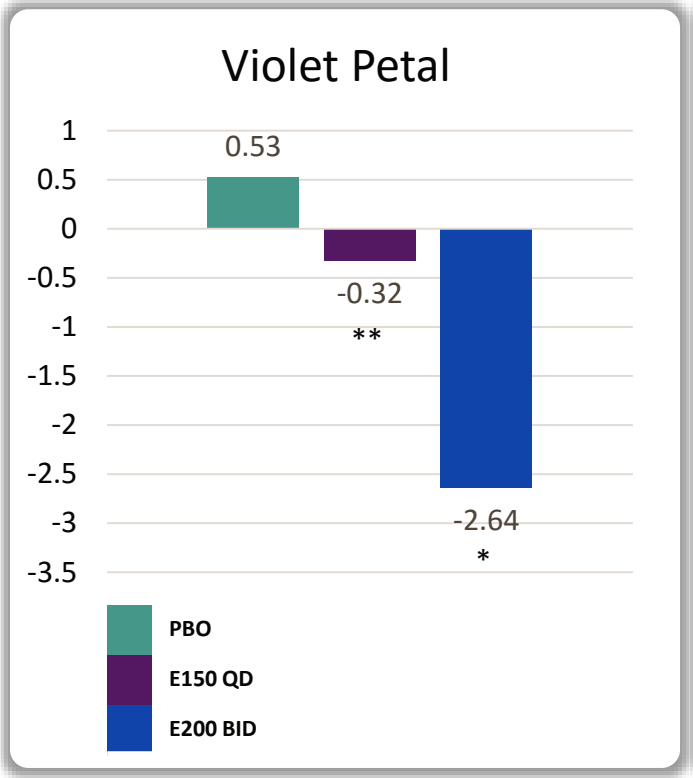


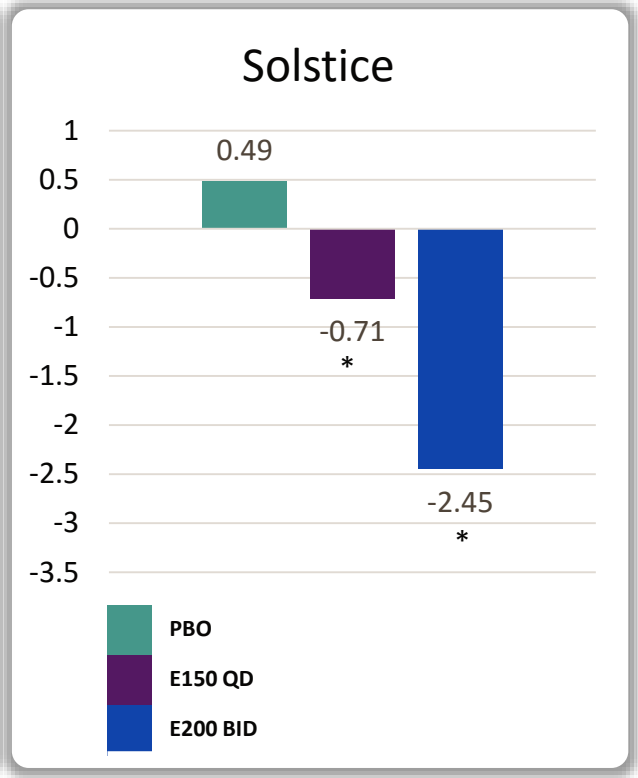
PBO (n=353)
E150 QD (n=221)
E200 BID (n=225)
PBO (n=355)
E150 QD (n=221)
E200 BID (n=225)

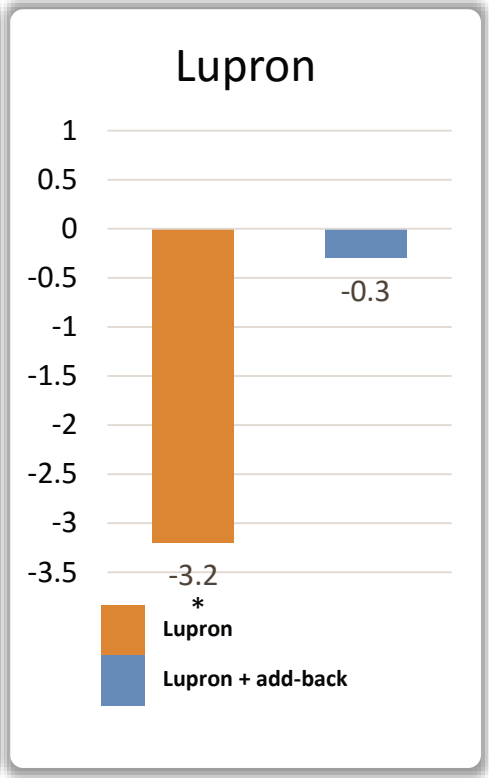
*P vs. PBO: <0.001;
**P vs. PBO: <0.01;
***P vs. PBO: 0.003

Solstice

Elagolix Endometriosis Phase 3 Pivotal Studies
Mean Percent Change from Baseline in Bone Mineral Density







- Limited BMD decrease at Elagolix 150 mg QD
- Higher BMD decrease at 200 mg BID
  - Options for bone protection are under evaluation, including hormonal add-back therapy
- Lupron 3.75 mg IM dosed monthly, is approved for 6 months when used without hormonal add-back therapy

Lupron approved for 6mo use

*P vs. PBO: <0.001
**P vs. PBO: 0.002

BMD measured in Lumbar Spine

Elagolix for the Management of Uterine Fibroids

Uterine Fibroids

Benign uterine tumors

- One or multiple tumors
- Tumors are estrogen and progesterone responsive
- Resolve after menopause

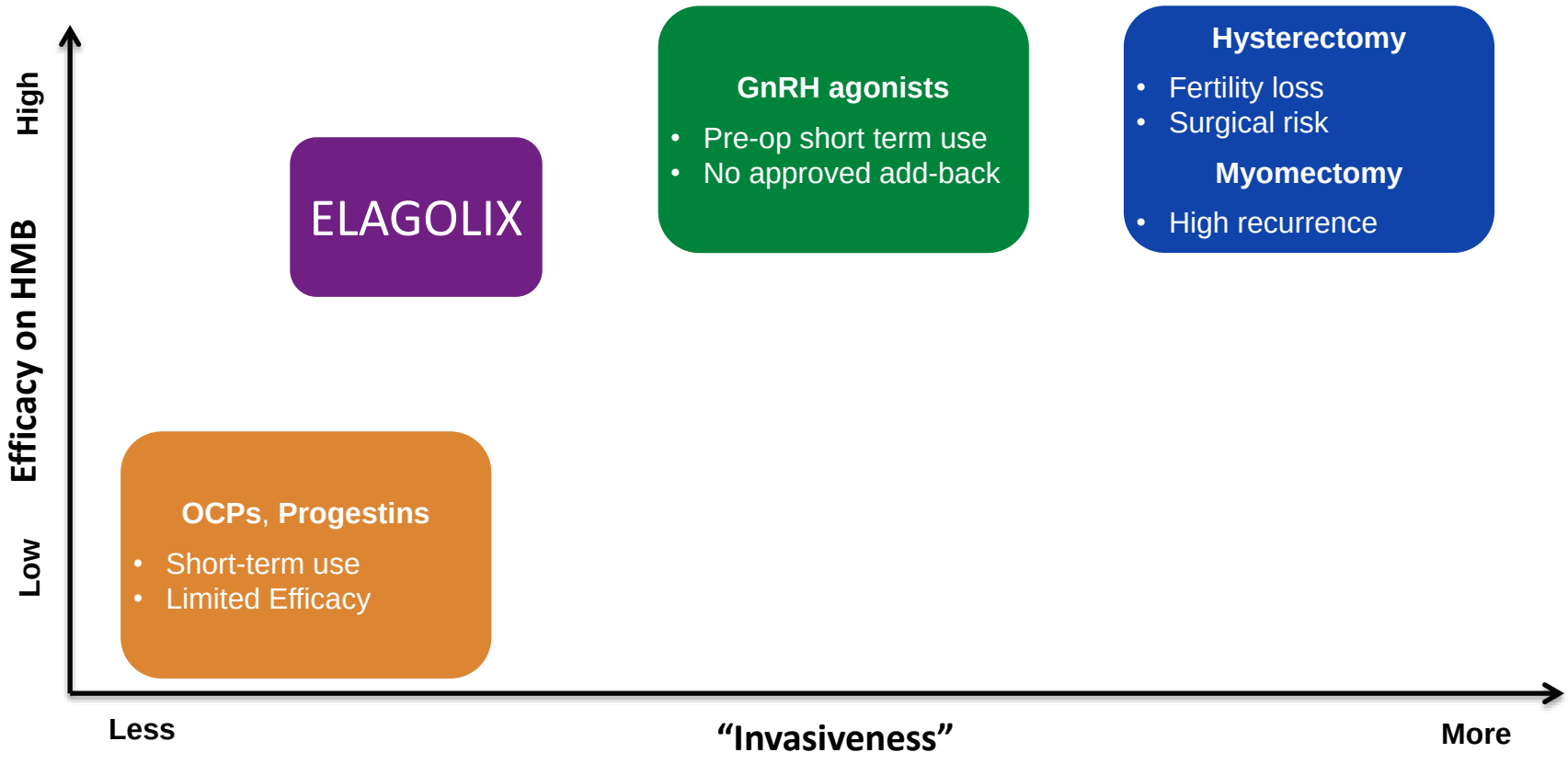
Epidemiology

- Estimated that the lifetime incidence in pre-menopausal women is 50–80%

Symptoms:

- **Heavy menstrual bleeding, often with anemia**
- Bulk symptoms (e.g., pelvic pressure, urinary frequency, etc.)
- Early pregnancy loss and infertility

Elagolix Has the Potential to Provide a Continuously Effective Treatment for Heavy Menstrual Bleeding (HMB) Associated with Uterine Fibroids (UF)

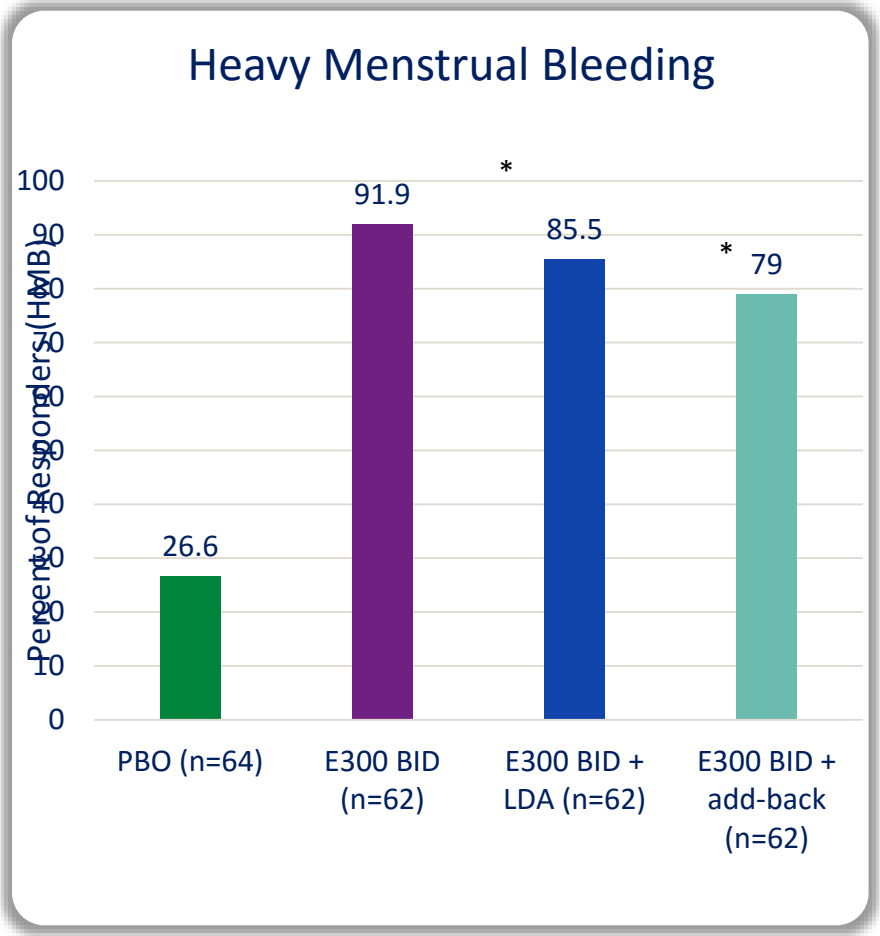


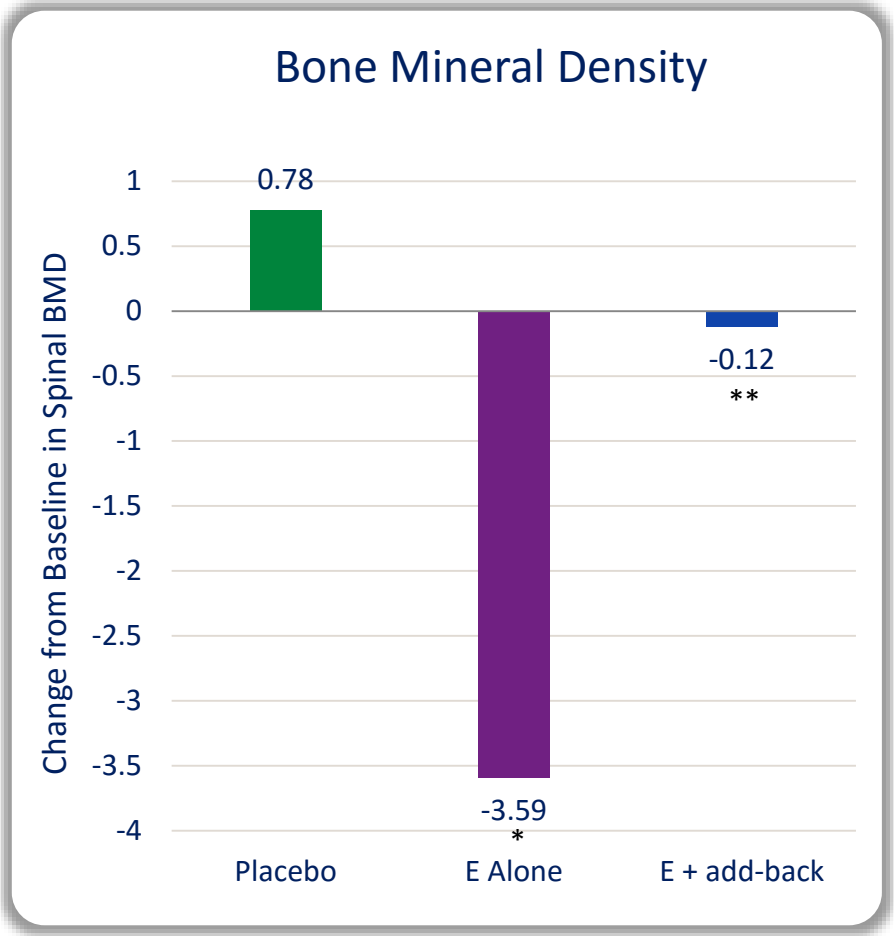
Unmet Need

- Long-term efficacy without surgery

Elagolix Demonstrated Marked Efficacy in Uterine Fibroids in Ph2b

Add-back Therapy Is Effective in Preventing Loss of Bone Density



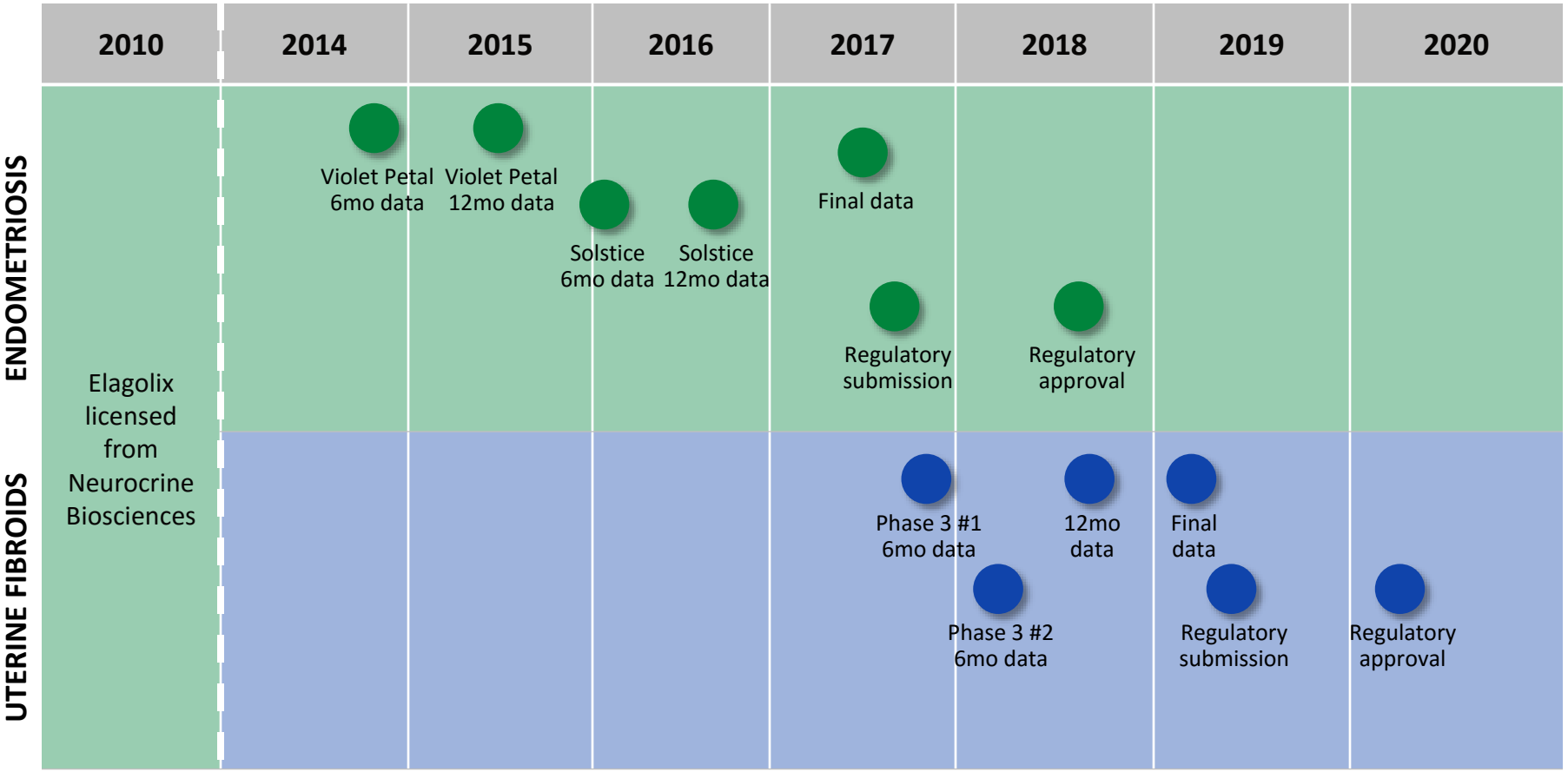


E = Elagolix 300 mg BID

Add-back = standard dose Activella (E2 1.0 mg/ NETA 0.5 mg) QD

***P vs. PBO: <0.001;**
****P vs. PBO: 0.148**

Elagolix on Track to Be the First Approval for Endometriosis Since Lupron in 1990



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NEUROSCIENCE

Oncology

Immunology

HCV

Elagolix

Neuroscience

abbvie

Zinbryta and ABT-555

Laura Gault, M.D., Ph.D.
Development

Eric Karran, Ph.D.
Discovery

AbbVie Neuroscience: Providing Novel and Effective Treatments for Neurodegenerative Disorders

Parkinson's Disease
Symptomatic Treatments
Disease Modification

- Less invasive, efficacious symptomatic treatments
- Halt disease progression

Multiple Sclerosis
Immunomodulation, Neuroprotection, Neuroregeneration

- Higher efficacy and manageable safety
- Improve function

Alzheimer's Disease
Disease Modification

- Maintain function
- Identify appropriate time to initiate treatment

AbbVie Neuroscience Pipeline
Marketed Products and Select Clinical Development Programs

Parkinson's Disease

Duodopa/Duopa: Levodopa-Carbidopa Intestinal Gel

- Marketed worldwide
- Improves function

Duodopa®
Duopa™

Multiple Sclerosis

Zinbryta: Anti-CD25 mAb

- Partnered with Biogen
- Demonstrated reduction in relapse and disability progression

ABT-555: RGMa mAb

- Phase 1
- Extensive preclinical evidence of neuroprotection and regeneration
- Based on biology pioneered at AbbVie*

Alzheimer's Disease

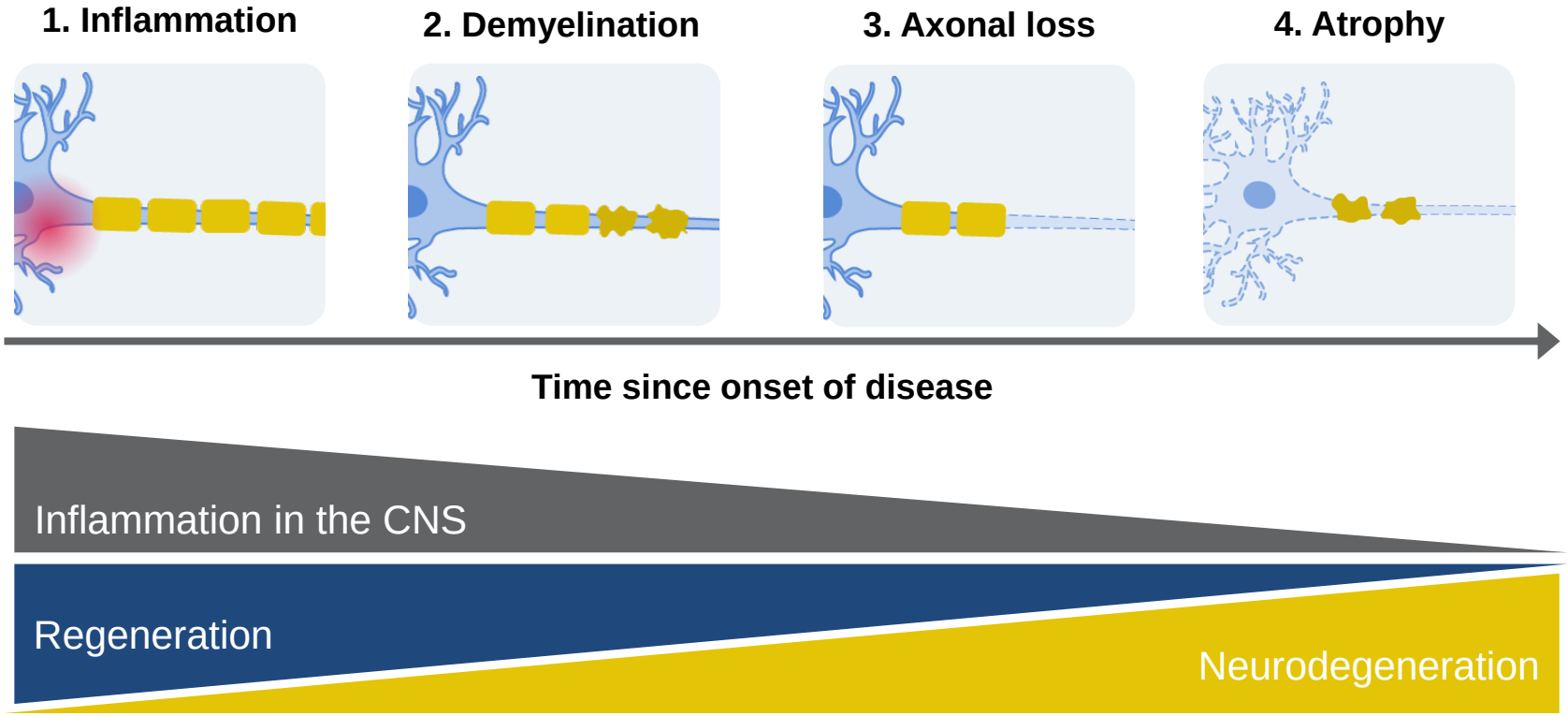
ABBV-8E12: Anti-tau mAb

- Phase 1
- Targets tau pathology
- Initial antibody development in Holtzman lab at Washington University

* Demicheva et al., 2015, Cell Reports 10:1-12

MS Is an Unpredictable, Progressive, Immune-mediated Disease

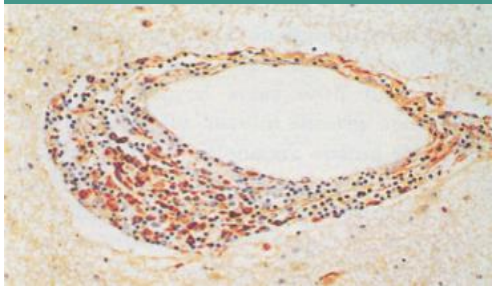
MS progression over time



MS = Multiple Sclerosis CNS = Central Nervous System

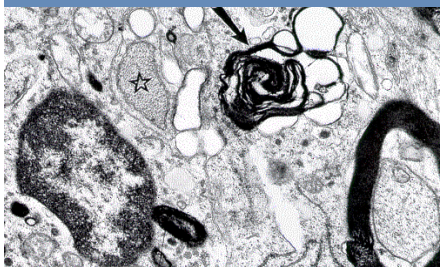
Current Treatments Are Immunomodulatory; Future Treatments Will Also Promote Neuroprotection and Neuroregeneration

Inflammation

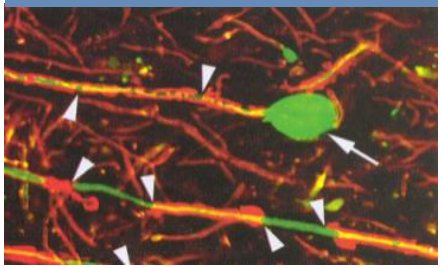


Platform agents such as interferons reduce the number of inflammatory relapses

Demyelination



Neuronal Loss



Drugs that promote remyelination or neuronal regeneration will be an important component of the future treatment paradigm

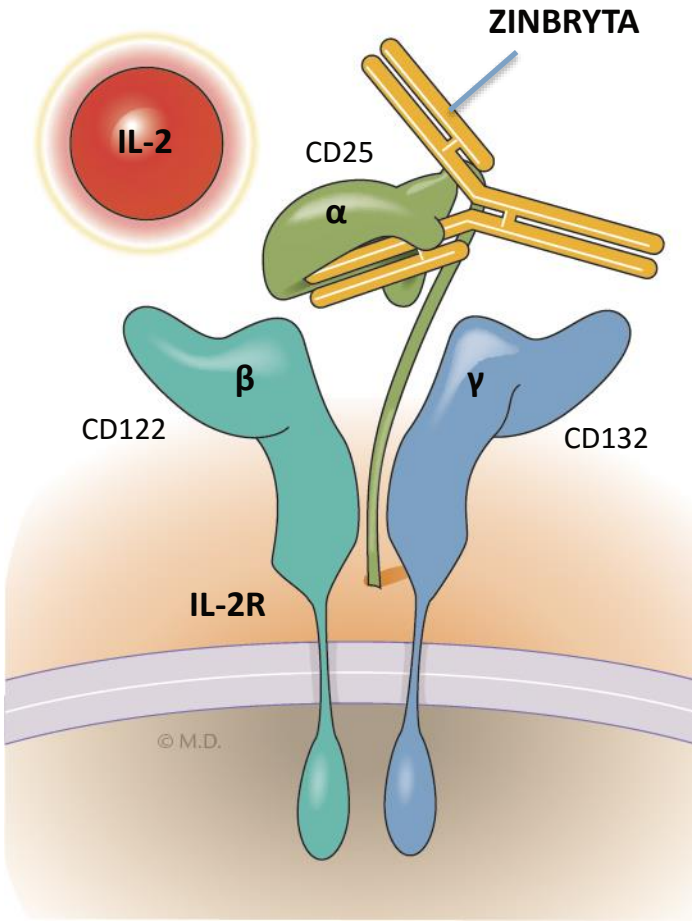
AbbVie is committed to meeting all the needs of patients with MS:

- Zinbryta will provide a novel immunomodulatory treatment option for patients
- ABT-555 under evaluation for neuroprotective and neuroregenerative effects

People with MS Need Additional Innovative Therapies

- Age of onset in the 30s, with unpredictable severity and progression
- Relapses often occur on initial therapies, prompting switch to another medication
- Drug efficacy/safety profiles inform the right choice for each patient
- New treatments with novel mechanisms of action are needed to provide additional individualized treatment options

Zinbryta (daclizumab)
Novel Mechanism to Address Unmet Needs in Multiple Sclerosis

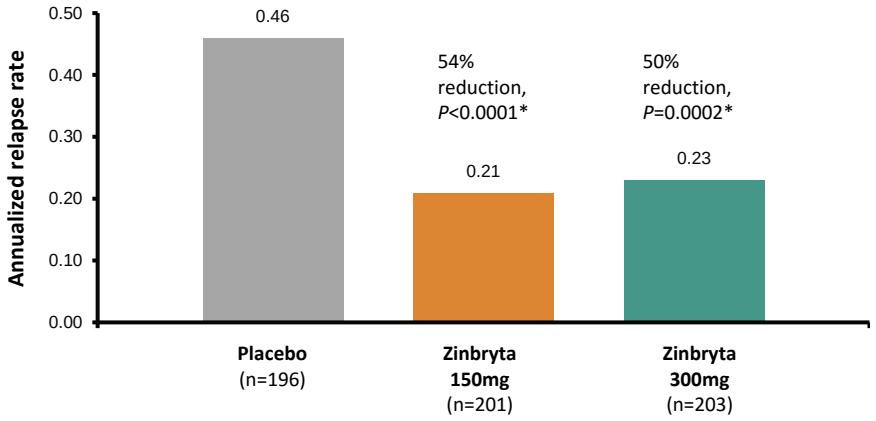


Bielekova B, et al. Proc Natl Acad Sci U S A. 2006;103:5941-5946.
Bielekova B. Neurotherapeutics. 2013;10:55-67.

- Humanized IgG1 mAb that binds specifically to the α-subunit of the interleukin-2 receptor (CD25, IL-2Rα)
- Novel biology – selectively blocks high affinity IL-2 receptor signaling:
  - Specifically inhibits activated effector T cells
  - Expands immunoregulatory CD56brightNK cells
  - Decreases regulatory T (Treg) cells
  - Immunomodulatory effects without broad immune cell depletion

Zinbryta Demonstrated Efficacy in Two Pivotal Trials

SELECT STUDY

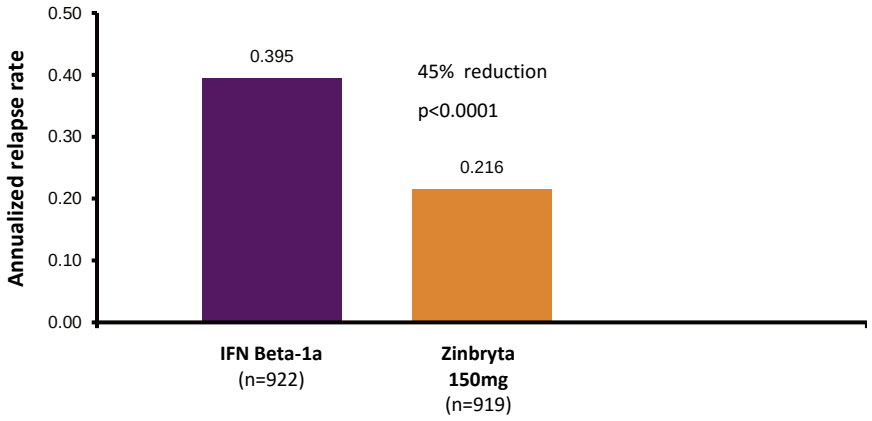


Zinbryta 150 mg demonstrated a 54% reduction in annualized relapse rate v placebo over 52 weeks

12 week confirmed disability progression

13% (placebo) v 6% (Zinbryta), p = 0.02

DECIDE STUDY



Zinbryta 150 mg demonstrated a 45% reduction in annualized relapse rate v IFN beta-1a at 2-3 years

12 week confirmed disability progression

14% (IFN beta-1a) v 12% (Zinbryta), p = 0.16

Gold et al., *Lancet* 2013 (SELECT); Kappos et al., NEJM, 2015 (DECIDE)

Benefit/Risk of Zinbryta Consistent with Other High Efficacy Agents

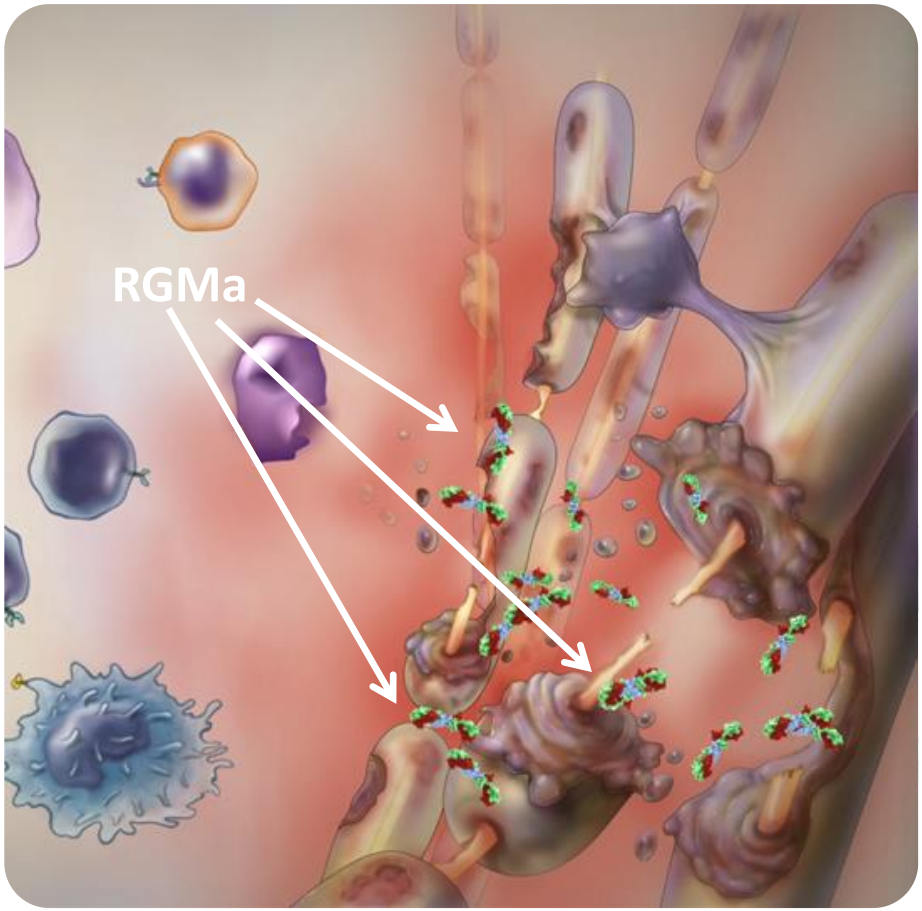
- Overall exposure in clinical trials is approximately 4,100 patient years
  - 2,133 MS patients treated with Zinbryta, for up to six years
- Warnings include: Hepatic injury, immune mediated disorders, acute hypersensitivity, infections, depression and suicide
- The most common adverse reactions (incidence ≥5% and ≥2% higher incidence than comparator) were: Nasopharyngitis, upper respiratory tract infection, influenza, dermatitis/rash, oropharyngeal pain, bronchitis, eczema, lymphadenopathy, depression, pharyngitis, and increased alanine aminotransferase (ALT)
- Zinbryta risks and side effects are generally manageable, including a REMS program with monthly monitoring

Zinbryta: A New Efficacious Treatment Option for People with Relapsing Forms of Multiple Sclerosis

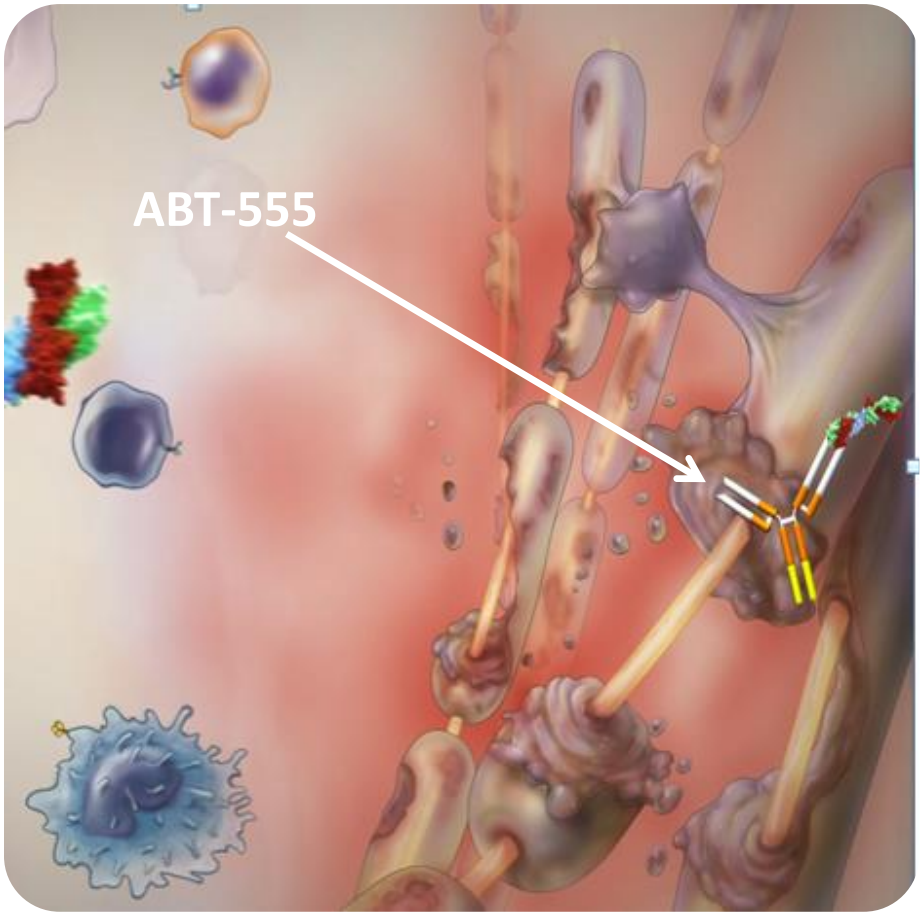
Increased efficacy (v IFN beta-1a) with a unique mechanism of action and convenient administration

- Novel mechanism of action that inhibits activated T-cells, while major immune cell subsets (T, B, NK) remained within normal ranges
- Zinbryta has shown superior, sustained efficacy versus IFN beta-1a (a standard first line therapy)
- Zinbryta risks and side effects are generally manageable, including a REMS program with monthly monitoring
- Monthly, self-administered subcutaneous dosing

A Fundamental Abnormality in MS and Spinal Cord Injury is Increased RGMa; Neutralizing RGMa Is a Way to Allow Nerves to Regenerate



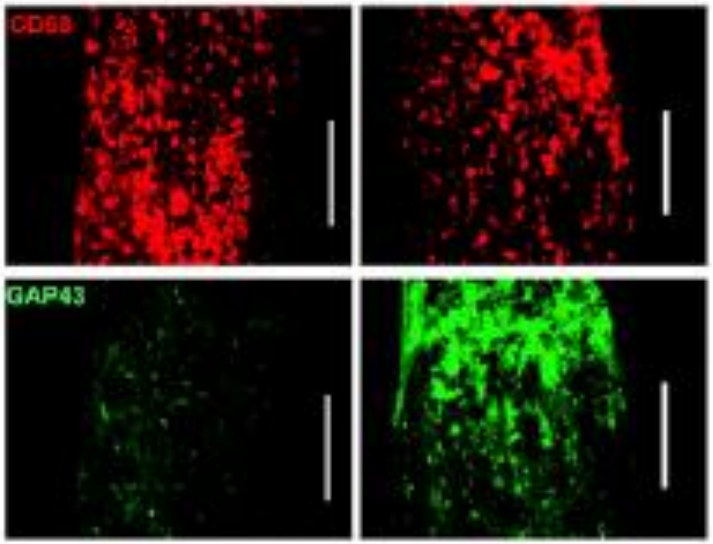
RGMa expression in MS promotes degeneration and inhibits axon regrowth and remyelination



ABT-555 blocks the effects of RGMa enabling axonal regeneration and remyelination

Anti-RGMa mAbs Demonstrated Neuroprotective and Neuroregenerative Effects in Preclinical Models of Neuroinflammatory Injury

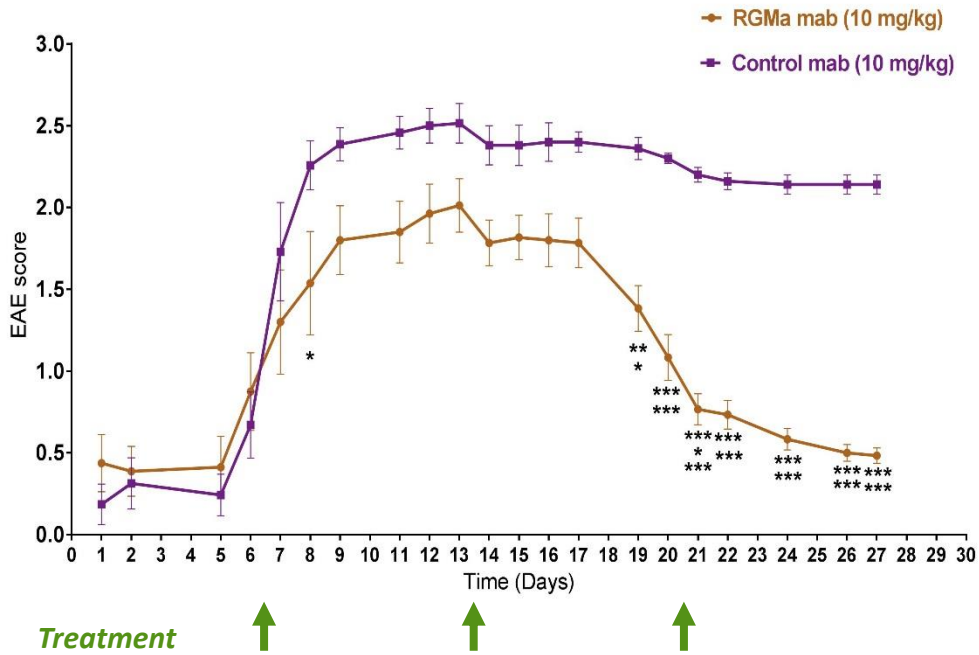
Targeted Optic Nerve Model



Control Ab Anti-RGMA Ab

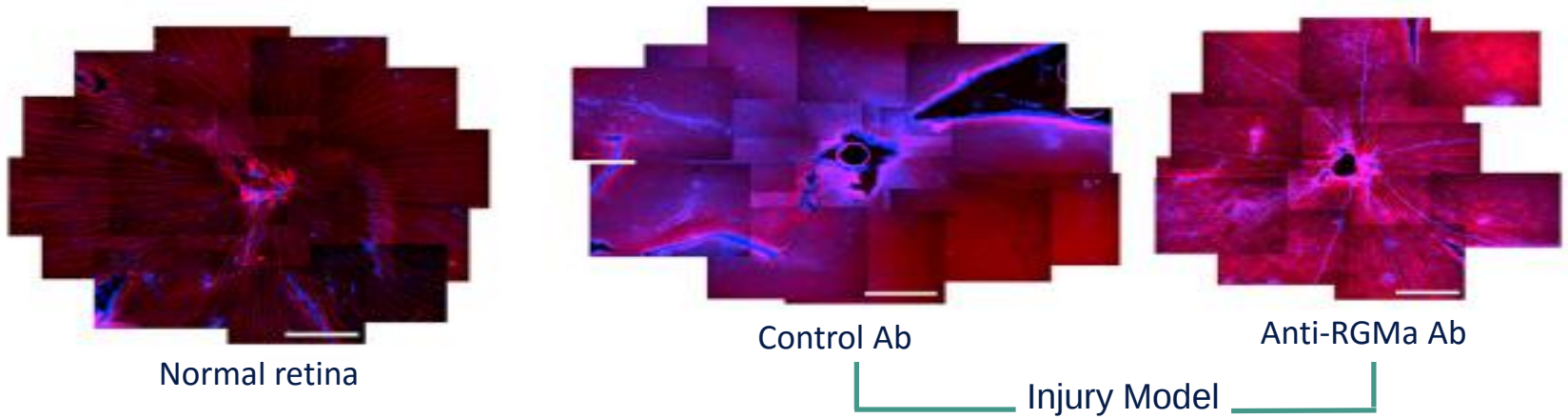
- Inflammatory cytokines injected into optic nerve
- Rats treated systemically with anti-RGMa antibody showed increased growth of nerve fibers into inflammatory lesion

Targeted Spinal EAE Model

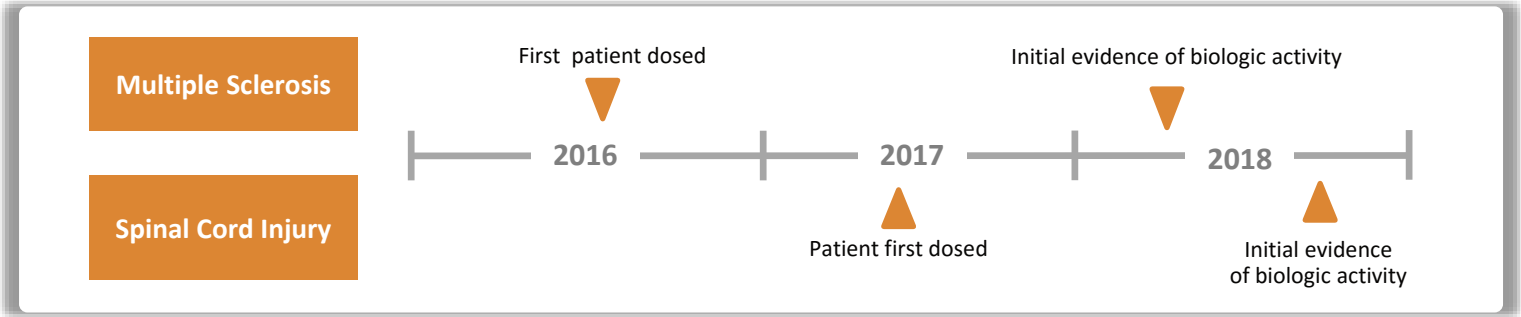


- Injection of inflammatory cytokines into rat spinal cord
- Anti-RGMa antibody administered after injury at weekly intervals improved recovery

Anti-RGMa mAbs Demonstrated Neuroprotective and Neuroregenerative Effects in Preclinical Models related to MS



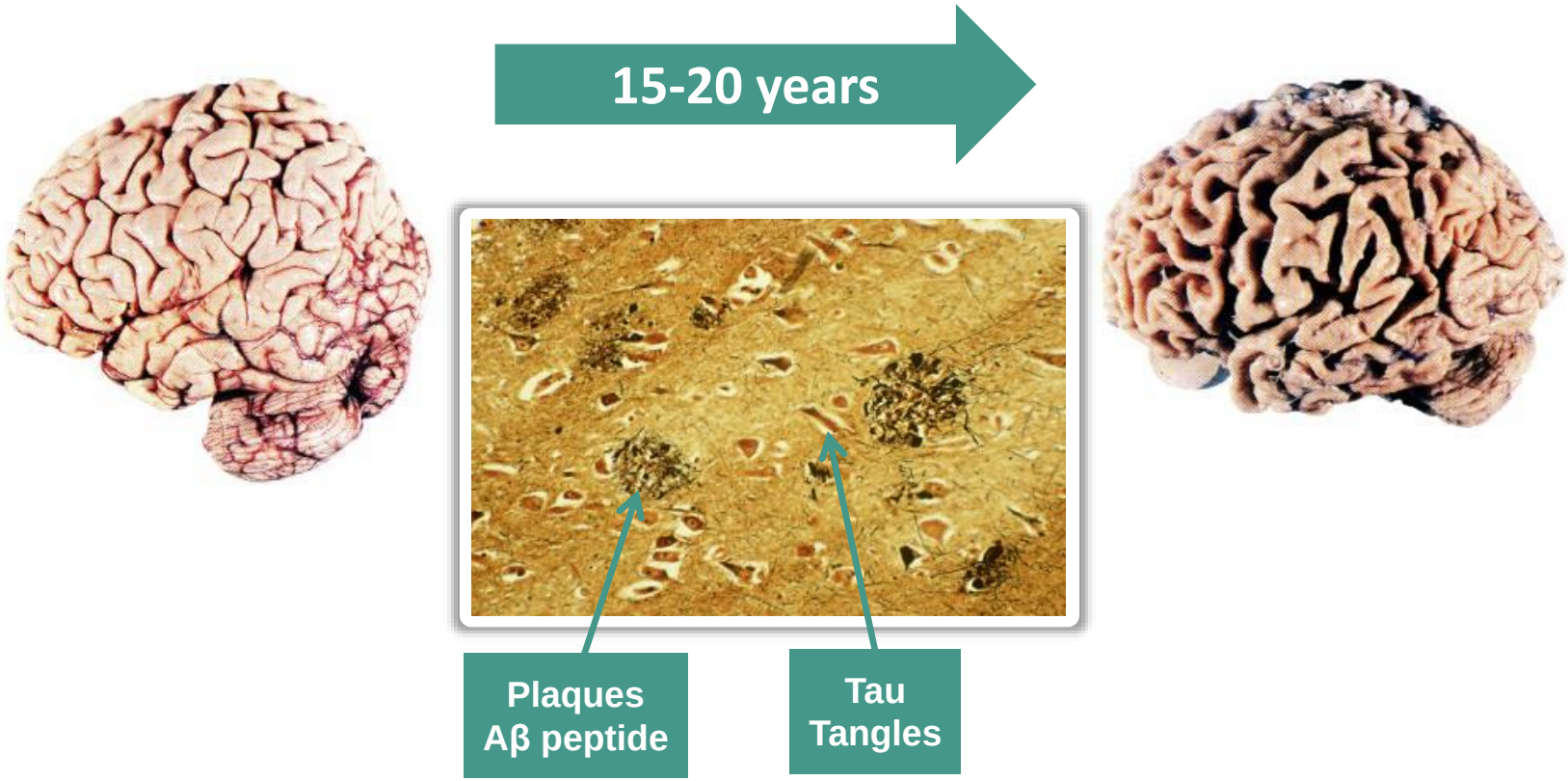
- Preclinical experiment in rats that recapitulates aspects of optic neuritis
- Treatment with anti-RGMa antibody preserved approximately 80% of axons compared to only 10% in control antibody treatment group
- Anti-RGMa antibody treatment prevents degeneration of the retinal fiber layer measured by optical coherence tomography (OCT)



Alzheimer's Disease Is an Emerging Global Crisis

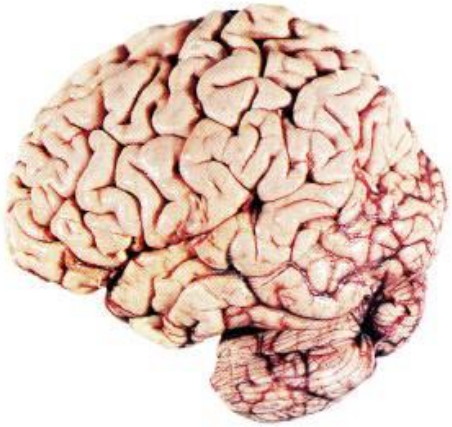
- **115 million** AD patients by 2050
- Cost of care in the US was **$225 billion** in 2015; will be **$1.1 trillion** by 2050
- **Therapeutic options** for AD are **limited**; progress lags well behind successes in oncology, inflammation, metabolic diseases and cardiology

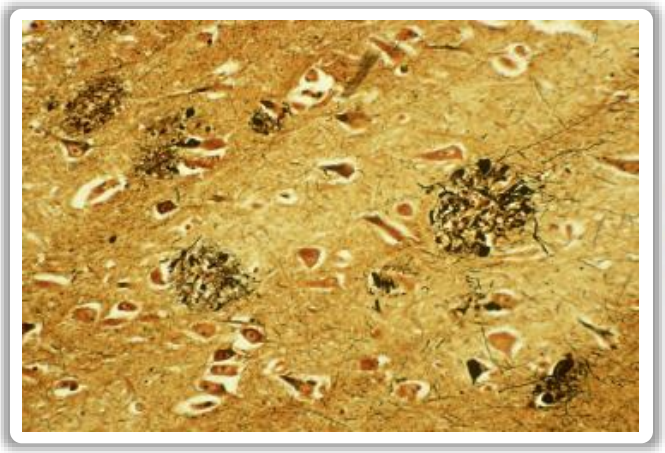
Alzheimer's Disease

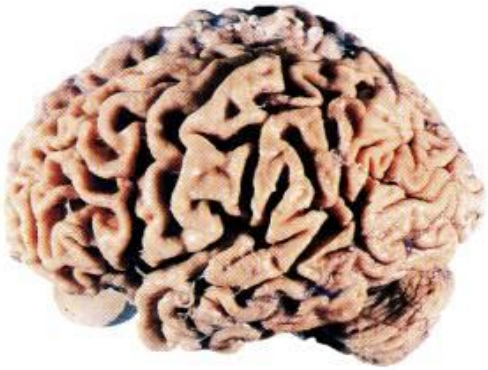


- Amyloid plaques - **do not correlate** with death of neurons or clinical symptoms
- Tau tangles - **do correlate** with death of neurons and clinical symptoms

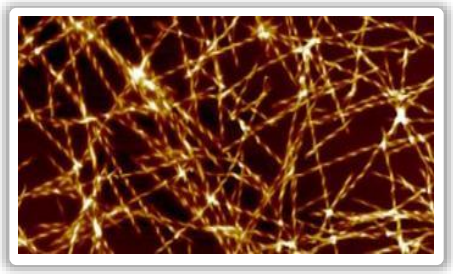
Alzheimer's Disease



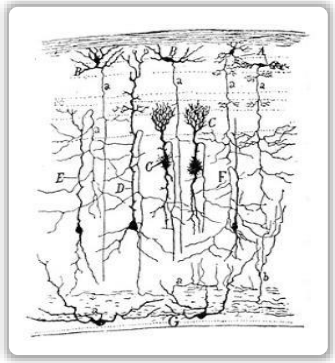




Biochemical phase



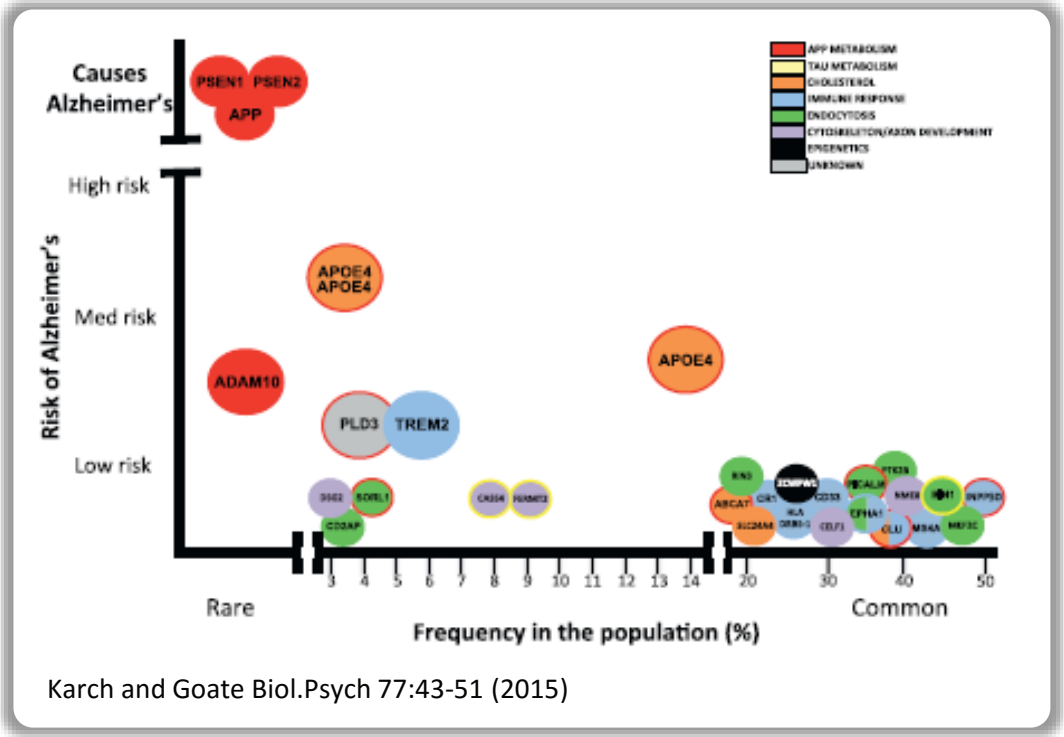
Cellular phase



Clinical phase

Recent Advances in Alzheimer's Research Are Promising

2010 → 2016



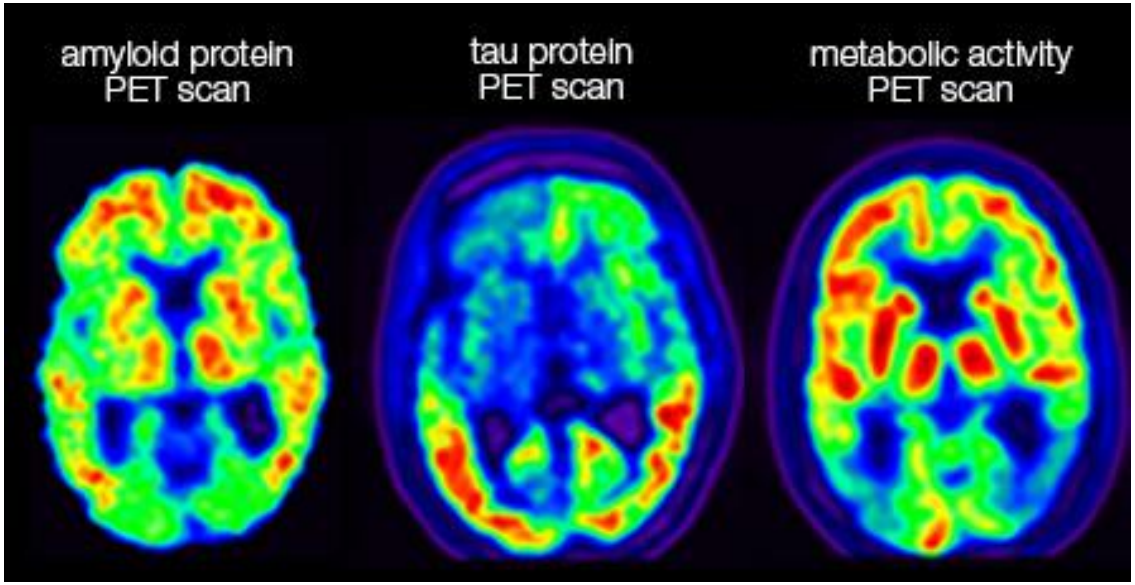
Karch and Goate Biol.Psych 77:43-51 (2015)

Recent Advances in Alzheimer's Research Are Promising

2010 → 2016

Growing understanding of the underlying pathobiology

Primarily Aβ approaches → Increased target diversity



http://memory.ucsf.edu/research/studies/eoad

Recent Advances in Alzheimer's Research Are Promising

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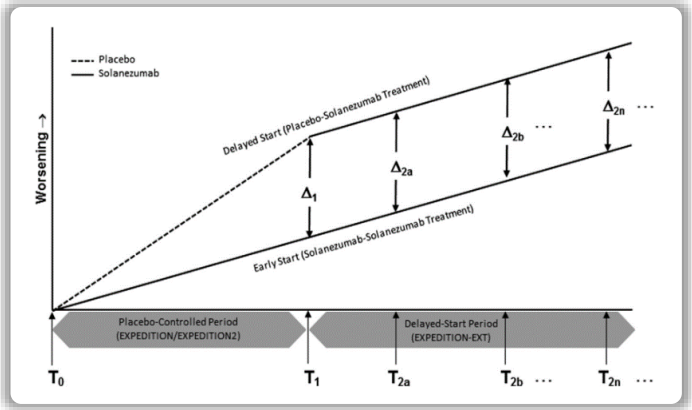
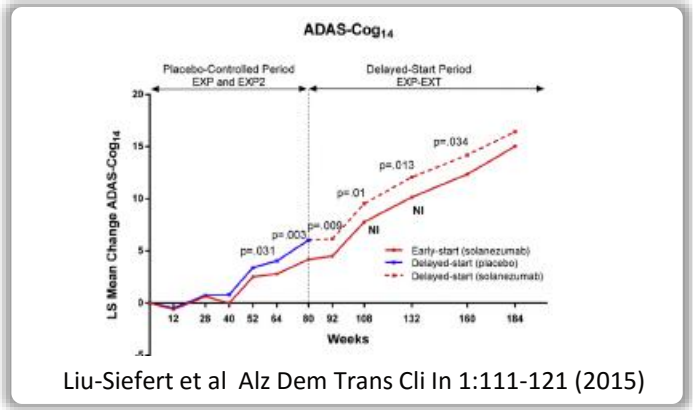
Availability of biomarkers

Trials frequently omit biomarkers of target engagement & efficacy → Amyloid imaging broadly available, tau imaging emerging, CSF biomarkers





Liu-Siefert et al Alz Dem Trans Cli In 1:111-121 (2015)

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Novel clinical trial designs

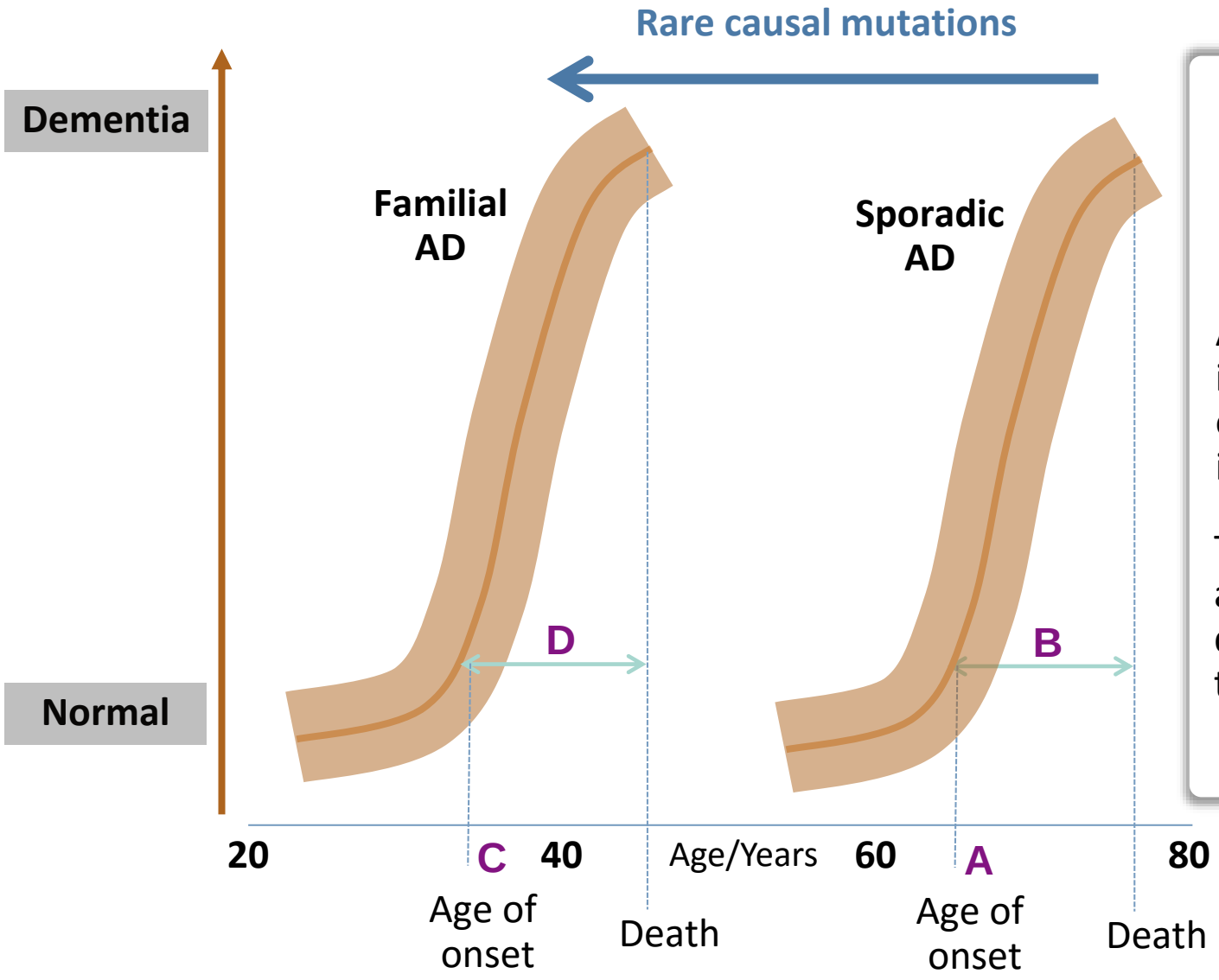
Mild to moderate patients → MCI/presymptomatic patients

Foundational Neuroscience Center

- To **gain** a fundamental understanding of disease processes and targets.
- To **execute** the highest caliber science internally and with world-class academic researchers and biotechs.
- To **populate** the AbbVie Neuroscience portfolio with innovative drug targets.
- Three focus areas:
  - **Tau pathobiology** spreading through the brain
  - **Neuroinflammation:** Microglial biology informed by new genetic findings
  - **Autophagy**: Why can't brain cells clear abnormal, toxic protein aggregates?

Amyloid/Aβ-based Therapeutics – AbbVie's Perspective

Amyloid/Aβ-based Therapeutics – AbbVie's Perspective



C < A

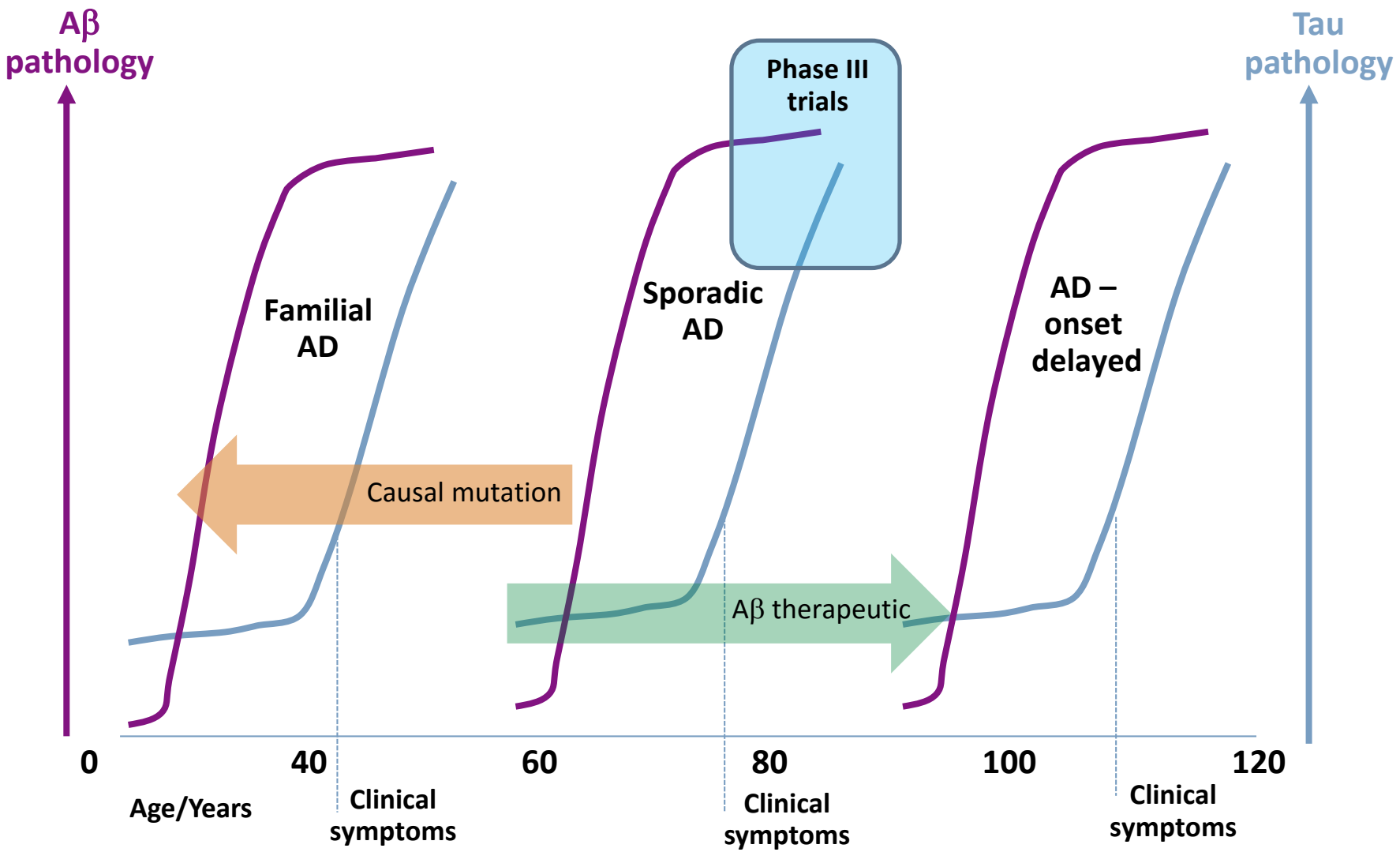
D = B

All causal mutations increase the probability of amyloid depositing in the brain.

This is consistent with amyloid ***triggering*** the disease process, rather than driving it.

Karran et al Nat Rev Drug Dis 10:698-712 (2011)

Amyloid/Aβ-based Therapeutics – AbbVie's Perspective



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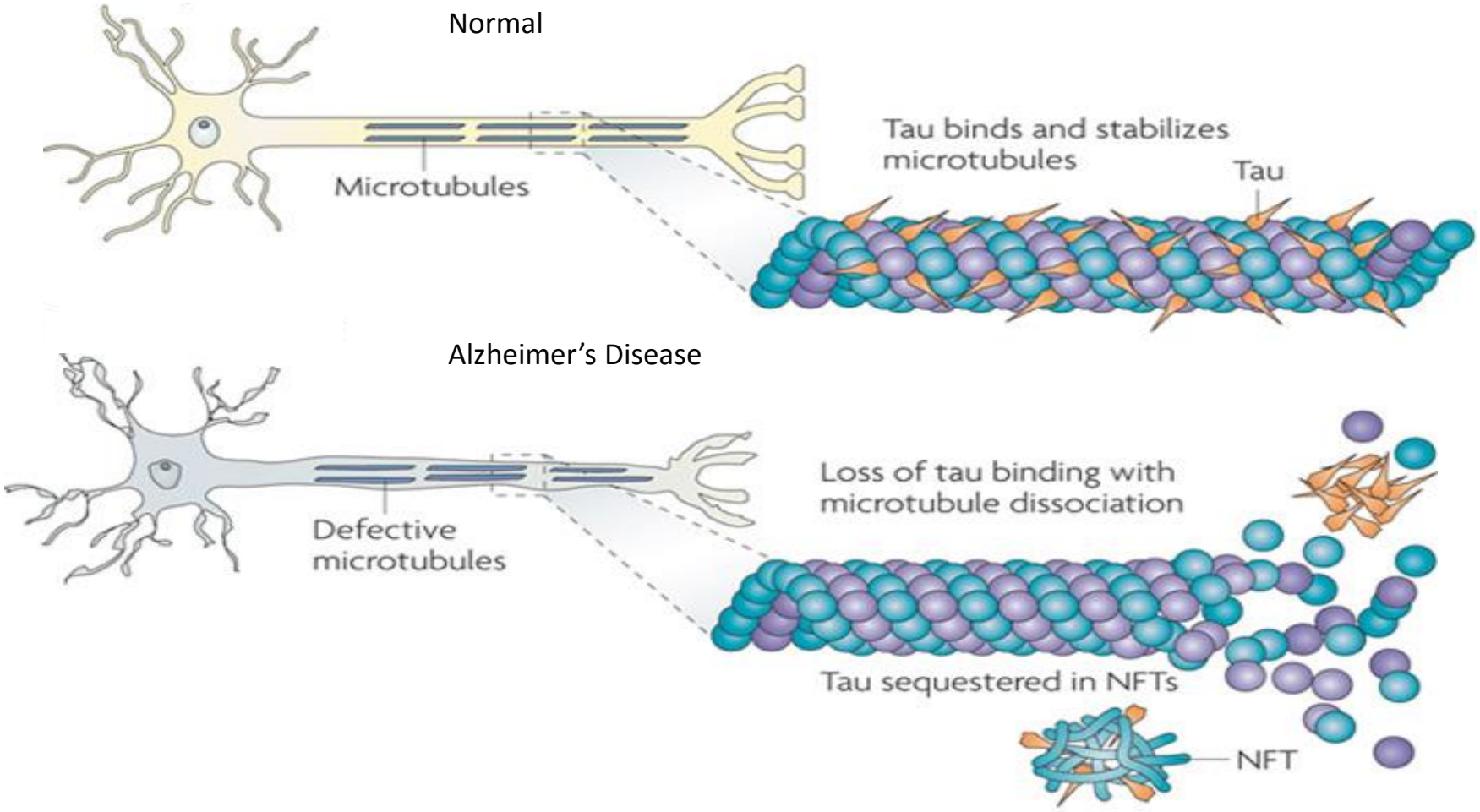
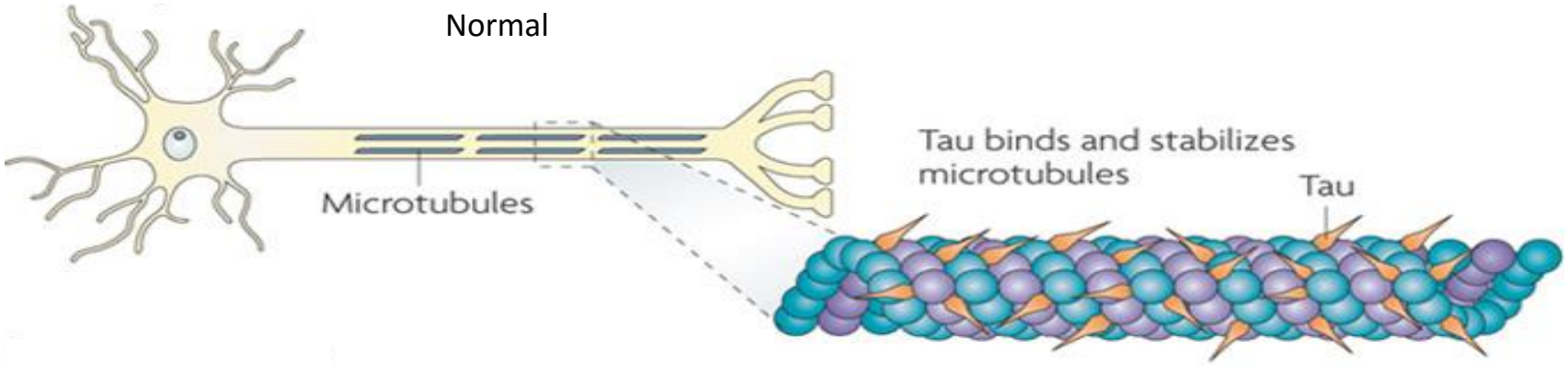
Tau Protein Supports the Intracellular "Skeleton" of Neurons



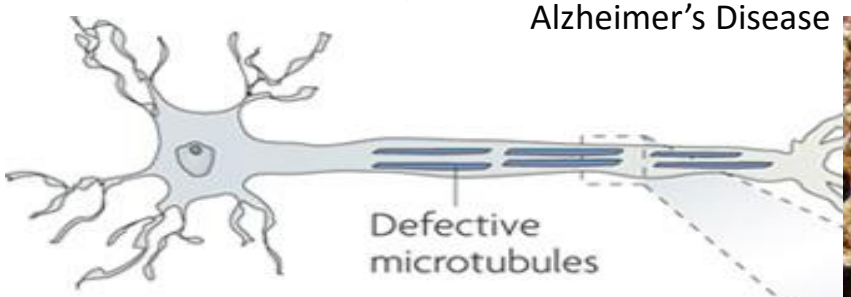
Brunden et al Nat Rev Drug Disc 8:783-793 (2009)

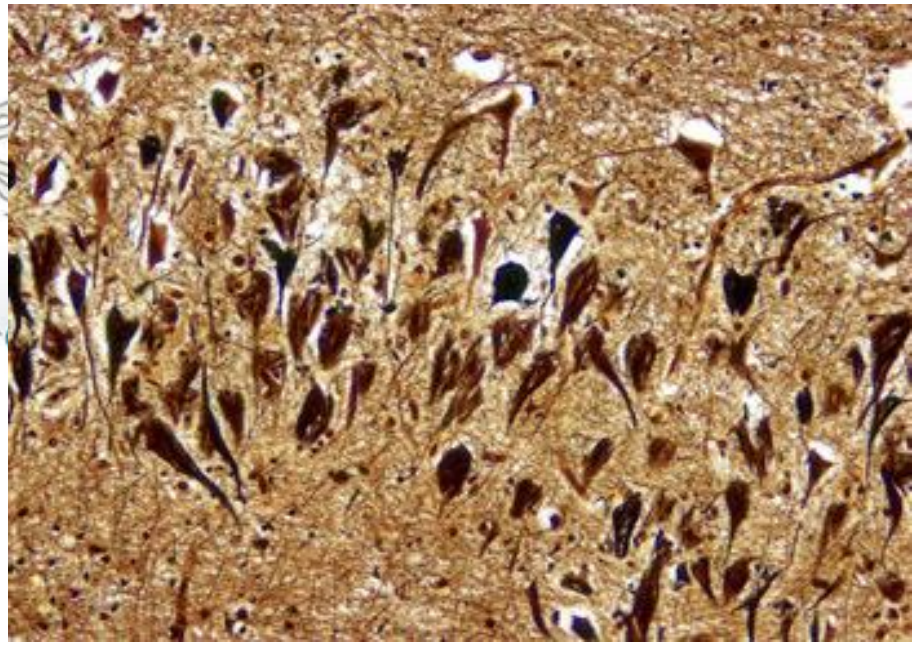
Tau Protein Supports the Intracellular "Skeleton" of Neurons

Normal



Alzheimer's Disease

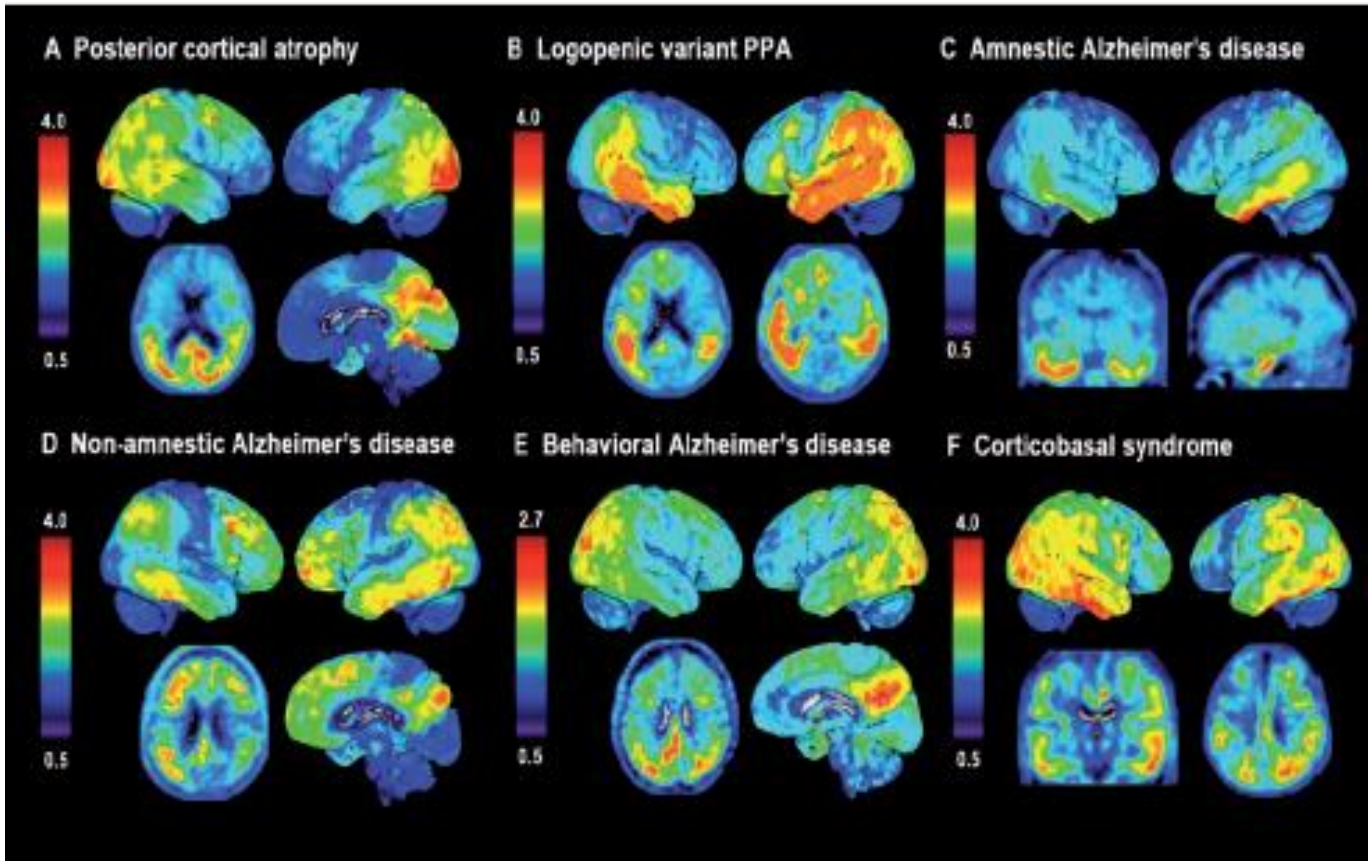




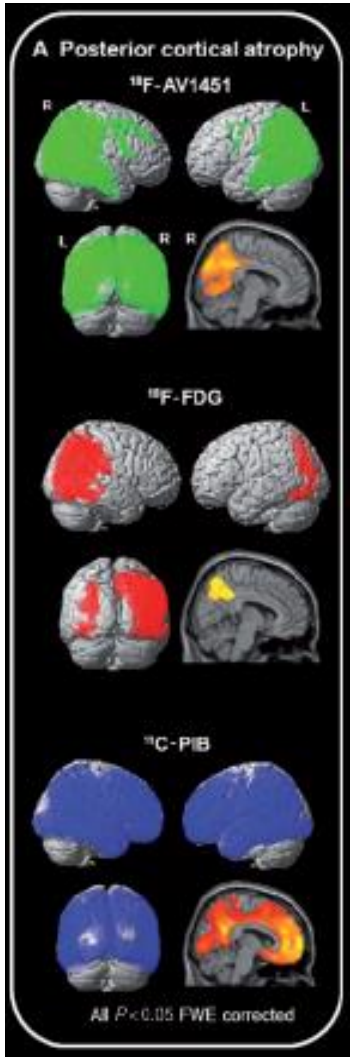
Brunden et al Nat Rev Drug Disc 8:783-793 (2009)

The Potential for Tau Therapeutics

- Tau pathology correlates spatially with symptomatology
- Amyloid does not

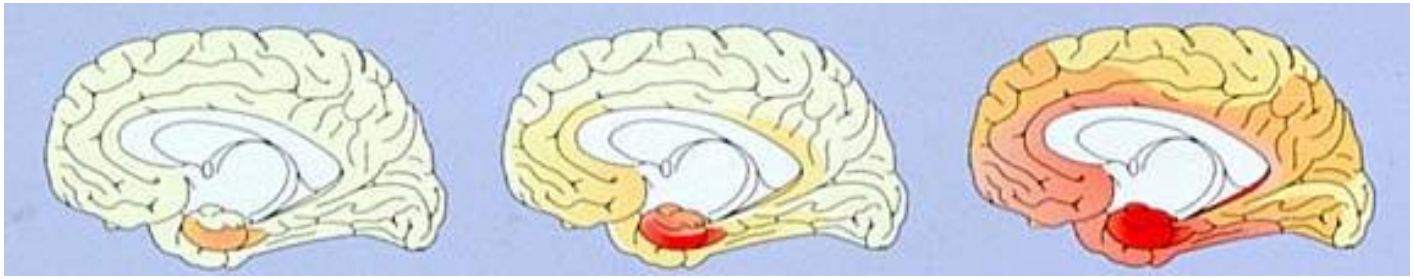


Ossenkoppele et al Brain 139: 1551-1567 (2016)



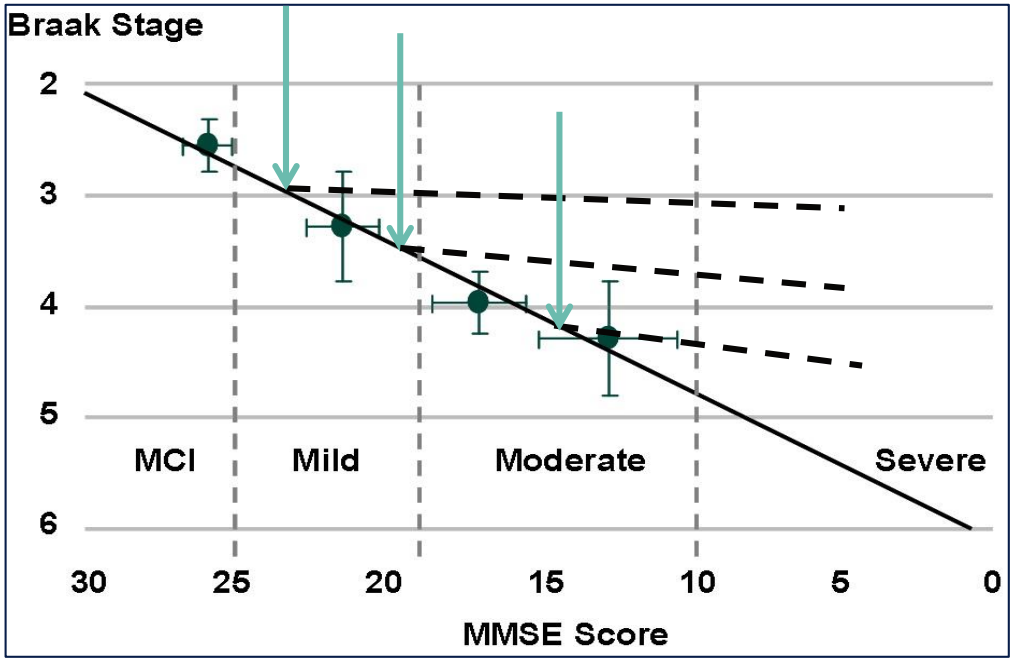
The Potential for Tau Therapeutics

Braak stages I-II III-IV V-VI



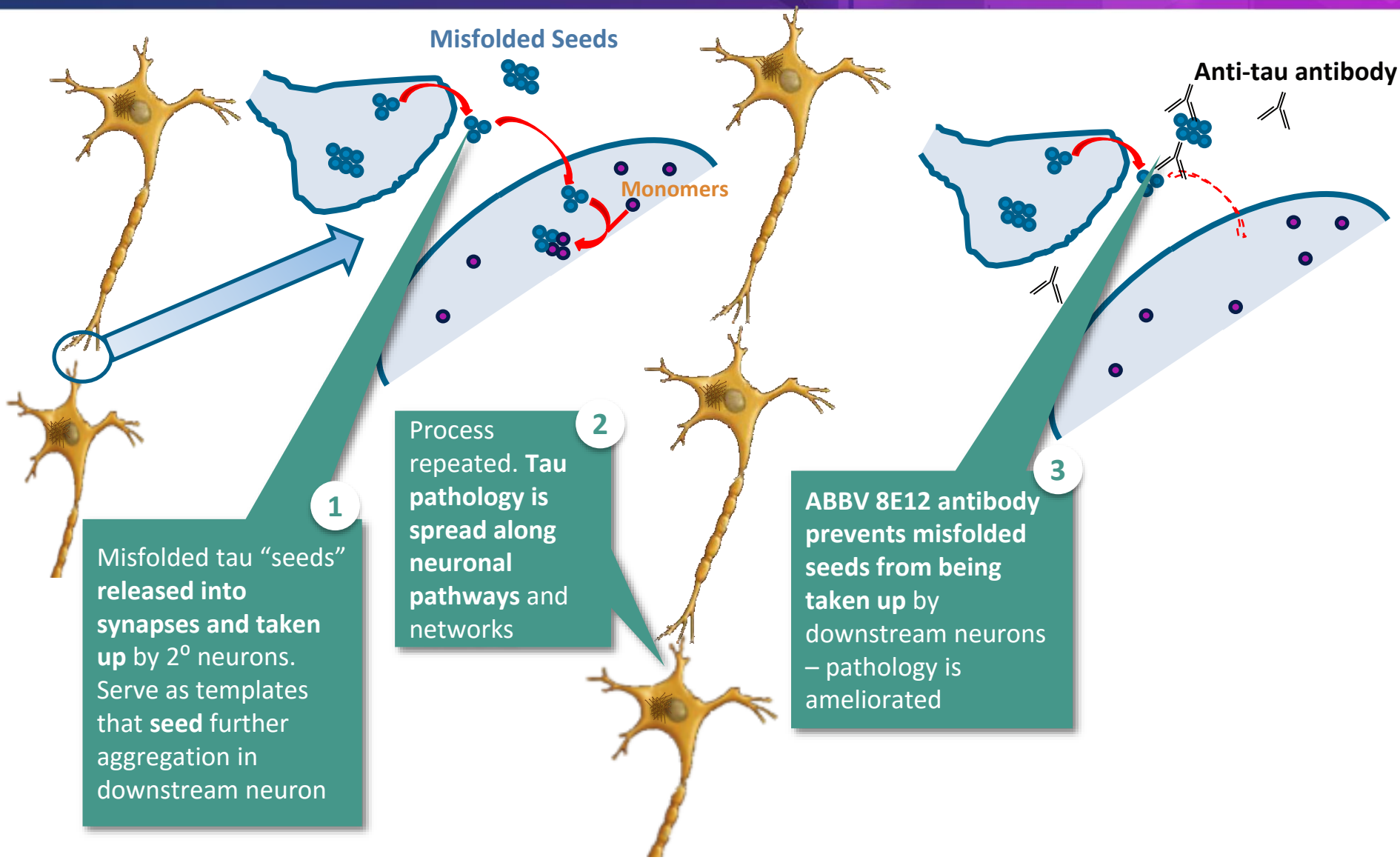
Braak & Braak Acta Neu 82:239-259 (1991)

Therapeutic intervention



Wischik et al Em Drugs & Targets For AD 1:210-232 (2010)

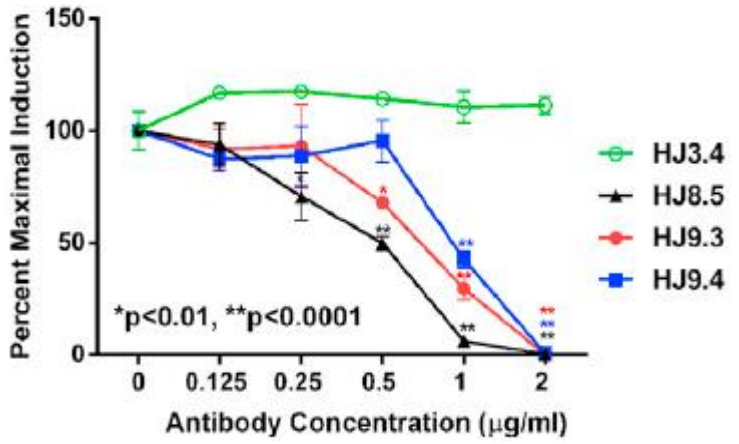
ABBV-8E12 Proposed to Prevent Spread of Tau Pathology by Disrupting Transcellular Propagation of Misfolded Tau



ABBV-8E12 History and Preclinical Data

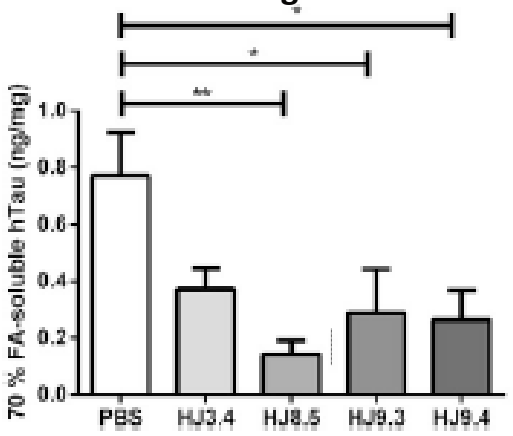
In-licensed from C2N in March 2015

Anti-tau antibody inhibits tau seeding in vitro



Yanamandra et al Neuron 80:402-414 (2013)

Anti-tau antibody reduces tau aggregates in vivo (P301S) tau transgenic mouse



Alzheimer's Disease

- 2015: First patient dosed
- 2016: Initial evidence of biologic activity
- First patient dosed (2016)
- 2017: Additional evidence of biologic activity
- Initial evidence of biologic activity (2018)
- 2018: First opportunity to demonstrate clinical efficacy

Progressive Supranuclear Palsy

Summary

- The inauguration of the Foundational Neuroscience Center in Cambridge exemplifies AbbVie's commitment to finding effective disease-modifying therapies for Alzheimer's disease.
- The FNC will grow over the next two years and deliver new therapeutic targets to the neuroscience portfolio.
- Neuroscience is developing a suite of anti-tau antibodies to augment our first clinical candidate ABBV 8E12.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