AbbVie R&D Deep Dive

March 10, 2020

abbvie

Forward-Looking Statements and Non-GAAP Financial Information

Some statements in this presentation are, or may be considered, 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 2019 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. This presentation contains GAAP and certain non-GAAP financial measures. Non-GAAP financial measures are adjusted for certain non-cash items and for factors that are unusual or unpredictable, and exclude those costs, expenses and other specified items presented in AbbVie’s reconciliation tables. AbbVie’s management believes non-GAAP financial measures provide useful information to investors regarding AbbVie’s results of operations and assist management, analysts and investors in evaluating the performance of the business. Non-GAAP financial measures should be considered in addition to, and not as a substitute for, measures of financial performance prepared in accordance with GAAP. Reconciliations of these non-GAAP financial measures to the most comparable GAAP measures are available in the appendix to this presentation and on the company’s website at www.abbvieinvestor.com.

abbvie

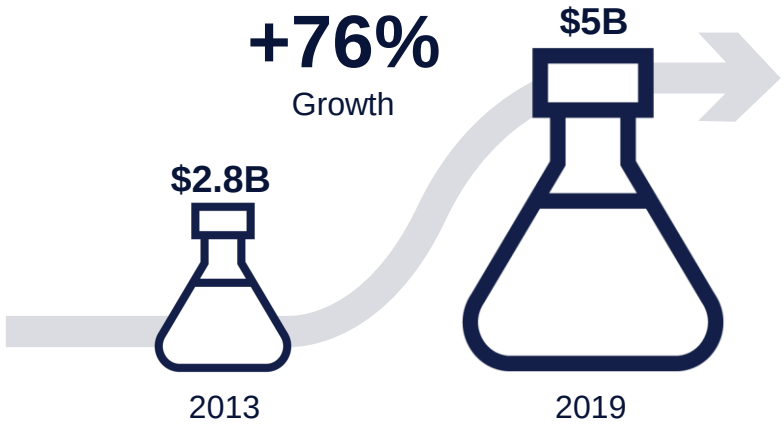
Evolution of AbbVie R&D

Mike Severino, M.D., Vice Chairman and President

We have consistently increased R&D investments and productivity since inception

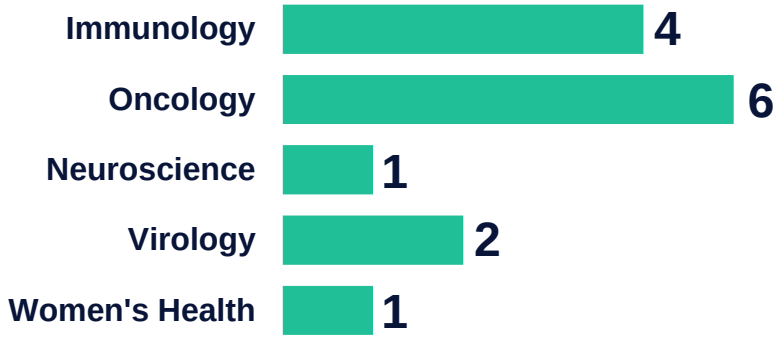
We have built an innovation-driven R&D organization with outstanding execution and a consistent stream of new medicines that elevate the standard of care and address significant unmet need

Annual R&D Investment (adjusted)



14 Major Approvals Since 2013

Therapeutic Focus Areas



Revenues from products launched since inception are growing robustly

Totaled ~$9 billion in 2019

Recently Launched Medicines	Current Approved Indications
Skyrizi™ risankizumab-rzaa 75mg/0.83mL Injection	Psoriasis
RINVOQ™ upadacitinib 15mg tablets	Rheumatoid arthritis
VENCLEXTA® venetoclax tablets 10mg, 50mg, 100mg	CLL and transplant ineligible AML
imbruvica® (ibrutinib) 140mg capsules	CLL, MCL, MZL, cGVHD
MAVYRET® glecaprevir/pibrentasvir 100 mg/40 mg tablets	HCV
Orilissa™ elagolix tablets 150mg 200mg	Endometriosis

AbbVie's recently launched medicines will expand into numerous important new disease areas

	Current Approved Indications	Future Disease Areas	
Skyrizi™ risankizumab-rzaa 75mg/0.83mL Injection	• Psoriasis	• Psoriatic arthritis • Crohn's disease • Ulcerative colitis	
RINVOQ™ upadacitinib 15mg tablets	• Rheumatoid arthritis	• Atopic dermatitis • Psoriatic arthritis • Ankylosing spondylitis • Non-radiographic Axial SpA	• Crohn's disease • Ulcerative colitis • Giant cell arteritis
VENCLEXTA® venetoclax tablets 10mg, 50mg, 100mg	• CLL and transplant ineligible AML	• AML (1L fit, r/r) • MM t(11;14) • MDS	• MCL
Orilissa™ elagolix tablets 150mg 200mg	• Endometriosis	• Uterine fibroids	

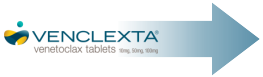
~$3.2Bn in 2020 → **New Indications Represent Significant Growth Opportunity**

We have built a healthy and productive pipeline

Existing Therapies Expanding into Important New Areas

PsA AD
CD HS
UC

AD CD
PsA UC
AS GCA
AxSpA



AML MCL
MM MDS
Solid Tumors

1L MCL
1L cGvHD
FL

UF
PCOS

Launching New Assets

Navitoclax

- Current therapies provide symptom relief, with minimal impact on underlying course of the disease
- Compelling POC data illustrate opportunity to transform the treatment of myelofibrosis
- Potential for accelerated approval in 2022

ABBV-951

- Innovative, subcutaneous delivery system for L-dopa / C-dopa prodrug
- Represents a transformational improvement to current treatments for advanced PD
- Potential to significantly broaden addressable patient population beyond those treated with DUOPA today

Veliparib

- Developed to combine with chemo earlier in treatment paradigm, as well as to expand into non-BRCA deficient tumors
- BRCA breast and 1L ovarian cancers represent a several hundred-million-dollar opportunity for our oncology franchise

Anticipated POC Readouts from Early-Stage Pipeline

- **ABBV-3373** (TNF/steroid ADC) RA Ph2
- **ABBV-599** (JAK/BTK) RA Ph2
- **Ravagalimab** (ABBV-323; CD40) UC Ph2
- **ABBV-157** (RORγt) Ps Ph1
- **Teliso-V** (cMet ADC) Solid Tumor Ph2
- **ABBV-155** (BCL-xLi ADC) Solid Tumor Ph1
- **ABBV-927** (CD40 agonist) Ph1
- **Elezanumab** (RGMa) MS Ph2
- **ABBV-8E12** (Tau) AD Ph2
- **VENCLEXTA** Solid Tumor Ph1
- **ABBV-368** (OX40) Ph1
- **ABBV-621** (TRAIL) Ph1
- **ABBV-647** (PTK7 ADC) Ph1
- **ABBV-011** (SEZ6 ADC) Ph1
- **TNB-383B** (CD3-BCMA) Ph1
- **ABBV-321** (EGFR ADC) Ph1
- **TTX-030** (CD39) Ph1
- **ABBV-151** (GARP+TGF-β1) Ph1
- **ABBV-CX-2029** (CD71) Ph1
- **ABBV-599** (JAK/BTK) SLE Ph2
- **ABBV-2222/ABBV-3067** CF Ph2
- **Elagolix** (GnRH) PCOS Ph2
- **ABBV-467** (MCL-1) Ph1
- **ABBV-744** (BET) Ph1
- **ABBV-184** (Survivin-CD3) Ph1
- **Scripps** (DUPA-CD3) Ph1
- **Harpoon** (Survivin-CD3) Ph1
- **Harpoon** (BCMA-CD3)
- **Calibr** (CD19 sCAR-T) Ph1
- **AL002** (TREM2) AD Ph1
- **AL003** (CD33) AD Ph1

2020
2021
2022

Our early-stage pipeline will drive additional growth in oncology

First and best-in-class assets in apoptosis that will expand into solid tumors

- Navitoclax, a BCL-XL inhibitor, moving to pivotal studies
- BCL-XL inhibition in solid tumors require higher levels; addressed using ADC modality
- TRAIL and MCL-1 are expressed in solid and heme malignancies

Immuno-oncology

- Novel assets that restore T-cell killing activity in the tumor microenvironment (i.e., GARP, CD39)
- Superior CD3 bispecific for both heme and solid tumors

ONCOLOGY

Late-Stage Pipeline

Navitoclax
Myelofibrosis

Veliparib
BRCA Breast Ovarian

Select Early- to Mid-Stage Pipeline

ABBV-151 (GARP+TGF-β1)
ABBV-155 (B7H3 BCL-XLi ADC)
ABBV-321 (AM1 PBD)
ABBV-368 (OX40)
ABBV-621 (TRAIL)
ABBV-744 (BET)
ABBV-927 (CD40)
ABBV-CX-2029 (CD71)
ABBV-647 (PTK7)
ABBV-011 (SEZ6)
TNB-383B* (CD3-BCMA)
TTX-030* (CD39)
Teliso-V (cMet)

*Partnered assets

Our leadership in immunology will drive significant indication expansion for existing therapies

SKYRIZI and RINVOQ

- Meaningful improvements over the standard of care
- Indication expansion/adjacencies

Next-generation assets:

- Novel platforms: Steroid ADCs to drive deeper responses without steroid adverse effects
- New mechanisms (i.e., barrier function in IBD)
- Combinations for indications where many pathways are implicated (i.e., lupus)

IMMUNOLOGY

Select Early- to Mid-Stage Pipeline

- **ABBV-3373** is a TNF steroid ADC. We believe this technology can serve as a platform to take us into a broad set of diseases, including rheumatoid arthritis, lupus and multiple other TNF-mediated diseases
- **ABBV-599** is a BTK JAK1 combination being studied for rheumatoid arthritis and lupus
- **Ravagalimab** is a CD40 antagonist being studied in inflammatory bowel disease
- **ABBV-157** is a small molecule (RORγt) in development for psoriasis

Our neuroscience research focuses on identification of novel disease modifying therapies

- Near-term assets such as ABBV-951 for Parkinson's disease (PD)
- Neural protection for MS, SCI and stroke
- Discovery focused on disease-modifying treatments for Alzheimer's disease (AD) and PD
- Beyond the beta amyloid hypothesis
- Misfolded proteins, such as tau and α-synuclein
- Genetically validated mechanisms such as neuro-inflammation

NEUROSCIENCE

Late-Stage Pipeline

- **ABBV-951** is a non-surgical option to deliver levodopa/carbidopa, offering predictable symptom control without the need for surgery. ABBV-951 is being investigated for the treatment of PD

Early- to Mid-Stage Pipeline

- **Elezanumab:** mAB RGMa inhibitor being investigated to treat spinal cord injuries and multiple sclerosis
- **Tau:** We are pursuing multiple approaches to modify pathogenic tau, including mAB (8E12) in Phase 2, vectorized delivery of mAB and gene knockdown
- **TREM2 and SIGLEC3/CD33:** Genetically validated targets being studied for their potential as disease modifying agents in AD
  - **AL003*:** mAB that works by blocking the function of SIGLEC3/CD33 to increase the activity of microglia and treat AD
  - **AL002*:** mAB that enhances the activity of TREM2 and is being developed for the treatment of AD
- **ABBV-0805:** A humanized mAB targeting α-synuclein being investigated for the treatment of PD

*Partnered assets

Our R&D organization has evolved significantly since 2013

Retained **core capabilities** and **built additional key competencies** in computational biology, immuno-oncology, genetics and genomics and clinical trial simulation

Decreased the lead optimization time to first in human cycle time in our discovery portfolio by approximately **6 months**

Investigated nearly **300 new targets from 2014 to 2018** (approximately 60 per year)

Expanded our presence in biotech hubs on the East and West Coasts

Introduced **important new modalities in our discovery portfolio**, including small interfering RNA (siRNA), cell-based therapies, next-generation iADCs, CD3 bispecifics and gene delivery

60% of our global R&D organization is new to AbbVie since 2013

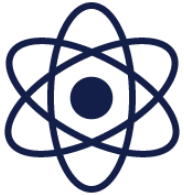
We have R&D sites across the globe with an expanded presence on the east and west coasts

Our top talent has allowed us to build industry-leading capabilities in important scientific areas

Our capabilities will help drive the next phase of our strategy focused on pipeline advancement and driving industry-leading performance

Bioinformatics

Genetics and Genomics



Molecular Modeling and Medicinal Chemistry

Protein Engineering

Precision Medicine

Innovation in Clinical Trials

Key R&D leadership recruited since inception

Our support for basic scientific research is attracting leading scientific talent

Thomas Hudson M.D.
Senior Vice President, R&D
Chief Scientific Officer

- Led team at MIT that mapped the human genome, an early milestone of the Human Genome Project
- Foundational work in understanding human genetic diversity that led to the haplotype map project and genome-wide association study (GWAS) methods to discover genes involved in common diseases such as asthma, diabetes, Crohn's disease and colon cancer
- Founder of the International Cancer Genome Consortium, a global effort to discover new cancer genes for diagnostics and drug development

Jose-Carlos Gutierrez-Ramos, Ph.D.
Vice President, Discovery

- Immunochemist with strong academic track record and diverse senior R&D leadership roles across a range of biotech start-ups and peer biopharma companies
- Deep expertise in translating new areas of science into successful drug discovery programs, from inflammasome and epigenetics to decoding the human immune to enable a new generation of curative immune medicines
- Founding CEO of two biotech companies (Synlogic, Cogen) focused on transformational science, led from academic science to clinical stage programs, raised capital and took the companies in the public market or M&A, respectively
- Teams under his direction discovered and developed marketed products Entyvio/Vedolixumab and Xeljanz/Tofacitinb; in addition, teams under his management across three companies have produced four Phase III assets and 11 Phase II programs

Neil Gallagher, M.D., Ph.D.
Vice President, Development
Chief Medical Officer

- Gynecological oncologist with more than 15 years of leadership experience at peer biopharma companies developing oncology drugs across all phases of development, including cytotoxics, small molecule kinase inhibitors and biologics
- Deep expertise in developing oncology drugs in hematological malignancies, such as AML and CML
- Oversaw the Novartis Oncology development portfolio, including Tasigna, Glivec, ABL001, Arzeera and Odomzo
- Foundational work in the role of CD40 signaling in cancer cells and the potential therapeutic use of a trimerized CD40 ligand

Our leaders have deep expertise in therapeutic areas and key capabilities

Oncology

Heather Maecker, Ph.D.
Director, Immuno-Oncology Discovery

Genentech, Stanford University

Mohamed Zaki, M.D., Ph.D.
Vice President, Global Head
of Hematology Development

Celgene, Sanofi

Mirella Lazarov, DDS, Ph.D.
Head, Companion Diagnostics
Center of Excellence

Gilead, Stanford University

Immunology

Timothy Radstake, M.D., Ph.D.
Senior Medical Director

UMC Utrecht, Radboud University

Lisa Olson, Ph.D.
Vice President, Discovery,
Site Head, East Coast

University of Illinois at Urbana-Champaign,
University of Chicago

Neuroscience

Eric Karran, Ph.D.
Vice President, Discovery
Neuroscience Research

Alzheimer's Research UK, Johnson & Johnson

Tammy Dellovade, Ph.D.
Director, Research Fellow,
In Vivo Pharmacology

Merck, University of Virginia

Genetics & Genomics

Howard Jacob, Ph.D.
Vice President, Head of Computational Biology Group and the Genomics Research Center
Harvard Medical School, Medical College of Wisconsin, The Whitehead Institute

Innovation in Clinical Trials

Kyle Holen, M.D.
Head, Development Design Center
Columbia University College of Physicians and Surgeons, Memorial Sloan-Kettering Cancer Center

Precision Medicine

Ian McCaffery, Ph.D.
Vice President, Precision Medicine
Janssen, Genentech, University of Leeds

AbbVie R&D Pipeline - 2013

Select Pipeline Assets and Programs

As of January 15, 2013

Phase 1	Phase 2	Registrational / Phase 3	Submitted
ABT-493/ABT-530 (NS3/4A / NS5A): HCV	BT-061 (CD4): RA	VIEKIRA PAK: HCV	DUOPA (dopamine receptor): PD (US)
ABT-122 (TNF/IL-17): RA	BT-061 (CD4): Ps	HUMIRA (TNF): HS	
VENCLEXTA (BCL-2): Lupus	GLPG0634 (JAK1)*: RA	HUMIRA (TNF): SpA peripheral	
RINVOQ (JAK1): RA	ABT-126 (a7 NNR): AD	HUMIRA (TNF): Uveitis	
ABT-981 (IL-1 α/β): Osteoarthritis	ABT-126 (a7 NNR): Schizophrenia	Daclizumab (CD25): MS	
ABT-354 (5-HTG): AD	ABT-436 (V1b): MDD	ORILISSA* (GnRH): Endometriosis	
ABT-419 (GlyT1): Schizophrenia	ABT-110 (NGF)*: Pain		
ABT-957 (Calpain): AD	Veliparib (PARP): BRCA Breast Cancer		
VENCLEXTA* (BCL-2): CLL	Veliparib (PARP): Lung Cancer		
ABT-348 (Aurora): Solid/Heme Tumors	Veliparib (PARP): Brain Metastasis		
ABT-414 (EGFR)*: GBM	ABT-719 (MCR)*: Acute Kidney Injury		
ABT-700 (cMet)*: Solid Tumor	Atrasentan (ETA): Diabetic Kidney Disease		
ABT-767 (PARP): Solid Tumor	ORILISSA (GnRH): Uterine Fibroids		

Oncology
Immunology
Neuroscience
Other

*Partnered Asset; Partnership Summary Below:
Venclexta – Developed by AbbVie and Roche, commercialized by AbbVie and Genentech, a member of the Roche Group; ABT-414 – Developed by AbbVie researchers with components in-licensed from Life Sciences Pharmaceuticals and Seattle Genetics; ABT-700 – Licensed from Pierre Fabre SA, development and commercialization led by AbbVie; GLPG0634 – Discovered, developed and commercialized in a global alliance with Galapagos NV; ABT-110 – Developed in partnership with PanGenetics; ABT-719 – Developed in partnership with Action Pharma and Zealand Pharma; Viekira Pak and Mavyret – In partnership with Enanta; Daclizumab – Developed in partnership with Biogen; Elagolix – Developed in cooperation with Neurocrine Biosciences

AbbVie R&D Pipeline - 2020

Select Pipeline Assets and Programs

As of February 7, 2020

Phase 1

- ABBV-157 (RORγT)
- ABBV-154 (TNF-Steroid ADC)
- ABBV-151 (GARP+TGFβ1): Solid Tumor
- ABBV-155 (BCL-xLi ADC): Solid Tumor
- ABBV-181 (PD-1): Solid Tumor
- ABBV-321 (EGFR ADC): Solid Tumor
- ABBV-368 (OX40): Solid Tumor
- ABT-165 (DLL4/VEGF): Solid Tumor
- ABBV-621 (TRAIL): Solid/Heme Tumor
- ABBV-744 (BET): Heme Tumor
- ABBV-927 (CD40): Solid Tumor
- ABBV-CX-2029* (CD71): Solid/Heme Tumor
- ABBV-647* (PTK7 ADC): NSCLC
- ABBV-011 (SEZ6 ADC): SCLC
- VENCLEXTA* (BCL-2): ALL
- VENCLEXTA* (BCL-2): Solid Tumor
- CCW702* (CD3-PSMA): Prostate Cancer
- CLBR001/SWI019* (sCAR-T): Heme Tumor
- TNB-383B* (CD3-BCMA): MM
- TTX-030* (CD39): Solid Tumor
- ABBV-0805* (α-Synuclein): PD
- AL002* (TREM2): AD
- AL003* (CD33): AD
- ABBV-4083 (TylAMac): Filarial Diseases

Phase 2

- SKYRIZI* (IL-23): Atopic Derm
- SKYRIZI* (IL-23): HS
- ABBV-3373 (TNF-steroid ADC)
- ABBV-599 (BTK/JAK): RA
- ABBV-599 (BTK/JAK): SLE
- Ravagalimab (CD40): UC
- IMBRUVICA* (BTK): Solid Tumors
- VENCLEXTA* (BCL-2): MDS
- Teliso-V (cMet ADC): NSCLC
- ABBV-8E12* (Tau): AD
- Elezanumab (RGMa): MS
- ABBV-2222/ABBV-3067 (CFTR-C1/CFTR-P): Cystic Fibrosis
- ELAGOLIX* (GnRH): PCOS

Registrational / Phase 3

- RINVOQ (JAK 1): PsA
- RINVOQ (JAK 1): CD
- RINVOQ (JAK 1): Atopic Derm
- RINVOQ (JAK 1): UC
- RINVOQ (JAK 1): GCA
- RINVOQ (JAK 1): AS
- RINVOQ (JAK 1): Axial SpA
- SKYRIZI* (IL-23): CD
- SKYRIZI * (IL-23): UC
- SKYRIZI * (IL-23): PsA
- IMBRUVICA* (BTK): 1L cGvHD
- IMBRUVICA* (BTK): 1L FL
- IMBRUVICA* (BTK): 1L MCL
- IMBRUVICA* (BTK): R/R MCL
- IMBRUVICA* (BTK): R/R FL/MZL
- IMBRUVICA* (BTK): 1L CLL
- Veliparib (PARP): NSCLC
- Veliparib (PARP): BRCA Breast Cancer
- Veliparib (PARP): 1L Ovarian Cancer
- VENCLEXTA* (BCL-2): 1L CLL
- VENCLEXTA* (BCL-2): 1L AML
- VENCLEXTA* (BCL-2): AML Maintenance
- VENCLEXTA* (BCL-2): R/R MM t(11;14)
- Navitoclax (BCL-2/BCL-xL): Myelofibrosis
- ABBV-951 (dopamine receptor): PD
- ELAGOLIX* + Hormonal Add-Back (GnRH): Endometriosis

Submitted

- ORILISSA* (GnRH): Uterine Fibroids (US)

Recently Approved

- RINVOQ: RA (US, EU, JPN)
- SKYRIZI*: Ps (US, EU, JPN)
- VENCLEXTA*: 1L CLL (US)
- IMBRUVICA* + Gazyva: 1L CLL (US)

Oncology
Immunology
Neuroscience
Other

We continue to focus on the quality of our medicines, while doubling our early-stage pipeline since 2013, with more than 30 assets currently in late discovery and preclinical development

*Partnered Asset; Partnership Summary Below:
Imbruvica jointly developed and commercialized with Janssen Biotech; Elagolix developed in cooperation with Neurocrine Biosciences; Venclexta developed by AbbVie and Roche, commercialized by AbbVie and Genentech, a member of the Roche Group; Skyrizi developed in cooperation with Boehringer Ingelheim; ABBV-8E12 developed in cooperation with C_2N Diagnostics; ABBV-0805 developed in cooperation with BioArctic; CCW702 / CLBR001 / SWI019 developed by Calibr in a first-in-patient trial and AbbVie holds option to license the program; TNB-383B developed by TeneoOne through Phase 1 and AbbVie holds exclusive right to acquire TeneoOne; AL002/AL003 developed by Alector through Phase 2 and AbbVie holds option for additional development and commercialization; TTX-030 developed by Tizona Therapeutics through Phase 1b and AbbVie has option to lead global development and commercialization; ABBV-2029 developed in cooperation with CytomX Therapeutics; ABBV-647 developed in cooperation with Pfizer.

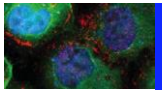
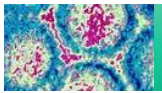
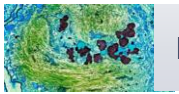
Anticipated key pipeline events

	2020	2021	
Regulatory Approvals	IMBRUVICA ECOG Approval (1L CLL vs. FCR) VENCLEXTA 1L CLL (EU) Elagolix UF	IMBRUVICA 1L cGvHD VENCLEXTA 1L AML (EU) VELIPARIB 1L Ovarian Cancer VELIPARIB BRCA Breast Cancer	RINVOQ PsA RINVOQ AD RINVOQ AS Elagolix + Hormonal Add-Back EM
Regulatory Submissions	IMBRUVICA 1L cGvHD (iNTEGRATE) VENCLEXTA 1L AML unfit (EU) Veliparib 1L Ovarian Cancer Veliparib BRCA Breast Cancer RINVOQ PsA RINVOQ AD RINVOQ AS Elagolix + Hormonal Add-Back EM	IMBRUVICA + VENCLEXTA r/r MCL (SYMPATICO) IMBRUVICA + VENCLEXTA 1L CLL (CAPTIVATE) IMBRUVICA r/r FL/MZL (SELENE) ABBV-951 PD SKYRIZI CD SKYRIZI PsA Navitoclax R/R MF	
Ph3/Registrational Data Readouts	SKYRIZI Ph3 CD induction (MOTIVATE) SKYRIZI Ph3 PsA (KEEPSAKE2) SKYRIZI Ph3 Ps H2H vs Cosentyx RINVOQ Ph3 PsA RINVOQ Ph3 Atopic Derm VENCLEXTA Ph3 AML unfit (VIALE-A; VIALE-C) IMBRUVICA + Venclexta Ph2 1L CLL (CAPTIVATE) IMBRUVICA Ph3 1L cGvHD (iNTEGRATE)	IMBRUVICA Ph3 1L MCL (SHINE) IMBRUVICA Ph3 r/r FL/MZL (SELENE) IMBRUVICA + VENCLEXTA Ph3 r/r MCL (SYMPATICO) IMBRUVICA + VENCLEXTA Ph3 1L CLL (GLOW) VENCLEXTA + IMBRUVICA Ph3 1L CLL (CLL13) VENCLEXTA Ph3 3L+ MM t(11;14) (CANOVA) ABBV-951 Ph3 PD	
Ph3/Registrational Study Starts	VENCLEXTA Ph3 AML fit VENCLEXTA Ph3 MDS Navitoclax Ph3 1L and r/r MF SKYRIZI Ph3 UC	VENCLEXTA Ph3 r/r MM t(11;14) w/ Darzalex VENCLEXTA Ph3 Solid Tumors SKYRIZI Ph3 AD SKYRIZI Ph3 HS Ravagalimab (ABBV-323; CD40) Ph3 UC	
Early-Stage Data Readouts	ABBV-3373 (TNF/Steroid ADC) RA Ph2 ABBV-599 (JAK/BTK) RA Ph2 Ravagalimab (ABBV-323; CD40) UC Ph2 ABBV-157 (RORgt) Ps Ph1 Teliso-V (cMet ADC) Solid Tumor Ph2 ABBV-155 (BCL-xLi ADC) Solid Tumor Ph1	ABBV-927 (CD40 Agonist) Ph1 ABBV-368 (OX40) Ph1 ABBV-647 (PTK7 ADC) Ph1 ABBV-011 (SEZ6 ADC) Ph1 TNB-383B (CD3-BCMA) Ph1 ABBV-321 (EGFR ADC) Ph1 TTX-030 (CD39) Ph1 VENCLEXTA Solid Tumor Ph1 ABBV-621 (TRAIL) Ph1	ABBV-151 (GARP+TGF-β1) Ph1 ABBV-CX-2029 (CD71) Ph1 ABBV-599 (JAK/BTK) SLE Ph2 ABBV-8E12 (Tau) AD Ph2 Elezanumab (RGMa) MS Ph2 ABBV-2222/ABBV-3067 (CFTR-C1/CFTR-P) CF Ph2 Elagolix (GnRH) PCOS Ph2

Existing and new capabilities

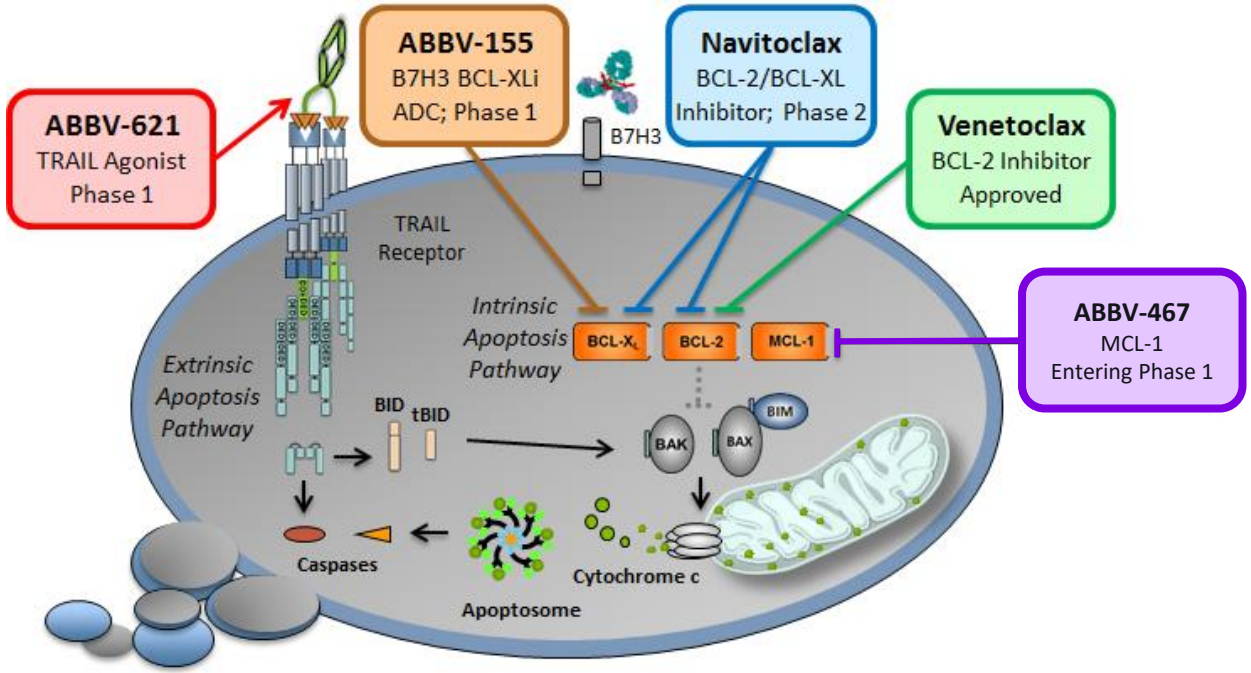
Tom Hudson, M.D., Senior Vice President, R&D and Chief Scientific Officer

Our existing and new capabilities drive results

Therapeutic areas	Capabilities	Vignettes
 Immunology	Medicinal Chemistry; Molecular Modeling	• VENCLEXTA • MAVYRET
 Oncology	Bioinformatics; Genetics & Genomics	• Computational Immuno-oncology • Genomics Research Center
 Virology	Precision Medicine; Innovation in Clinical Trials	• Development Design Center
 Neuroscience		

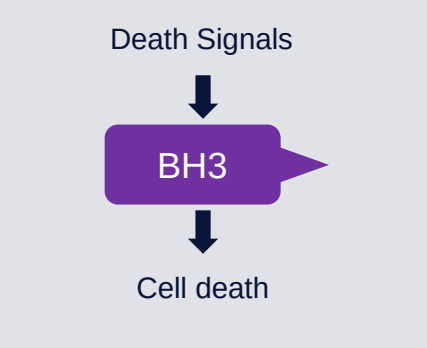
Discovery of VENCLEXTA: Breakthrough in drugging protein-protein interaction

Multiple innovations led to AbbVie's leadership in developing an industry-leading apoptosis portfolio

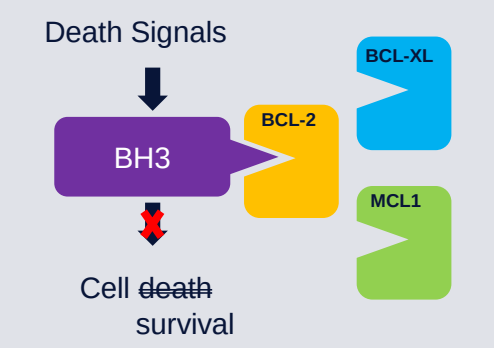


Building a portfolio of apoptosis tools and therapeutics

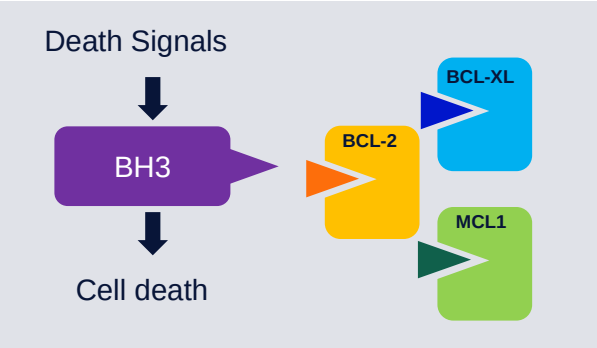
1. Apoptosis is a normal process



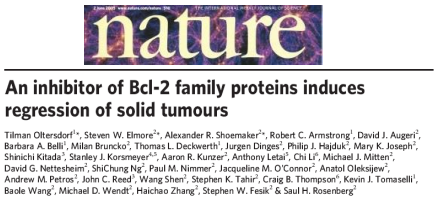
2. In cancer, BCL-2 family members can inhibit apoptosis



3. Compounds that block BCL-2 family members can induce apoptosis

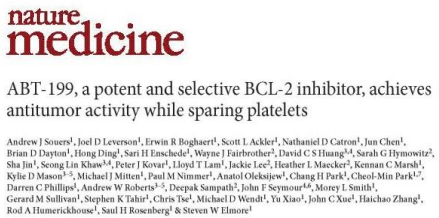


4. AbbVie scientists pioneered the discovery of BCL-2 family inhibitors and advanced the field of apoptosis for treating both heme and solid tumors


nature

An inhibitor of Bcl-2 family proteins induces regression of solid tumours

Tilman Oltersdorf[1]*, Steven W. Elmore[2]*, Alexander R. Shoemaker[2]*, Robert C. Armstrong[1], David J. Augeri[2], Barbara A. Belli[1], Milan Bruncko[2], Thomas L. Deckwerth[1], Jurgen Dinges[2], Philip J. Hajduk[2], Mary K. Joseph[1], Shinichi Kitada[1], Stanley J. Korsmeyer[2,3], Aaron R. Kunzer[2], Anthony Letai[2], Chi Li[2], Michael J. Mitten[2], David G. Nettesheim[2], ShiChung Ng[2], Paul M. Nimmer[2], Jacqueline M. O'Connor[2], Anatol Oleksijew[2], Andrew M. Petros[2], John C. Reed[1], Wang Shen[2], Stephen K. Tahir[2], Craig B. Thompson[3], Kevin J. Tomaselli[1], Baole Wang[2], Michael D. Wendt[2], Haichao Zhang[2], Stephen W. Fesik[2] & Saul H. Rosenberg[2]


nature medicine

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]


Science Translational Medicine

Exploiting selective BCL-2 family inhibitors to dissect cell survival dependencies and define improved strategies for cancer therapy

Joel D. Leverson[1†], Darren C. Phillips[2], Michael J. Mitten[2], Erwin R. Boghaert[2], Dolores Diaz[2], Stephen K. Tahir[2], Lisa D. Belmont[2], Paul Nimmer[2], Yu Xiao[1], Xiaoju Mac Ma[2‡], Kym N. Lowes[2§], Peter Kovar[2], Jun Chen[2], Sha Jin[2], Morey Smith[2], John Xue[2], Haichao Zhang[2], Anatol Oleksijew[2], Terrance J. Magoc[2], Kedar S. Vaidya[2], Daniel H. Albert[2], Jacqueline M. Tarrant[2], Nghi La[2], Le Wang[2], Zhi-Fu Tao[2], Michael D. Wendt[2], Deepak Sampath[2], Saul H. Rosenberg[2], Chris Tse[2], David C. S. Huang[3,4], Wayne J. Fairbrother[2], Steven W. Elmore[2] and Andrew J. Souers[1]

Lessons learned in our journey to drug apoptosis

Although we generated preclinical data on which BCL-2 family members are linked to specific tumor types, our current understanding of which inhibitors work best in different indications has come from multiple clinical studies

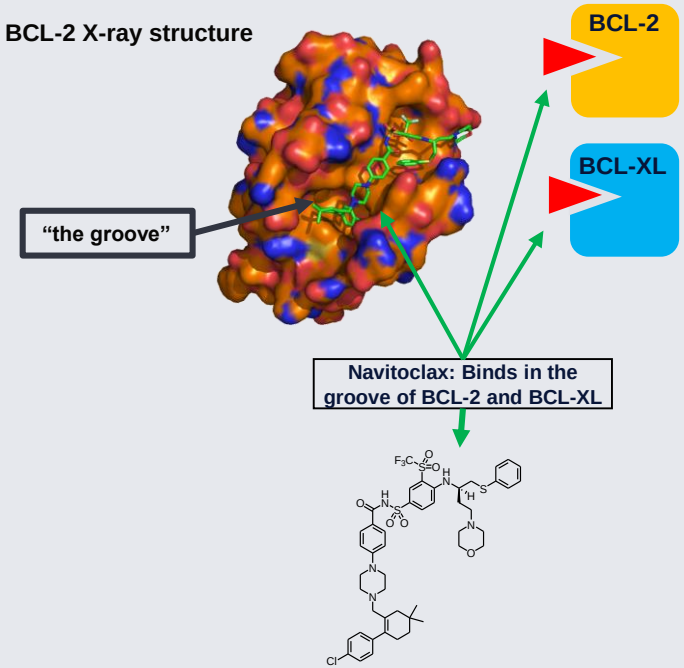
Target	Drug	Preclinical insights	Clinical insights	Additional clinical insights
BCL-2	VENCLEXTA	Heme	CLL, AML, MM (t11:14), Breast	
BCL-XL + BCL-2	Navitoclax	Heme and solid	Myelofibrosis	Solid tumor efficacy requires higher doses linked to platelet depletion
BCL-XL	ABBV-155 (ADC with BCL-XL)	Solid	Target indications to be determined in Phase 1	ADC modality avoids platelet effects
MCL-1	ABBV-467	Solid and heme	Target indications to be determined in Phase 1	

Discovery breakthrough #1: Drugging a protein-protein interaction

- AbbVie medicinal chemists developed new technology and broke drug discovery rules to identify the first-generation BCL-2 family inhibitors
- Our medicinal chemists discovered Navitoclax, the first orally active clinical BCL-2 family inhibitor
- BCL-2/BCL-XL inhibitor is clinically active in myelofibrosis
- Generated the first drug to inhibit a protein-protein interaction

Next challenge: BCL-2 selectivity

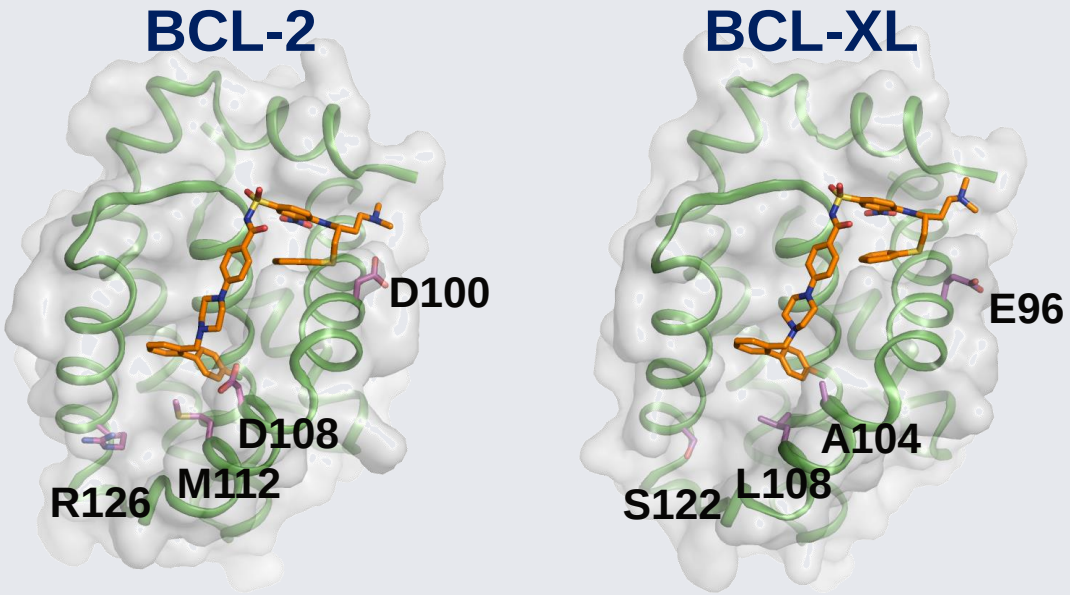
Challenge: BCL-2 family considered “undruggable” given the need to disrupt large, hydrophobic and high affinity protein-protein interactions



Quest for BCL-2 selective agents

- BCL-2 and BCL-XL are very similar proteins
- Only four residues differ within binding groove of BCL-2 and BCL-XL

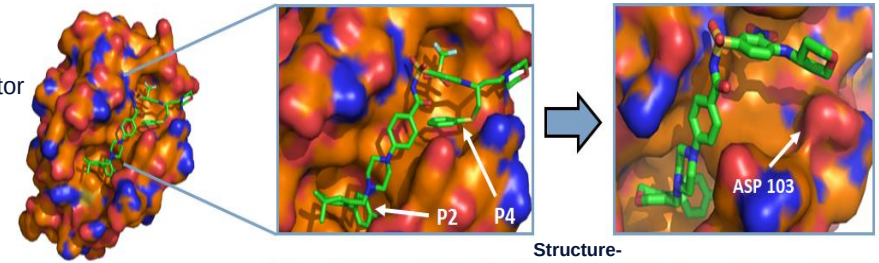
Challenge: Homology of BCL-2/BCL-XL binding groves presents a significant challenge



Discovery breakthrough #2:
Analyses of the protein structure provided insights into selectivity and potency, leading to the discovery of VENCLEXTA

AbbVie scientists generated unique X-ray crystal structures, leading to structural insights that facilitated discovery of first-in-class BCL-2 selective inhibitors

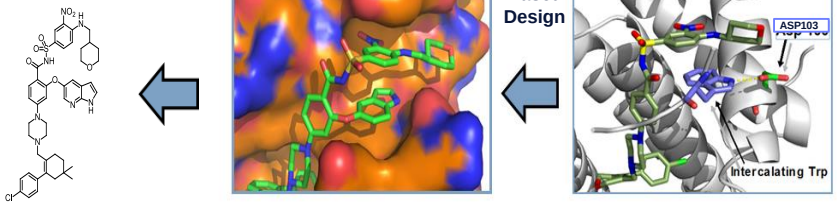
Navitoclax
BCL-2 and BCL-XL Inhibitor
(BCL-2 X-ray structure)



- Remove “bent-back” thiophenyl group
- ↑BCL-2 selectivity, ↓potency

Structure-Based Design

VENCLEXTA
First-in-Class
Selective BCL-2
Inhibitor

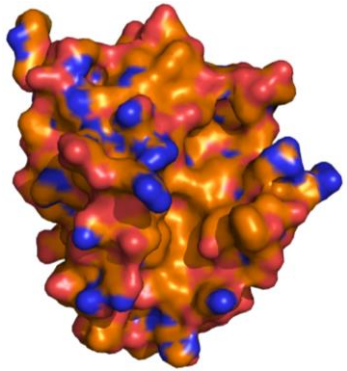


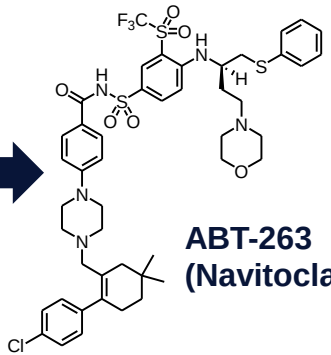
- X-ray shows amino acid (Trp) sidechain from neighbor BCL-2 protein
- Trp sidechain fills P4 pocket – makes BCL-2 selective H-bond with ASP103

Discovery of selective BCL-2 family inhibitor VENCLEXTA: Breaking new ground in medicinal chemistry

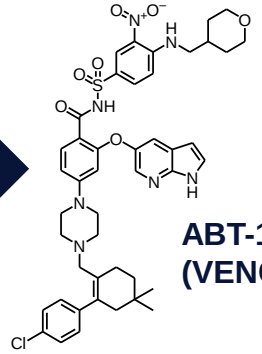
BCL-2 Protein Structures

Sattler, *Science* 1997, 275: 983





ABT-263 (Navitoclax)



ABT-199 (VENCLEXTA)

Insights and innovations leading to the discovery of VENCLEXTA

- Generation and full understanding of BCL-2 family member molecular structures
- Development of new technologies (SAR by NMR) to enable discovery of protein-protein interaction inhibitors
- Recognition of the role of BCL-XL in controlling the survival of circulating platelets
- Persistent “art of the possible” medicinal chemistry effort to discovery orally bioavailable, selective BCL-2 inhibitors

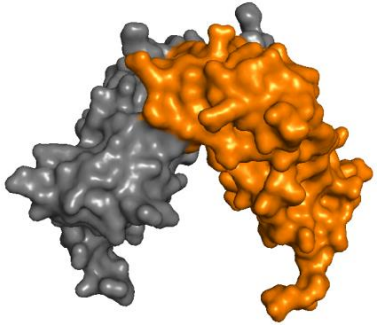
Discovery of MAVYRET: Using structure-based drug design to cure HCV

Clinical challenge:
The ability to increase potency and decrease resistance mutations was essential to create a two-drug next-generation HCV regimen

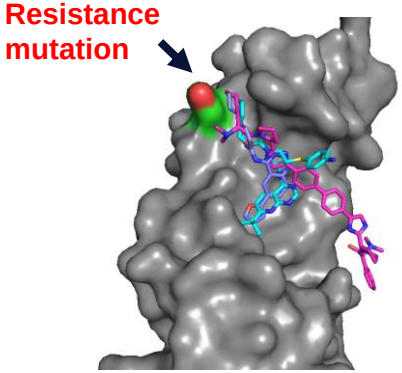
MAVYRET is focused on two protein drug targets, NS3 protease and NS5A, a protein of unknown function, but critical to viral survival

Numerous companies had lead compounds at the time we began research on NS5A

NS5A Homodimer



NS5A is a symmetrical dimer critical for viral life cycle, but of unknown function



One key resistance mutation appears with all known NS5A inhibitors at the time

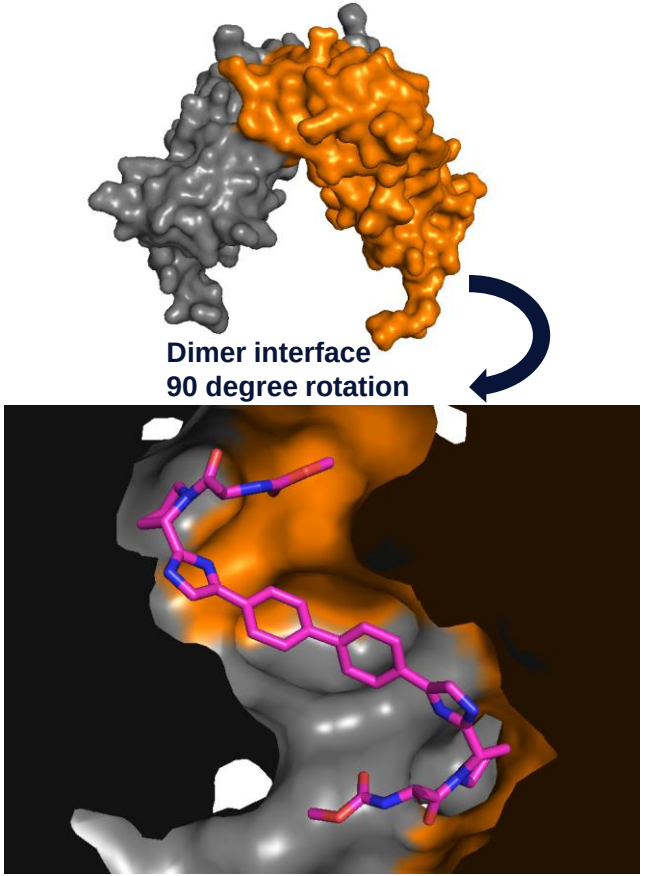
Attempts to discover a compound interacting with the resistance mutation were unsuccessful

Discovery of MAVYRET

Thinking differently, we went beyond established industry standards, abandoning the resistance mutation binding site

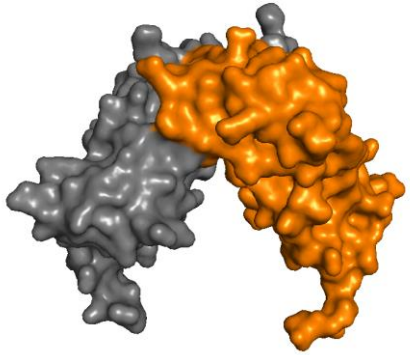
Our modelers generated compounds that would affect the dimer

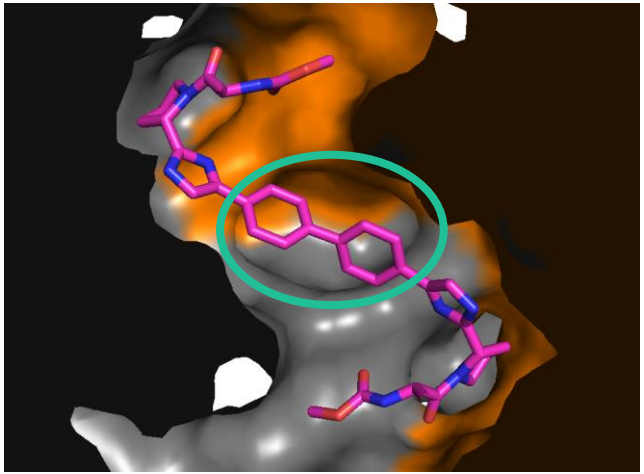
Since the molecules are symmetrical, we evaluated the dimer interface and found a perfect binding site for symmetrical molecules



Discovery of MAVYRET

Based on this model we identified a novel binding pocket



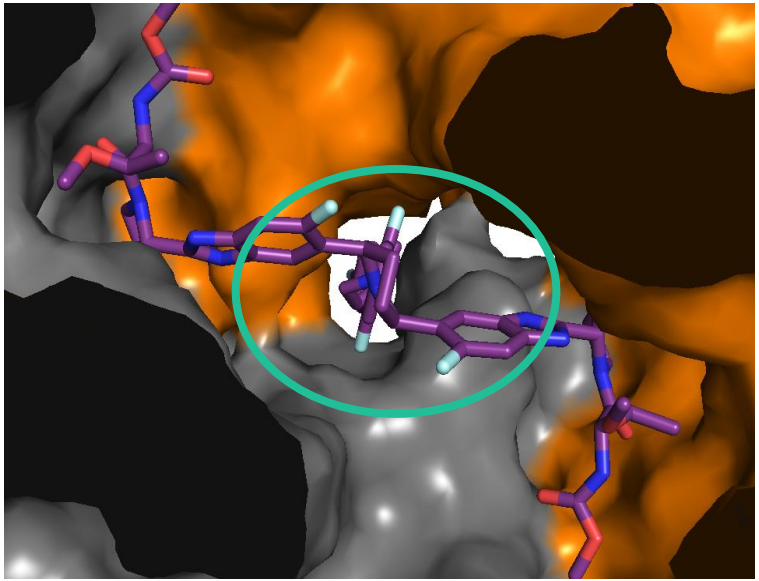


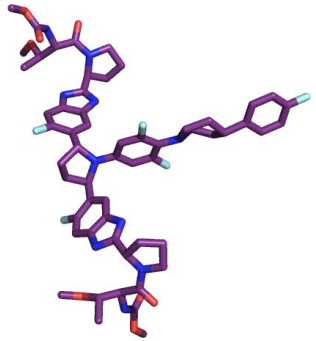
Discovery of MAVYRET

Building into this pocket brought high potency, broad genotype activity and reduced resistance

Success factors:

- Our scientists abandoned the resistance mutation binding site
- Having atomic resolution protein structure allowed us to use structure-based drug design to model compounds





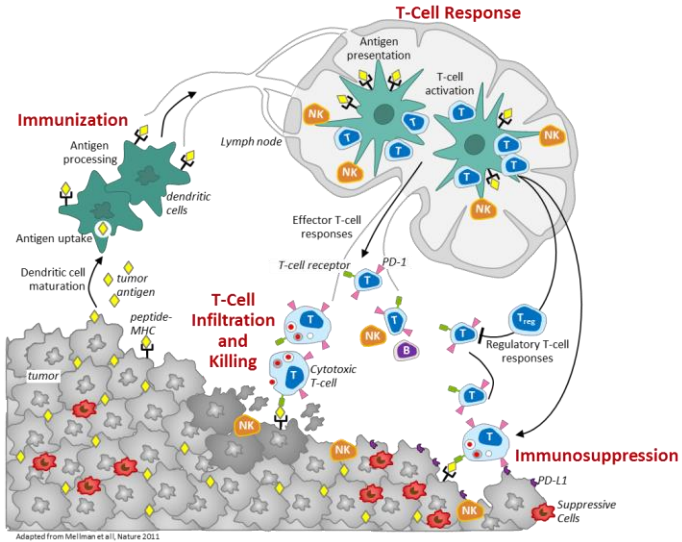
NS5A component of MAVYRET

MAVYRET is approved as a pan-genotypic 8-week treatment option for most HCV patients, supported by 98 percent cure rates (rates ranged between 92-100 percent)

Building new capabilities: Computational immuno-oncology as a basis for target identification and clinical trial design

Overview of AbbVie's Immuno-oncology (I-O) program

Generation and Regulation of Antitumor Immunity



AbbVie Approaches

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

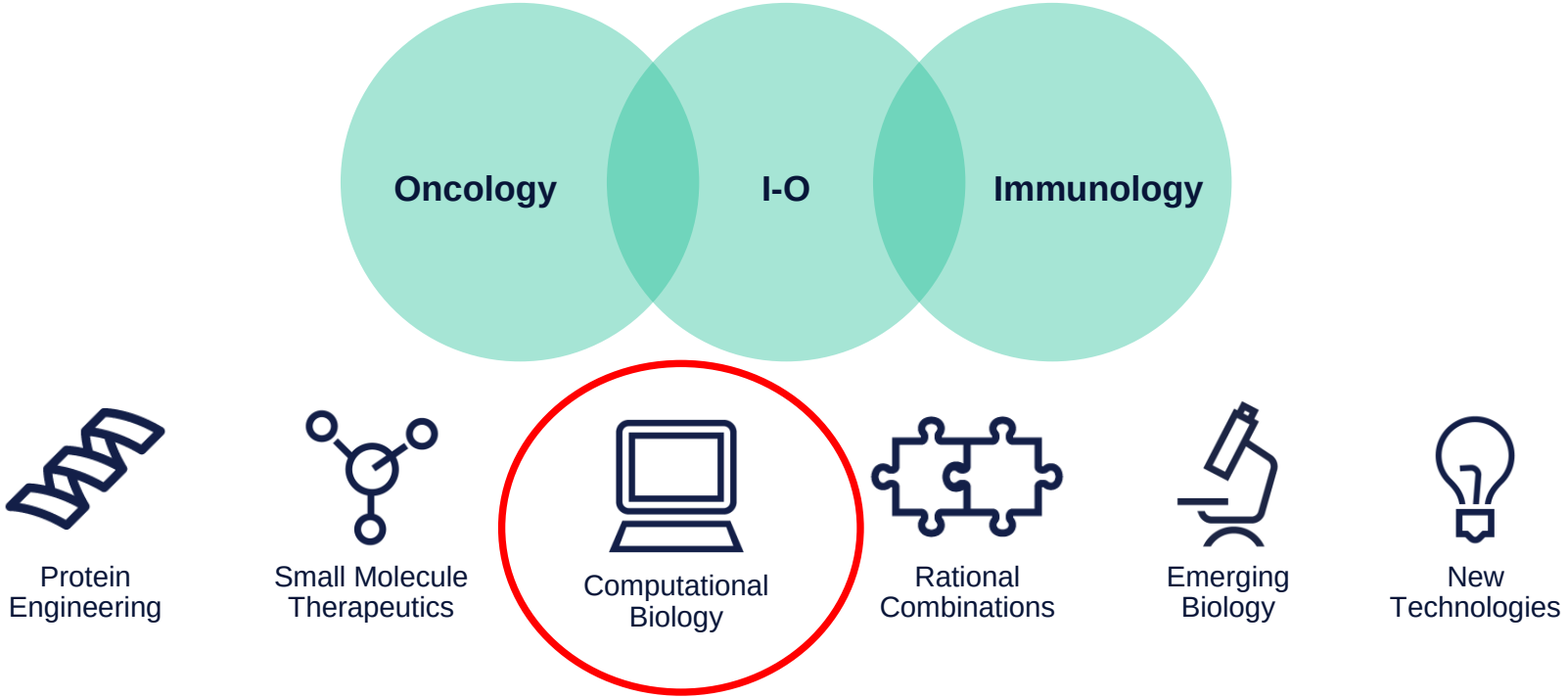
Disruptive Technologies: T-cell Receptor-based Biologics and Cell-based Therapies
e.g., soluble TCR bispecifics

Numerous Collaborations with Leaders in the Field*

MD Anderson Cancer Center
UCSF University of California San Francisco
FNIH Foundation for the National Institutes of Health
F-star BISPECIFIC. BY DESIGN.
The University of Chicago
Turnstone Biologics
Bristol-Myers Squibb
Harpoon Therapeutics
Calico
Cancer Moonshot

* Select collaborations

AbbVie I-O programs leverage existing and new capabilities



Computational I-O

Josue Samayoa
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Tolga Turan
Principal Scientist
Ph.D.: University of California Irvine

Kyle Halliwill
Principal Scientist
Ph.D.: University of California San Francisco

Sarah Kongpachith
Sr. Scientist II
Ph.D.: Stanford

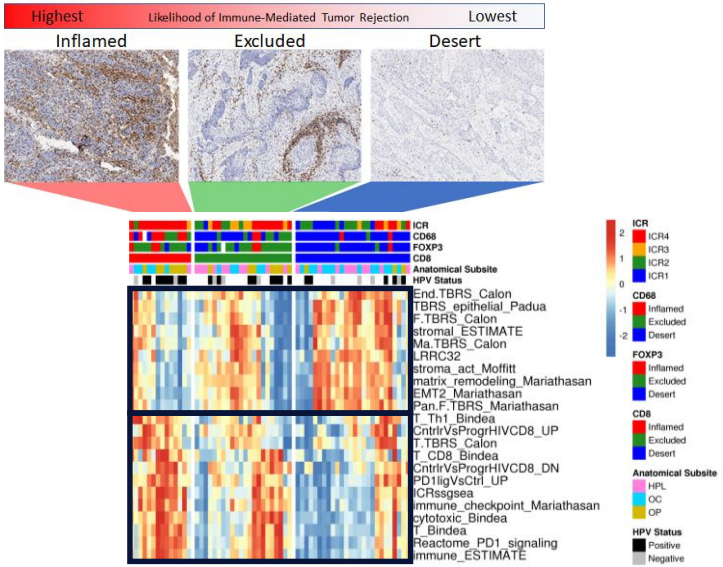
David Masica
Principal Scientist
Ph.D.: Johns Hopkins University

Tyler McLaughlin
Sr. Scientist
Ph.D.: Rice University

Zoltan Dezso
Principal Scientist
Ph.D.: Notre Dame University

Xu Shi
Sr. Scientist II
Ph.D.: Virginia Polytechnic Institute and State University

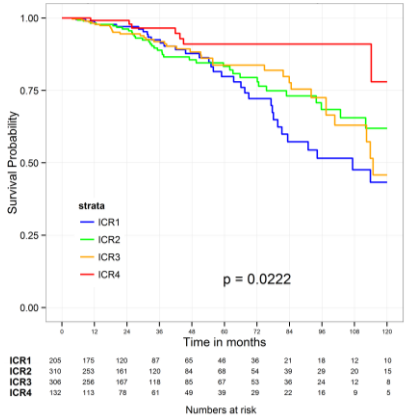
Multidimensionally-defined tumor-immune landscape for HNSCC
(based on RNAseq and IHC)

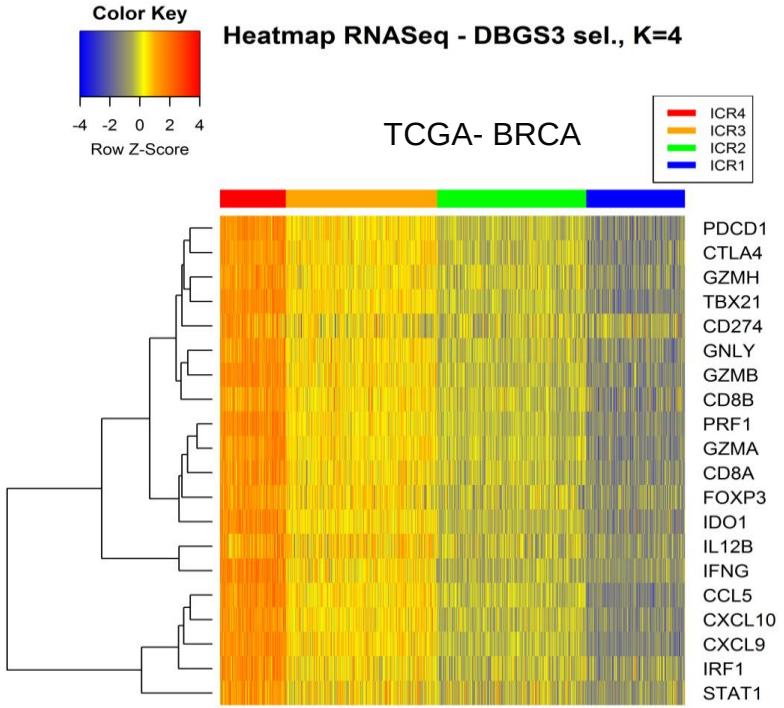


Computational I-O methods rely on genetic and genomic datasets obtained from tumor biopsies

Example: ICR gene signature

CXCR3/CCR5 Chemokines	Th1 signaling	Effector functions	Immune regulatory
CXCL9	IFNG	GNLY	CD274
CXCL10	TBX21	PRF1	CTLA4
CCL5	CD8	GZMA	FOXP3
	IL12B	GZMB	IDO1
	CD8	GZMH	PDCD1
	STAT1		
	IRF1		





Hendrickx et al, *Oncoimmunology* 2017

Using tumor-based computational analyses to define next-generation I-O targets and clinical studies

TCGA/IGCC/Clinical trial RNA, DNA and methylome datasets

↓

For each tumor type, we imputed:

- Cell types
- Pathways
- Gene expression

} **Drug target/ candidate**

↓

We prioritized these targets, both internally and externally

↓

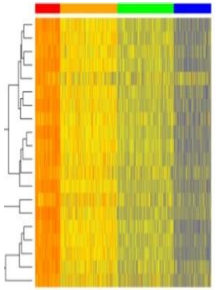
Defined paths to the clinic

↓

Clinical trial populations informed by computational analyses (i.e. tumor types where target is “active”)

↓

Translational studies (biomarker selection based on I-O hypotheses)



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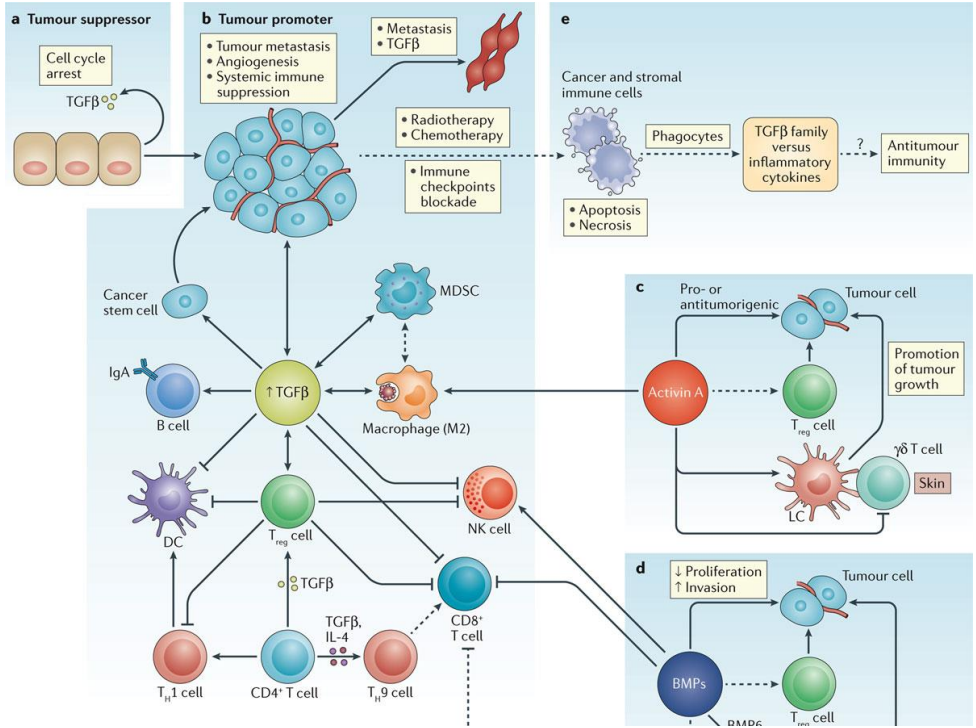
Example Phase 1 program	MOA	Indication(s)
Triple I-O combo (ABBV-927+368+181)	CD40, OX40, PD-1	**NSCLC**
ABBV-151	GARP/TGF-β	**TNBC, bladder, pancreatic, HNSCC**
ABBV-368/TLR9 combo	OX40, TLR9, PD-1	**HNSCC**
TTX-030	CD39	**Solid tumors**
MAVU-104	ENPP1/STING	**Solid tumors**

Effects of TGF-β on the immune response in cancer

- TGF-β plays a role in establishing and driving immunosuppression in the tumor microenvironment by several mechanisms
    - Suppression of cytotoxic T lymphocytes, T helper 1 cells, natural killer cells and dendritic cells
    - Enhancing the number and functions of pro-tumor regulatory T-cells, M2-like macrophages, and myeloid-derived suppressor cells (MDSCs)

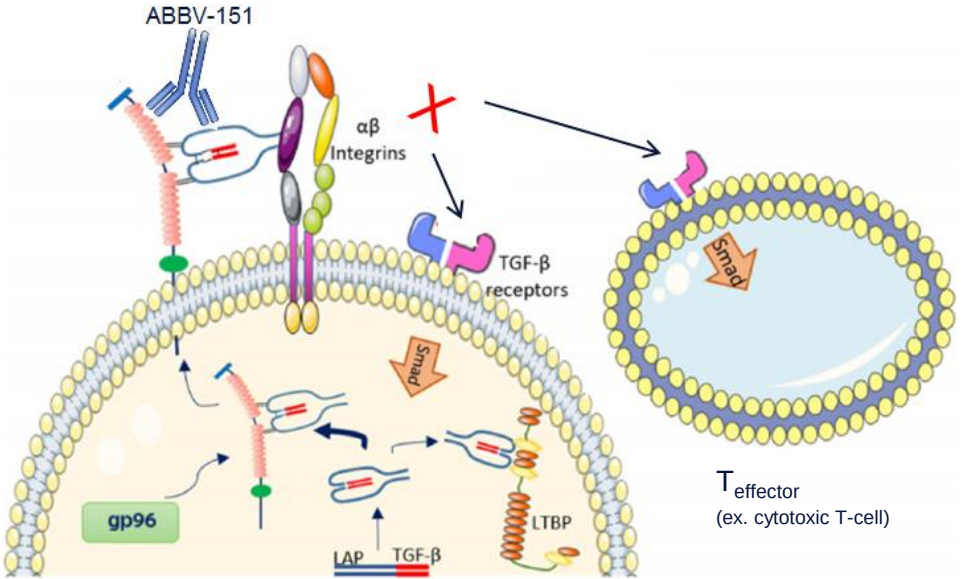


Application of computational immunology to ABBV-151 (MOA: GARP/TGF-β)

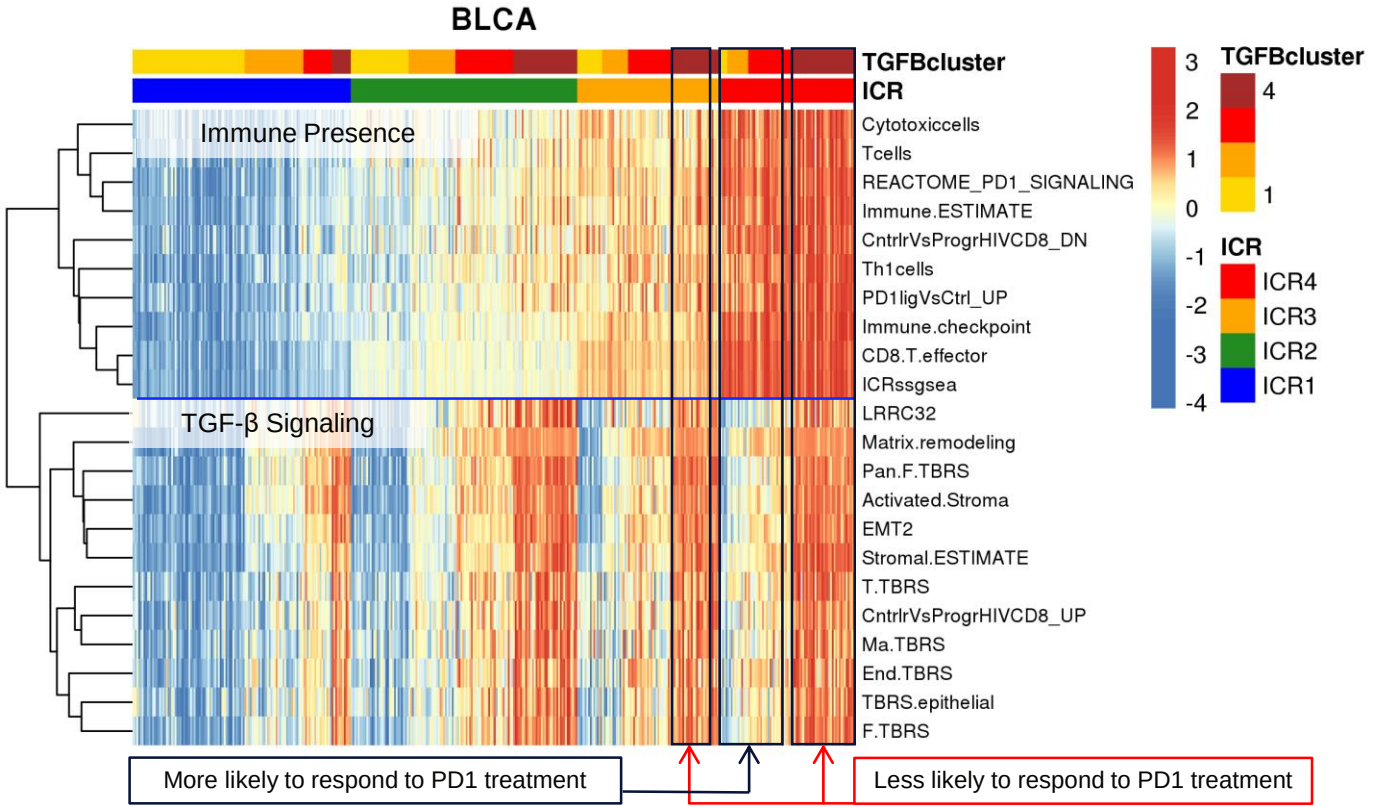
- GARP is a novel I-O target that is implicated in TGF-β biology
- ABBV-151 prevents GARP-mediated TGF-β-1 suppression of T effector cells
- ABBV-151 disables T regulatory cells and enables T effector cells

Role of Computational I-O team on ABBV-151 program:

- Characterized target biology
- Guided disease indication selection
- Analyzed clinical trial biomarker data



Tumor inflammation versus TGF-β signaling in bladder urothelial carcinoma



New capabilities: Genetics and genomics; innovation in clinical trials

Howard Jacob, Ph.D.,
Vice President and Head, Genomics Research Center

Kyle Holen, M.D., Head, Development Design Center

Genetics and genomics

Howard Jacob, Ph.D.,
Vice President and Head of the Genomics Research Center

Why is the rate of attrition across pharma pipelines constant?

- In medicine, knowledge is estimated to be doubling every 18 months
- There must be a better understanding of pathobiology in these data
- How can knowledge be doubling and pharma's success rate staying constant?
- There must be better ways to treat disease and manage healthcare with data

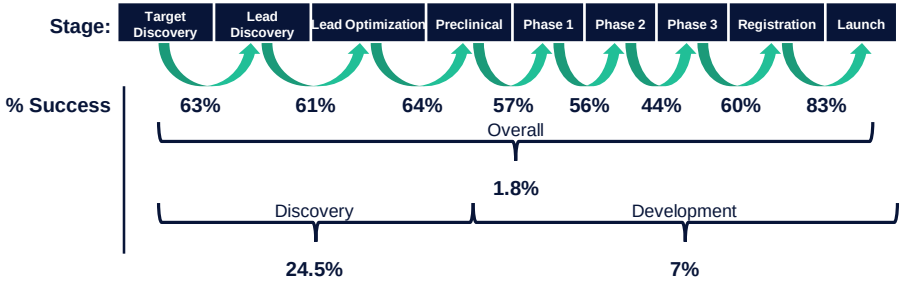


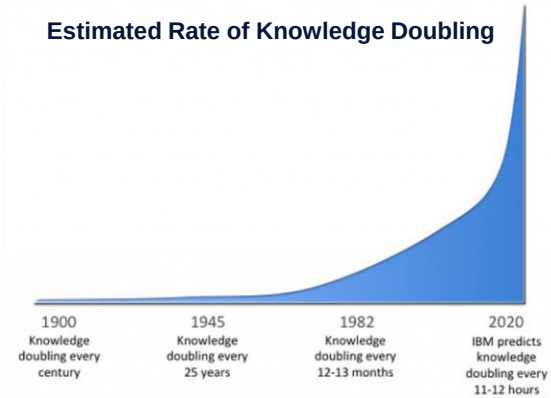
Figure1, Attrition Across the Pipeline.[1]

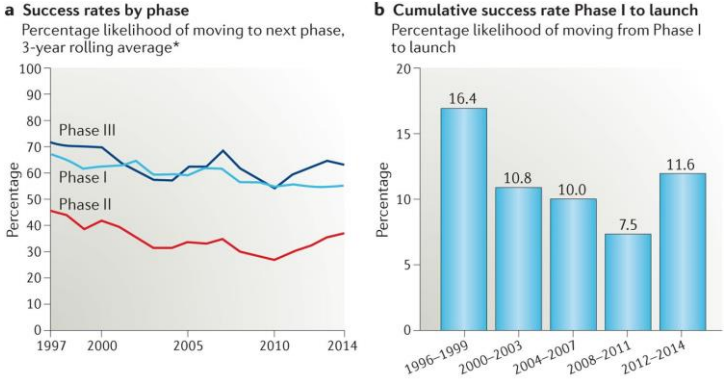
PLOS GENETICS

Are drug targets with genetic support twice as likely to be approved? Revised estimates of the impact of genetic support for drug mechanisms on the probability of drug approval

Emily A. King, J. Wade Davis, Jacob F. Degner

Published: December 12, 2019
https://doi.org/10.1371/journal.pgen.1008489





Nature Reviews Drug Discovery June 2016, Vol 15. pg. 379

Building a genomics capability at AbbVie

Since 2016, we have invested in people, technology, and cohorts totaling over $100M to date

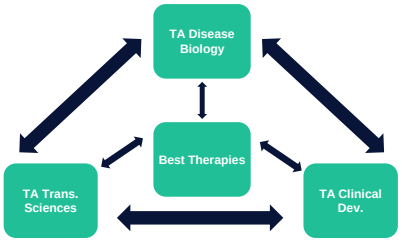
AbbVie is acquiring over 1 million genomes

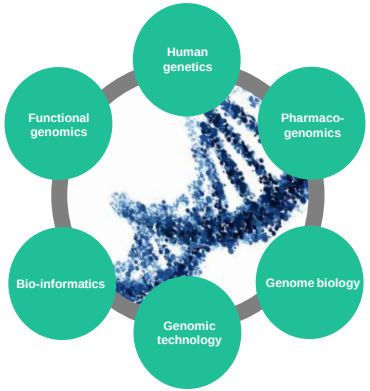
Genomics is now impacting:

- Discovery in three core therapeutic areas
- Development in all areas
- Process sciences to improve our CHO cells ability to make biologics
- Governance starting in March 2020
- Corporate Strategy: What indications, what targets, what companies
- Commercial: We are testing if Omics can be used to identify the best drug

The Genomics Research Center (GRC)

Six functional teams
Supports all therapeutic areas
Connects across R&D





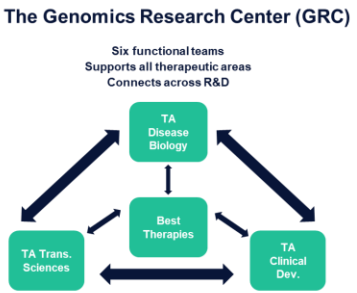
IT Infrastructure (IR)

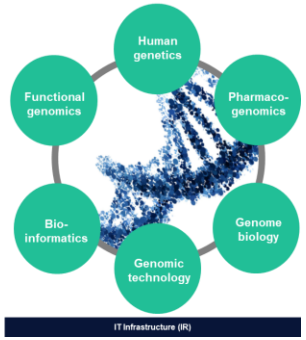
Massive data sets from:

- Real-world data (~350M claims)
- Large cohorts
  - 10% of Finland
  - ~1% of Ireland
  - 500,000 UK biobank
  - 30,000 cancer patients
- Whole genome sequencing
- Single-cell transcriptomics
- Epigenetics
- Imaging
- Wearables
- Longitudinal data
- EHRs: 150 million (globally)
- Whole genome CRISPR screens in cell lines, iPCS from patients, and in vivo models

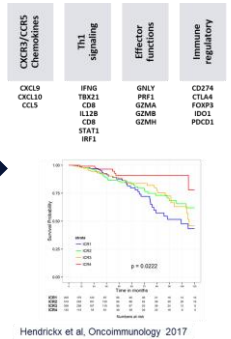
- Today, we are working from the single patient with deep phenotyping and molecular fingerprinting to national level healthcare data
- Creating the need to re-think our data strategy and pipeline
- Doubled the number of clinically validated targets

Building a genomics capability at AbbVie

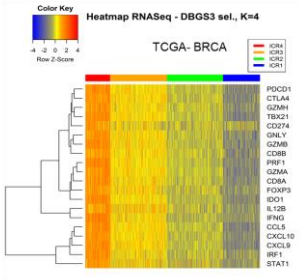




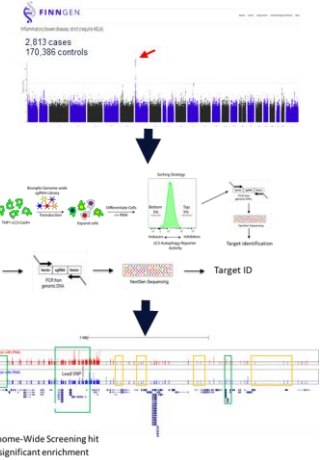
Stratify Patients



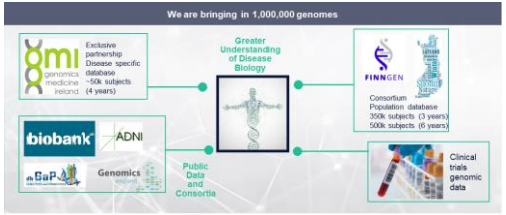
Oncology



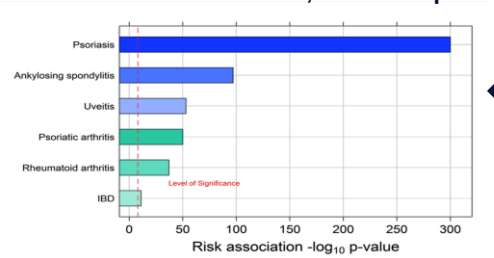
Immunology
Target ID and Confirmation



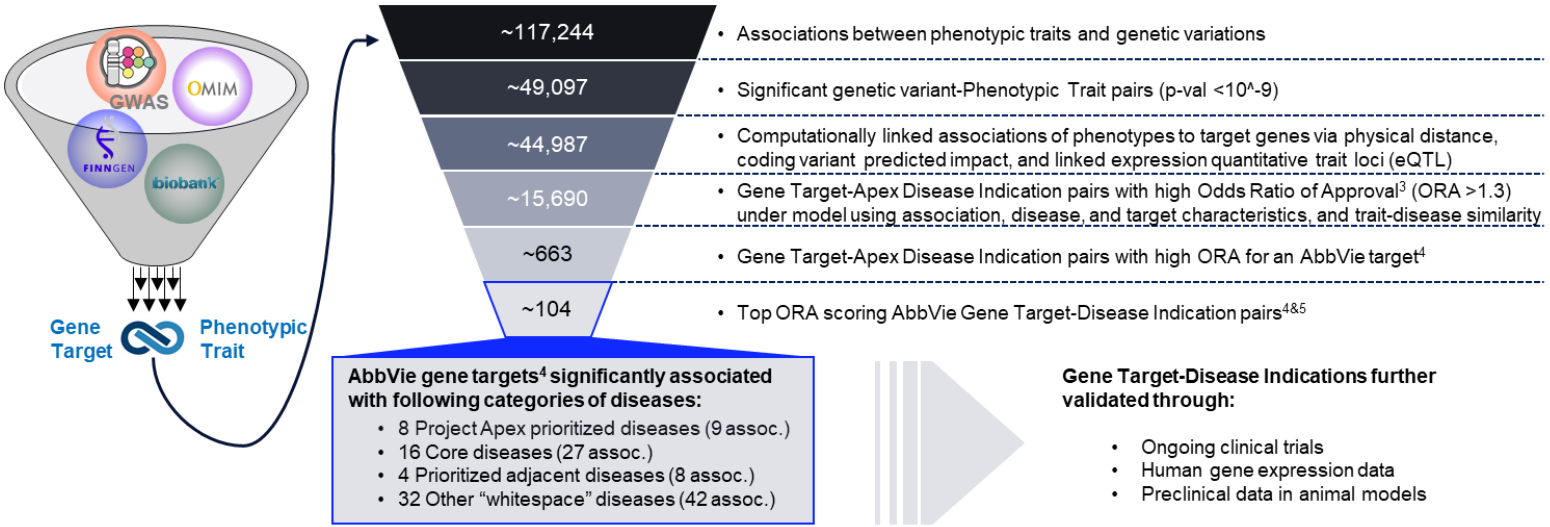
Population cohorts for new indications, target ID and confirmation



New Indications, TNF example



Using human genetics to select gene targets *in silico*



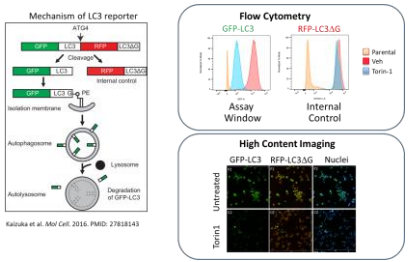
Using >500,000 genomes to evaluate large numbers of targets *in silico*
Increase accuracy and reduce time to identify

Functional genomics: Ongoing projects

IBD Target Discovery

Immunology

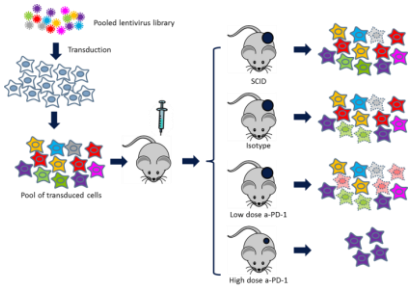
- **Overview:** Integrated genomics and genomics approach to IBD target discovery (genome-wide CRISPR screens, genome-wide association study and clinical expression profiling)
- **Outcome:** 3 new targets entering immunology discovery pipeline
- **Status:** Additional target validation efforts ongoing with human primary macrophage and *in vivo* approaches



In vivo Syngeneic Tumor Cell IO CRISPR Screens

Oncology

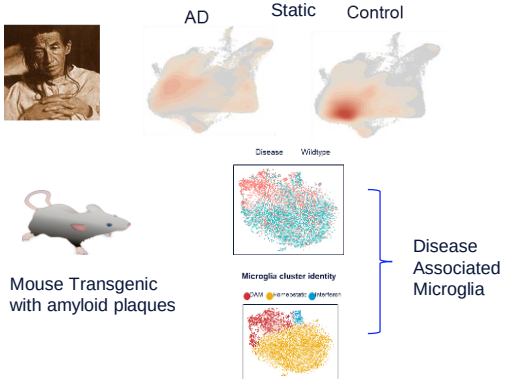
- **Overview:** *In vivo* CRISPR screens using multiple syngeneic tumor models to identify tumor cell targets under immune surveillance
- **Outcome:** Feasibility demonstrated for MC38 colon cancer model
- **Status:** Multiple new screens planned for 2020; additional model development in progress



Microglia Alzheimer Disease Target Discovery

Neuroscience

- **Overview:** Human AD vs Mouse APP transgenic – select targets from man and back-translate
- **Outcome:** sNuc/cell-Seq enables use of archived human AD brains, major regulatory pathways identified
- **Status:** Target validation ongoing



Innovation projects and new initiatives

Epigenetics

- Identify functional target (gene/s) of sequence variant nominated from FinnGen by mapping enhancers, promoters (ChIP-seq) and generation of 3D DNA interactions with Hi-C,PLAC-seq
- Deconvolute the genome-wide association study (GWAS) hits in patients with IBD by utilizing ATAC-seq, Hi-C, PLAC-seq, proteomics, and RNA-seq data from gut tissue samples in healthy individuals, non-inflamed individuals, and inflamed individuals

Image-based morphological profiling (cell painting)

- Multiple cellular features imaged simultaneously using fluorescent dyes
- Cellular signatures derived via automated feature extraction and machine-learning assisted image analysis
- Clustering of signatures to categorize phenotypically similar genetic or chemical perturbations

CHOmics: SUPERCHO expression platform

- Collaboration with Process Science team at ABC (Operations S&T)
- Leverage 'omics platforms to improve biologics product quality, yield, manufacture process
- CHO lipase KO to support risankizumab production completed in 2019; unbiased epigenetic characterizations, additional gene editing and screening projects in line for 2020

CRISPR screening in single cells

- Link genotype to molecular phenotype at high throughput
- Utilize the conventional CRISPR/Cas9 loss-of-function (LoF) screen
- Couple with single-cell RNA-Seq (scRNA-Seq)

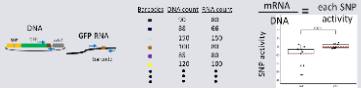
Gene Perturbation | Transcriptome Measurement | Molecular Phenotype

Deep mutational scanning (MITE-seq)

- Implement saturation mutagenesis approach to comprehensively assess the effect of nonsynonymous mutations on BCL-2 and its role in development of resistance to VENCLEXTA
- Confirm/discover findings as it correlates with novel mutations arising in the clinic

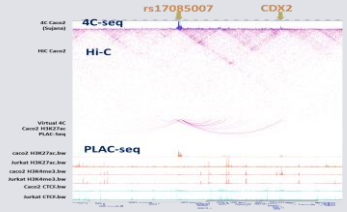
Lenti-MPRA

- Functionalization of GWAS non-coding variants using lentivirus based massively parallel reporter assay (Lenti-MPRA) in disease-relevant cells
- POC with 225 SNPs in IBD overlapping with H3K27Ac PLAC-seq data in Caco-2 cells, 38 SNPs from PANTS anti-TNFα response/ non-response in Chr12 and 45 SNPs from FinnGen IBD GWAS Chr7 TNRC18 locus



Linking non-coding variant to gene

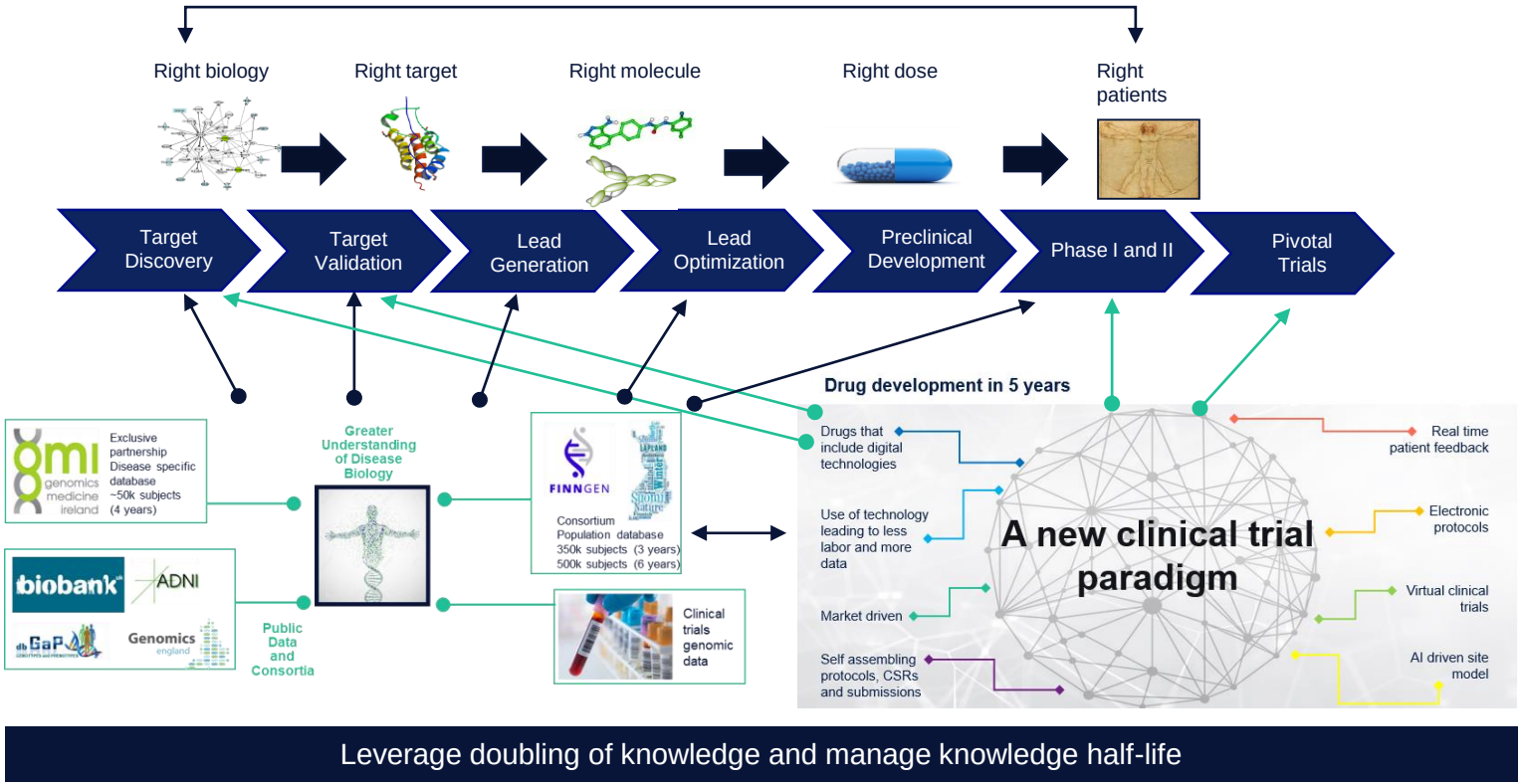
- Implement 3C (chromosome conformation capture) methods to link non-coding variants (IBD GWAS) to their target genes in disease-relevant cell system



Coordination center to develop animal models

- Utilizing knock-in, knock-out, CRISPR/Cas, BAC transgenesis etc. 13 genetically modified strains were delivered and 9 new one were started in 2019

Convergence: Disrupting the discovery and development paradigm



Leverage doubling of knowledge and manage knowledge half-life

What does this innovation mean for AbbVie?

- We can start our discovery pipeline with knowledge from human data
  - Real world data
  - EHR data or clinical trial data
  - Omics data
  - Molecular fingerprints
- The ability to gene edit in the cell, tissue and animal has changed our discovery platform
- Reduce our failure rates and accelerate the pipeline by using human data most of the time
- Increase the effectiveness of our treatments
- Move into new indications faster
- Produce better biologics faster
- Help physicians and patients use our medications

Becoming the best knowledge-based biopharma company

The Development Design Center: Shaping the future of clinical research

Kyle Holen, M.D., Head, Development Design Center

The Development Design Center (DDC): Tailored expertise, predictive analytics and machine learning to deliver efficient trial decisions

Growing Pipeline

AbbVie's growing pipeline demands efficiency and innovation

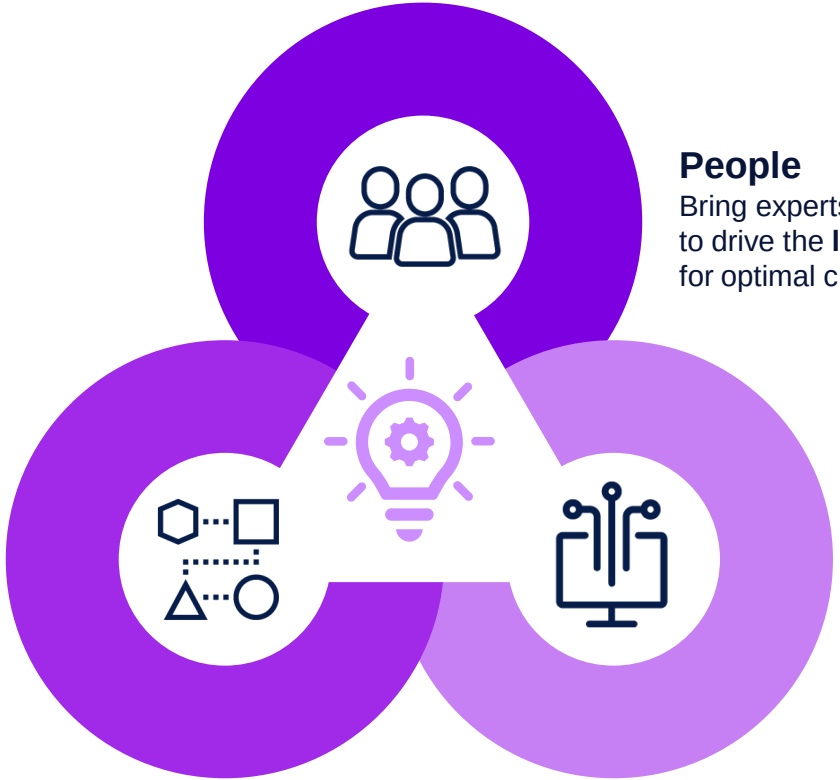
Drive Consistency

The entire portfolio must have access to innovative tools and cross-therapeutic learning

Exceptional Tools

Big Data allows for predictive analytics and machine learning: the future of AbbVie's success

The DDC approach



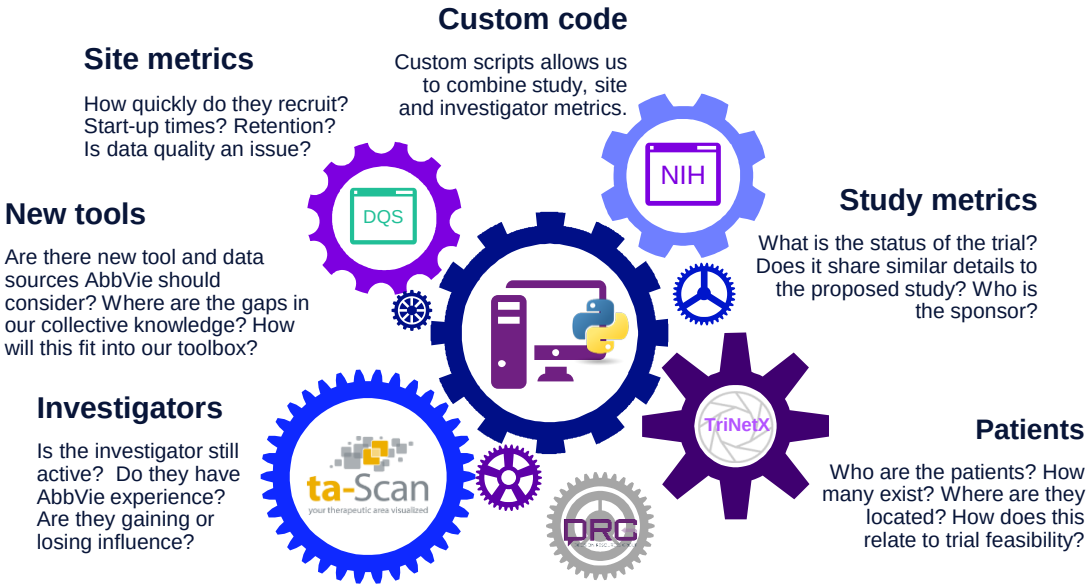
People
Bring experts together as partners to drive the **latest technology** for optimal clinical output

Process
Establish **a common approach** to clinical trial design

Technology
Leverage predictive analytics and real-world data to **strengthen and optimize clinical decisions**

DDC goal: Make the smartest decisions

We are consistently finding ways to leverage data and tools in combination to provide a more robust dataset for decision making



Using machine learning to accelerate clinical trials

Accelerating Study Enrollment By Better Site Selection

- We used more than 4 million data fields from 10-15 sources to better predict highest performing sites
- These models outperform historic performance by 5-7 months

Predicting Study Participants Who Drop-out

- We analyzed more than 11,000 patients with millions of data to better understand factors associated with dropping out of a study
- Solving industry wide problem of high drop out rates by using a risk score analysis

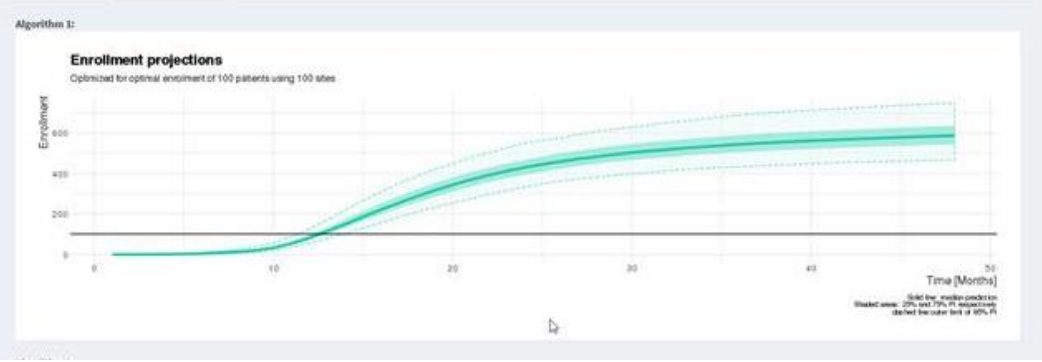
Finding Patients Pre-diagnosis

- By analyzing millions of patient medical records, we can identify patterns of health care engagement that can predict a diagnosis
- These patients can then be offered our clinical trial, or perhaps an AbbVie treatment that would benefit them

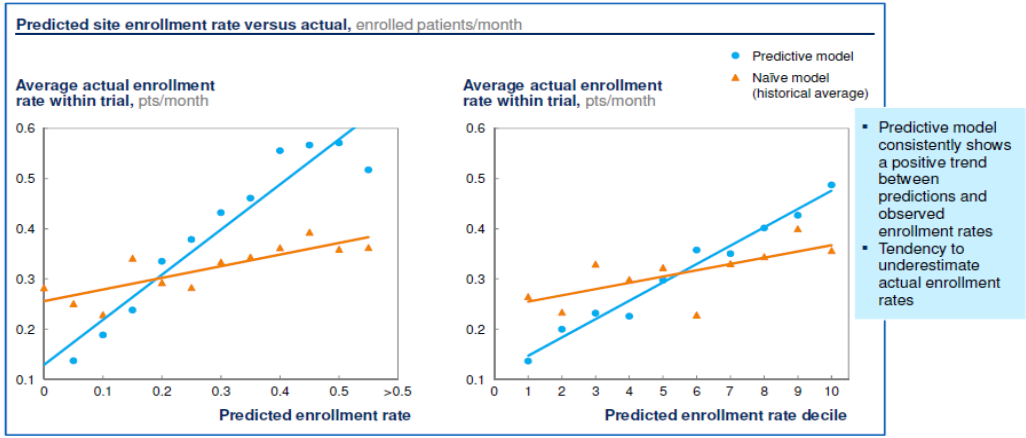
In Silico Control Arms

- We can predict patient placebo responses in our clinical trials by using machine learning to develop outcome algorithms
- These algorithms can be used to predict how our patients would have responded would they have not received our drugs

Programs dramatically accelerated by use of machine learning

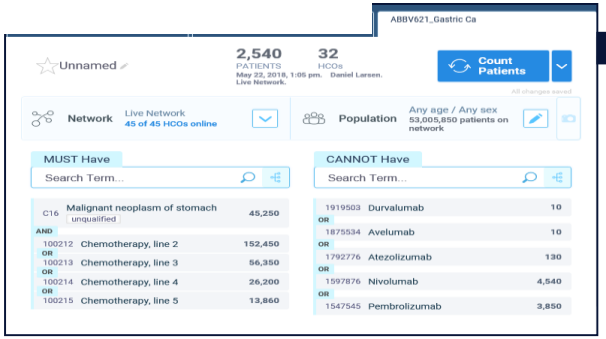


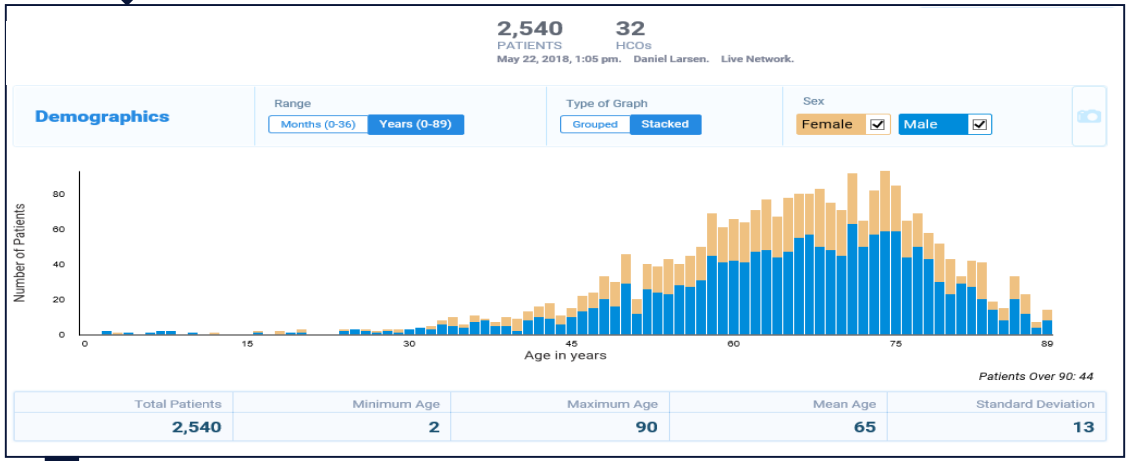
This machine learning model lead to a ~5 month acceleration of the clinical program



This machine learning model showed consistent improvements over using historical performance data

The DDC in action: Finding patients and designing ABBV-621 protocol





- The DDC worked with the study team for ABBV-621 (eftozanermin alfa or “Eftoza“) where time to proof of concept was critical
- Analytical insights from the DDC were utilized to accelerate the study design and find the patients

What's on the horizon: 2020 and beyond

Tokens

Personal identifiable information encrypted to create a unique code that can be used for anonymized research

The first company in the industry to utilize tokens for a 360 view of participants in our trials

Abbvie Design and Execution Platform (ADEPt)

Forecasting and trial simulation tool

Direct-to-Patient Trials

Gathering the building blocks for virtual studies

Patient Burden

Developing a tool to measure patient burden in our studies

In Silico Controls "Bookshelf"

Creating algorithms to predict disease outcomes

Tech-Enabled Medicine Development

Developing novel digital endpoints for our studies

Expansion of the pipeline

Tom Hudson, M.D., Senior Vice President, R&D
and Chief Scientific Officer

AbbVie R&D Pipeline - 2020

Select Pipeline Assets and Programs

As of February 7, 2020

Phase 1

- ABBV-157 (RORγT)
- ABBV-154 (TNF-Steroid ADC)
- ABBV-151 (GARP+TGFβ1): Solid Tumor
- ABBV-155 (BCL-xLi ADC): Solid Tumor
- ABBV-181 (PD-1): Solid Tumor
- ABBV-321 (EGFR ADC): Solid Tumor
- ABBV-368 (OX40): Solid Tumor
- ABT-165 (DLL4/VEGF): Solid Tumor
- ABBV-621 (TRAIL): Solid/Heme Tumor
- ABBV-744 (BET): Heme Tumor
- ABBV-927 (CD40): Solid Tumor
- ABBV-CX-2029* (CD71): Solid/Heme Tumor
- ABBV-647* (PTK7 ADC): NSCLC
- ABBV-011 (SEZ6 ADC): SCLC
- VENCLEXTA* (BCL-2): ALL
- VENCLEXTA* (BCL-2): Solid Tumor
- CCW702* (CD3-PSMA): Prostate Cancer
- CLBR001/SWI019* (sCAR-T): Heme Tumor
- TNB-383B* (CD3-BCMA): MM
- TTX-030* (CD39): Solid Tumor
- ABBV-0805* (α-Synuclein): PD
- AL002* (TREM2): AD
- AL003* (CD33): AD
- ABBV-4083 (TylAMac): Filarial Diseases

Phase 2

- SKYRIZI* (IL-23): Atopic Derm
- SKYRIZI* (IL-23): HS
- ABBV-3373 (TNF-steroid ADC)
- ABBV-599 (BTK/JAK): RA
- ABBV-599 (BTK/JAK): SLE
- Ravagalimab (CD40): UC
- IMBRUVICA* (BTK): Solid Tumors
- VENCLEXTA* (BCL-2): MDS
- Teliso-V (cMet ADC): NSCLC
- ABBV-8E12* (Tau): AD
- Elezanumab (RGMa): MS
- ABBV-2222/ABBV-3067 (CFTR-C1/CFTR-P): Cystic Fibrosis
- ELAGOLIX* (GnRH): PCOS

Registrational / Phase 3

- RINVOQ (JAK 1): PsA
- RINVOQ (JAK 1): CD
- RINVOQ (JAK 1): Atopic Derm
- RINVOQ (JAK 1): UC
- RINVOQ (JAK 1): GCA
- RINVOQ (JAK 1): AS
- RINVOQ (JAK 1): Axial SpA
- SKYRIZI* (IL-23): CD
- SKYRIZI * (IL-23): UC
- SKYRIZI * (IL-23): PsA
- IMBRUVICA* (BTK): 1L cGvHD
- IMBRUVICA* (BTK): 1L FL
- IMBRUVICA* (BTK): 1L MCL
- IMBRUVICA* (BTK): R/R MCL
- IMBRUVICA* (BTK): R/R FL/MZL
- IMBRUVICA* (BTK): 1L CLL
- Veliparib (PARP): NSCLC
- Veliparib (PARP): BRCA Breast Cancer
- Veliparib (PARP): 1L Ovarian Cancer
- VENCLEXTA* (BCL-2): 1L CLL
- VENCLEXTA* (BCL-2): 1L AML
- VENCLEXTA* (BCL-2): AML Maintenance
- VENCLEXTA* (BCL-2): R/R MM t(11;14)
- Navitoclax (BCL-2/BCL-xL): Myelofibrosis
- ABBV-951 (dopamine receptor): PD
- ELAGOLIX* + Hormonal Add-Back (GnRH): Endometriosis

Submitted

- ORILISSA* (GnRH): Uterine Fibroids (US)

Recently Approved

- RINVOQ: RA (US, EU, JPN)
- SKYRIZI*: Ps (US, EU, JPN)
- VENCLEXTA*: 1L CLL (US)
- IMBRUVICA* + Gazyva: 1L CLL (US)

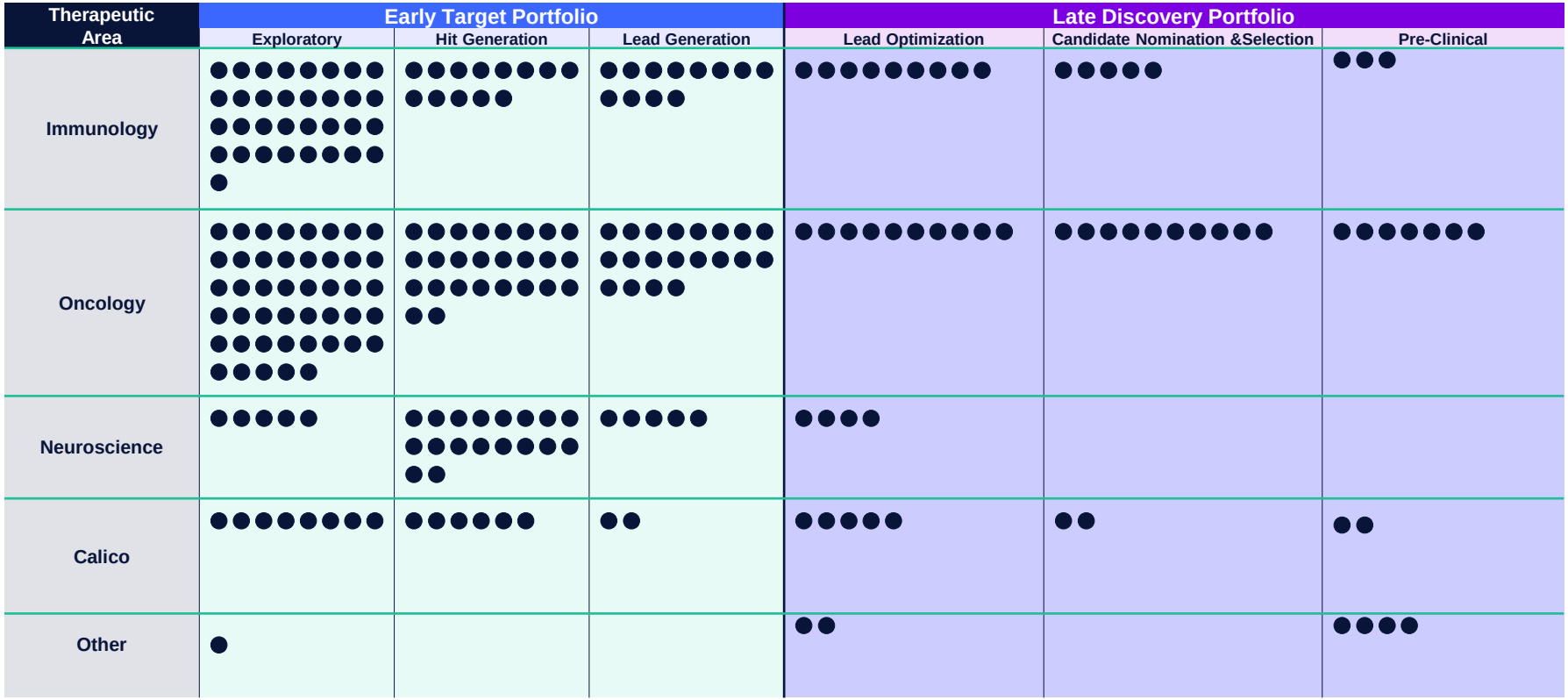
Oncology
Immunology
Neuroscience
Other

We continue to focus on the quality of our medicines, while doubling our early-stage pipeline since 2013, with more than 30 assets currently in late discovery and preclinical development

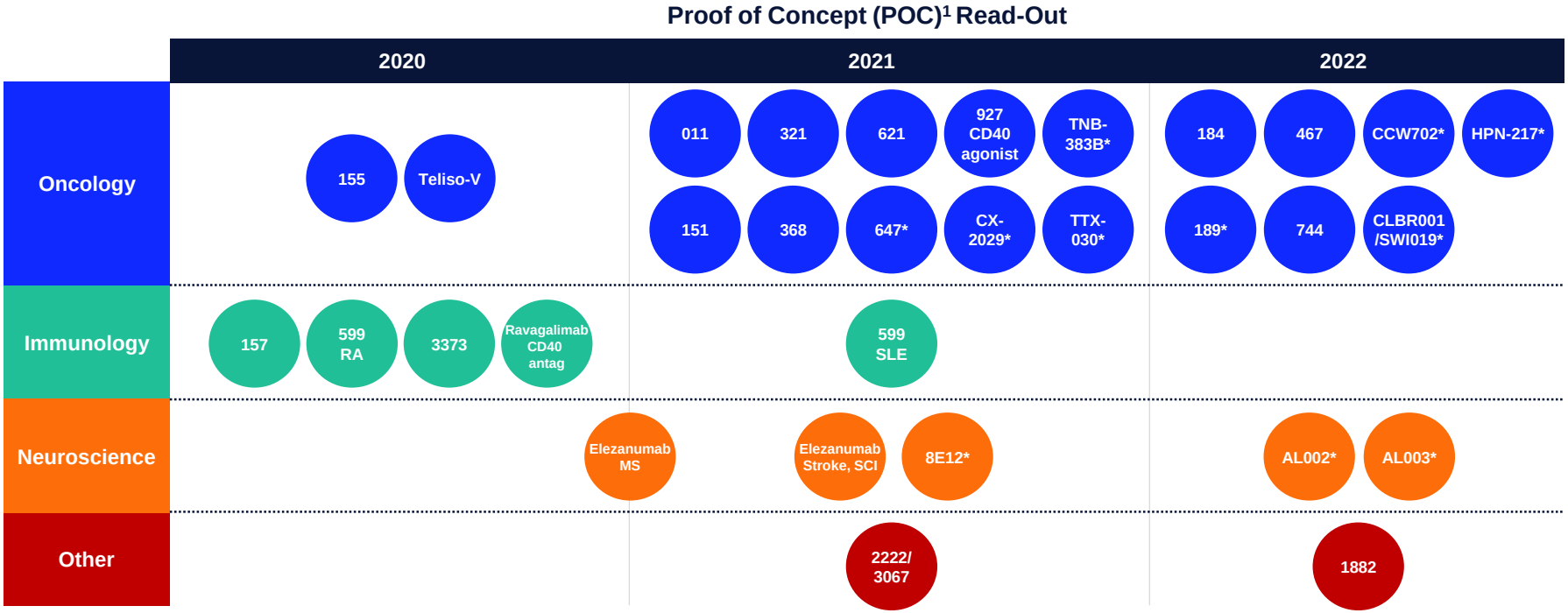
*Partnered Asset; Partnership Summary Below:
Imbruvica jointly developed and commercialized with Janssen Biotech; Elagolix developed in cooperation with Neurocrine Biosciences; Venclexta developed by AbbVie and Roche, commercialized by AbbVie and Genentech, a member of the Roche Group; Skyrizi developed in cooperation with Boehringer Ingelheim; ABBV-8E12 developed in cooperation with C_2N Diagnostics; ABBV-0805 developed in cooperation with BioArctic; CCW702 / CLBR001 / SWI019 developed by Calibr in a first-in-patient trial and AbbVie holds option to license the program; TNB-383B developed by TeneoOne through Phase 1 and AbbVie holds exclusive right to acquire TeneoOne; AL002/AL003 developed by Alector through Phase 2 and AbbVie holds option for additional development and commercialization; TTX-030 developed by Tizona Therapeutics through Phase 1b and AbbVie has option to lead global development and commercialization; ABBV-2029 developed in cooperation with CytomX Therapeutics; ABBV-647 developed in cooperation with Pfizer.

AbbVie's early target and preclinical portfolio snapshot

As of February 7, 2020



Our early pipeline will yield approximately 30 POC readouts in the near-term

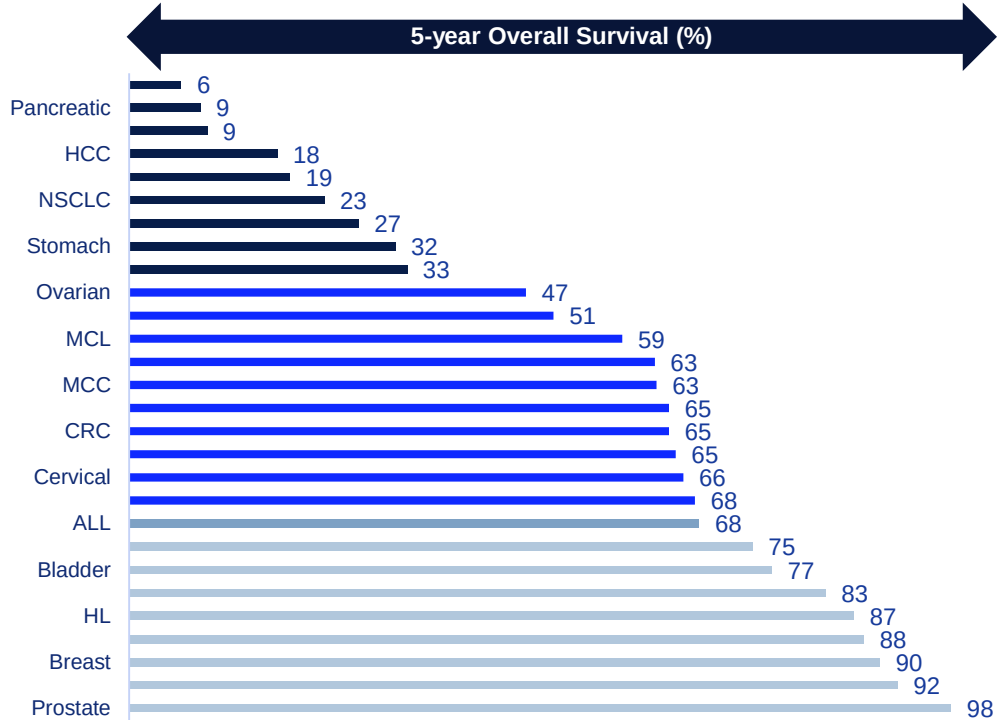


1. POC date corresponds to interim data readout; Only pipeline assets that have not already achieved POC represented
*Partnered Asset: ABBV-647 developed in cooperation with Pfizer; ABBV-CX-2029 developed in cooperation with CytomX Therapeutics; TNB-383B developed by TeneoOne through Phase 1 and AbbVie holds exclusive right to acquire TeneoOne; TTX-030 developed by Tizona Therapeutics through Phase 1b and AbbVie has option to lead global development and commercialization; ABBV-189 developed in cooperation with Harpoon Therapeutics; CCW702 / CLBR001 / SWI019 developed by Calibr in a first-in-patient trial and AbbVie holds option to license the program; HPN-217 developed by Harpoon Therapeutics through Ph 1/2 and AbbVie has option to license worldwide exclusive rights; ABBV-8E12 developed in cooperation with C_2N Diagnostics; AL002/AL003 developed by Alector through Phase 2 and AbbVie holds option for additional development and commercialization

Oncology

Neil Gallagher, M.D., Ph.D.,
Chief Medical Officer and Vice President of Development

Despite recent advances, unmet need and opportunity exists for all tumor types



Opportunity

- Improve survival

- Improve survival, especially for patients in later lines/later stages of disease

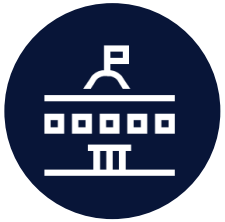
- Improve survival for sub-populations with high unmet need (e.g., metastatic stage, TNBC in breast)
- Improve safety, tolerability, QoL

Source: SEER (based on patients into 2015), STS = Soft Tissue Sarcoma; MCC = Merkel cell carcinoma

AbbVie oncology

2

approved oncology products worldwide



9

breakthrough designations by the FDA to date

20+

investigational compounds in the clinic

100+

AbbVie sponsored clinical trials in 50 countries

Additional 300+ IIS ongoing

Oncology key areas of biology

Apoptosis

Cancer cells often lose their ability to undergo apoptosis, thereby promoting tumor cell survival

A 20+ year commitment to apoptosis research led AbbVie scientists to the discovery and approval of VENCLEXTA – validating apoptosis as a compelling, new approach to treating cancer

We are now exploring other forms of cell death as next-generation anticancer agents

I-O

I-O therapies seek to overcome the ability of tumor cells to evade elimination by the immune system

AbbVie scientists are investigating novel approaches to manipulate the immune system

For example, we are using cutting-edge genomics technologies to understand how tumors suppress immune responses and to develop new I-O agents

Tumor Targeting

Tumor cells can be distinguished from normal cells by way of protein antigens on their cell surface

AbbVie scientists have developed novel systems to uncover tumor selective antigens for both solid tumors and hematologic malignancies

We are using novel biologics (drug conjugates, CD3 bispecific) and next-generation engineered T-cells to target tumor antigens and avoid killing normal cells

We have a compelling oncology pipeline

	Preclinical	Phase 1 / Phase 2	Phase 3 / Registrational	Submitted / Launched
Heme tumors	ABBV-467	ABBV-744 TNB-383B CLBR001/SWI019 HPN-217	VENCLEXTA (1L CLL, 1L AML, AML maintenance, R/R MM t(11;14), MDS) IMBRUVICA (1L CLL, R/R FL/MZL, R/R MCL, 1L MCL, 1L FL) Navitoclax (Myelofibrosis)	VENCLEXTA (1L CLL US) IMBRUVICA + Gazyva (1L CLL US)
Both	ABBV-184	ABBV-621 VENCLEXTA (ALL, solid tumors) ABBV-CX-2029		
Solid tumors	ABBV-637 ABBV-CLS-579 ABBV-189	Teliso-V ABBV-927 ABBV-321 ABBV-647 CCW702 ABBV-368 ABBV-155 ABBV-151 ABBV-011 ABBV-181 ABBV-165 TTX-030	Veliparib (1L ovarian, BRCA breast, NSCLC)	

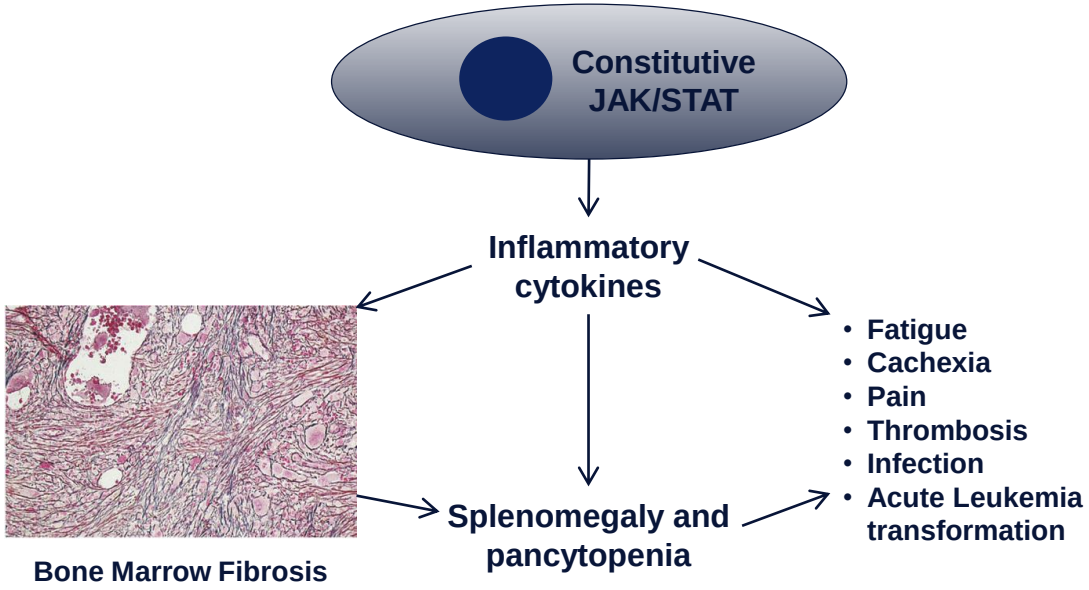
MOA

- **I-O**
- **Apoptosis**
- **Tumor Targeting**

Our goal is to transform the treatment of myelofibrosis with our BCL-XL inhibitor Navitoclax

Myelofibrosis (MF): a malignant, life-threatening bone marrow disorder

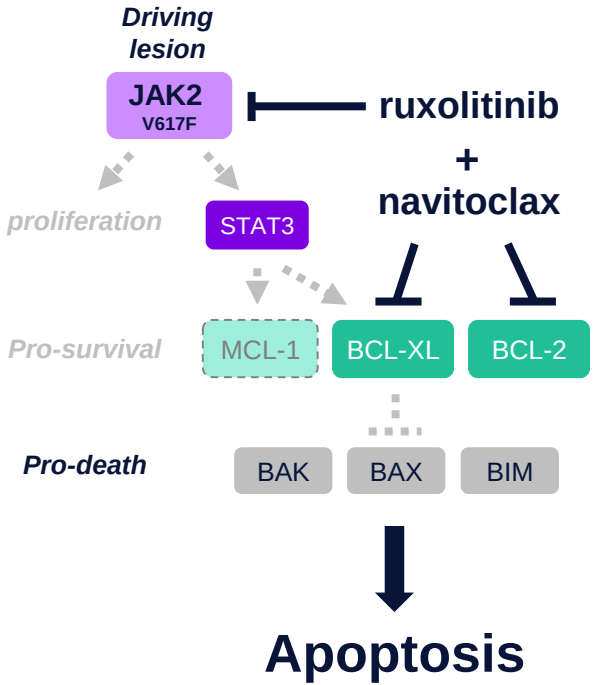
- MF disrupts production of blood cells by extensive scarring in the bone marrow
- This leads to severe anemia, weakness, fatigue, and splenomegaly (spleen enlargement)
- In MF, certain mutations (e.g., V617F) result in sustained signaling of the JAK/STAT pathway leading to increased cell division and growth
- The only approved class of therapies (JAK inhibitors) offers symptom relief, with minimal impact on underlying course of the disease
- Encouraging early indications of reduction in allelic burden



Navitoclax + ruxolitinib is a rational and potentially transformative combination in myelofibrosis therapy

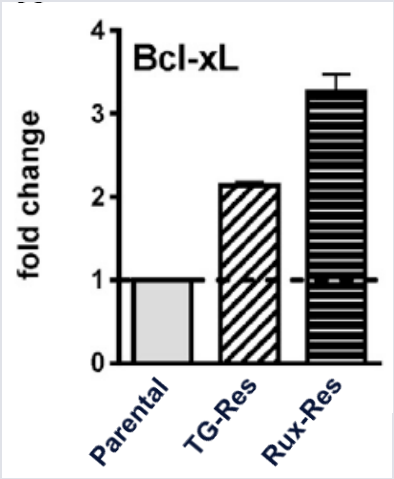
- JAK/STAT activating mutations drive proliferation and an anti-apoptotic effect via MCL-1 up-regulation
- JAK2 inhibitor ruxolitinib (Jakafi) reduces JAK/STAT signaling
- Combining navitoclax with ruxolitinib induces apoptosis in MPN cells, including malignant stem cells

Eradication of myeloproliferative neoplasms (MPN) cells and malignant stem cells may enable spleen normalization, remodeling of fibrotic bone marrow and improvement of hematologic parameters



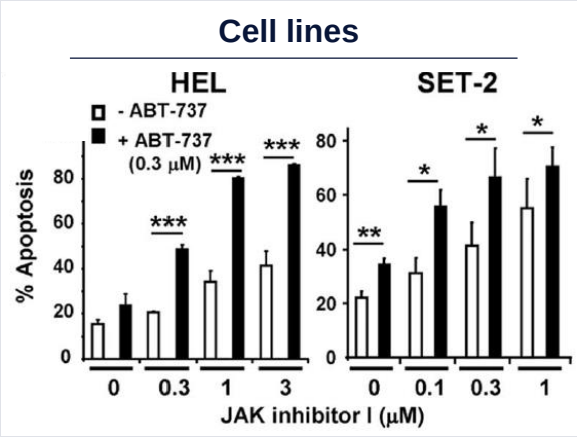
BCL-XL inhibition overcomes resistance to JAK2 inhibitors

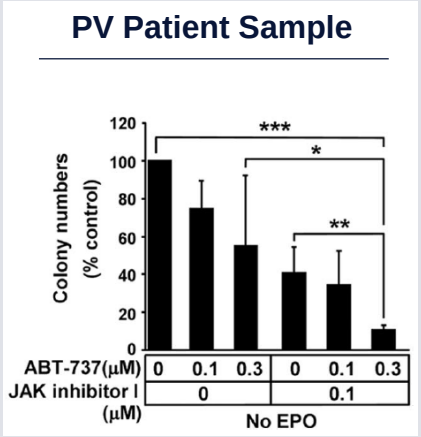
BCL-XL levels are elevated in cells with acquired resistance to JAK2 inhibitors



TG-Res: resistant to JAK2 inhibitor (TG101209)
Rux-Res: resistant to ruxolitinib

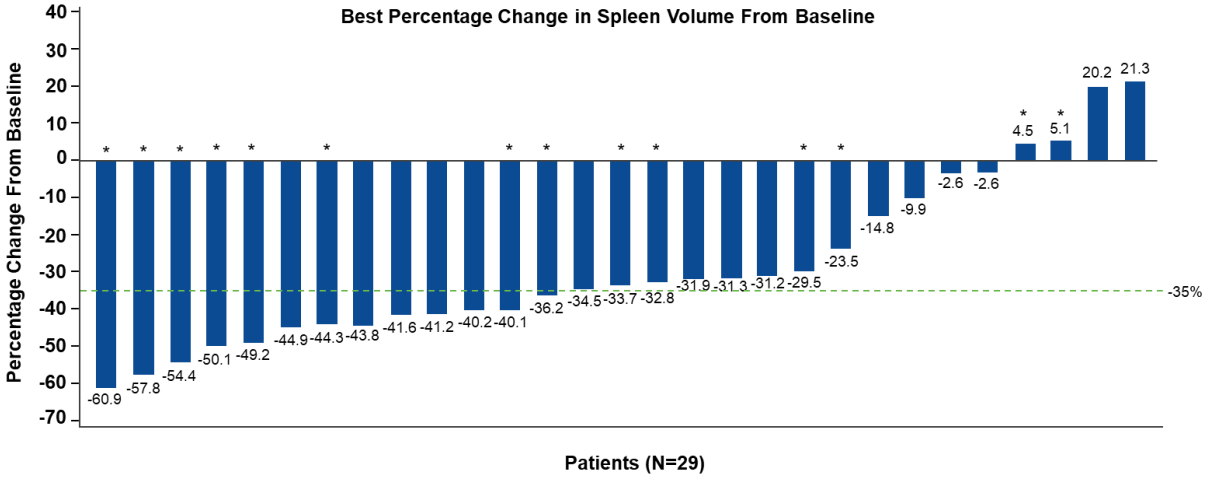
Dual BCL-2/BCL-XL inhibitors (ABT-263 and ABT-737) synergize with JAK2 inhibitor (JAKi-I) to kill JAK2 V617F cell lines (SET-2 and HEL) and PV patient samples





Navitoclax overcomes ruxolitinib resistance resulting in splenomegaly improvement for most patients

- SVR_{35} best on study: 43% (13/30)
- SVR_{35} at week 24: 30% (9/30)
- 53% (16/30) of patients resolved palpable splenomegaly during study treatment
- 25% (8/32) of patients demonstrated reduction in bone marrow fibrosis (local assessment)
  - 13% (4/32) with 1 grade reduction
  - 13% (4/32) with 2 grade reduction



Data cut: November 18, 2019.
Percentages calculated on the basis of efficacy analysis set (N=30).
Baseline is defined as the last non-missing observation collected on or prior to the date of the first dose of any component of study treatment.
*Denotes patients with high molecular risk (defined by the presence of mutations within *ASXL1*, *EZH2*, *IDH1/2*, *SRSF2*, *U2AF1*).

Building an industry-leading portfolio in apoptosis and regulated cell death

Program	MOA	Indication(s)	Opportunity	Stage
ABBV-621	TRAIL agonist	2L Mutant KRAS CRC	• Best-in-class pro-apoptotic agent	• Phase 1 – expansion and combos
ABBV-155	BCL-XL Inhibitor	SCLC, NSCLC and breast cancer	• First-in-class ADC delivering BCL-XL as cargo	• Phase 1 – expansion and combos
ABBV-467	MCL-1 Inhibitor	R/R AML	• Best-in-class combination with VENCLEXTA	• Entering Phase 1
Discovery	• Focus on targets that complement VENCLEXTA and IMBRUVICA resistance mechanisms • Pursue exploratory targets in under-explored forms of regulated cell death (e.g., necroptosis, ferroptosis)			

Leveraging BCL-XL inhibition to treat solid tumors requires tumor targeting

BCL-XL inhibition induces apoptosis

- We used structure-based design to discover first-in-class highly potent, selective BCL-XL inhibitors
- Pre-clinical efficacy in solid tumors
- In clinical studies with navitoclax, we observed platelet decreases at doses that are sub-optimal for treating solid tumors

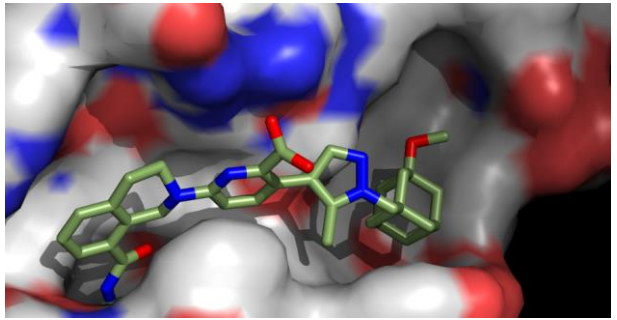
ADC technology used to deliver BCL-XL inhibitors to tumors

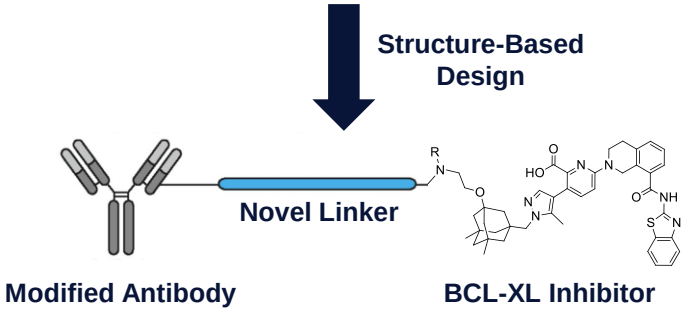
- Generation of novel enabling linkers allowed for first-ever ADCs possessing BCL-2 family inhibitor warheads
- ADCs show preclinical efficacy in mouse models of human lung cancer, with no platelet effect

ABBV-155 is a First-in-Class BCL-XL inhibitor ADC

- Currently in Phase 1 for solid tumors that express B7H3, which is expressed at high levels on many tumor cells but not platelets
- Differentiated safety vs cytotoxic ADCs in monkeys

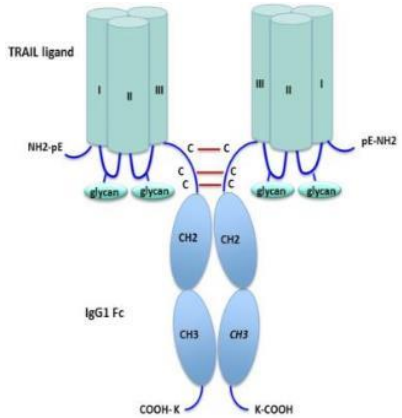
BCL-XL Inhibitor
X-ray structure





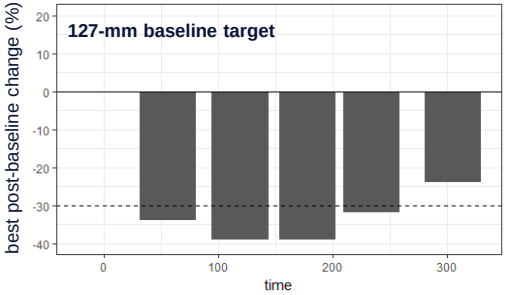
ABBV-621: TRAIL demonstrating monotherapy activity

ABBV-621

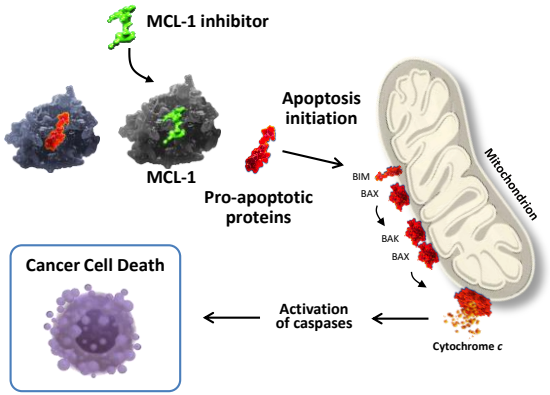


- Novel TRAIL agonist with a pair of trimerized receptor binding domains that optimize clustering of TRAIL receptors independent of Fc engagement, resulting in apoptotic cell death
- Phase 1 study in multiple tumor types, dose optimization in pancreatic cancer and $KRAS_{MT}$ CRC
- Encouraging preliminary monotherapy activity (including PRs) in $KRAS_{MT}$ CRC (see panel at right) triggered expansion in 2L setting in combination with FOLFIRI
- cPOC study initiated Q4 2019; targeting interim analysis for early cPOC declaration by end of 2021
- Anchor potential for AbbVie through ongoing study in CRC as well as potential expansion into myeloma based on encouraging preclinical combination data

Subject with $KRAS_{MT}$ CRC with confirmed PR, sustained for 200+ days after 3 prior lines of therapy

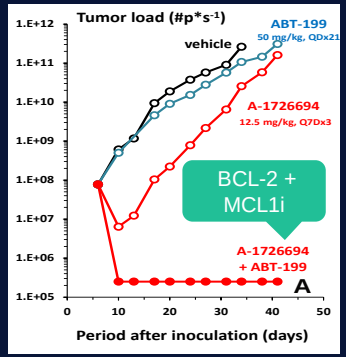


ABBV-467: Important apoptotic pathway in solid and heme tumors

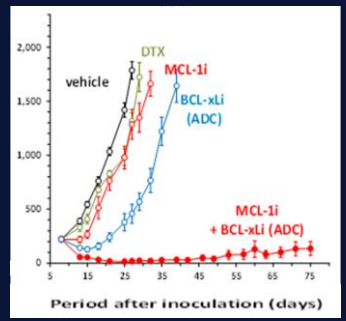


- MCL-1 is widely expressed in heme and solid tumors; allows cancer cells to evade apoptosis
- Mechanistic synergy between BCL-2 and MCL-1 inhibition across broad array of MM, AML and NHL
- *In vivo* efficacy observed across multiple preclinical models, both as monotherapy, and in combination with VENCLEXTA
- IND approved Q4 2019, on target for FSFD Q1 2020
- Anchor potential for AbbVie through key cPOC combination studies in MM and AML

Preclinical Systemic AML Model
(MV4;11)



Preclinical Docetaxel-Resistant NSCLC Model
(H1650-DTX^{r})



Summary of key opportunities in tumor-specific antigen targeting and next milestones

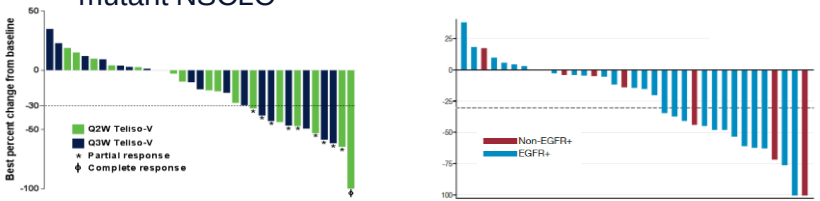
Program	MOA	Indication(s)	Opportunity	Next Data Milestone
Teliso-V	Anti-cMET ADC Warhead: auristatin	NSCLC	First-in-class ADC targeting cMET	• 2020: Go/No go registration trial decision
ABBV-647	Anti-PTK7 ADC Warhead: auristatin	Ovarian, NSCLC	First-in-class ADC targeting PTK7	• Phase 1: Ongoing • EOY 2021: If warranted by clinical data, cPOC early declaration
ABBV-011	Anti-SEZ6 ADC Warhead: calicheamicin	SCLC	First-in-class ADC targeting SEZ6	
ABBV-155	BCL-XL Inhibitor	SCLC, NSCLC and breast cancer	First-in-class ADC delivering BCL-XL as cargo	• Phase 1 – expansion and combos
Discovery	ADC strategy to focus on targets with higher tumor cell expression using warheads with intrinsic tolerability and novel mechanisms			

Leverage strengths in ADCs, novel target identification and engineering of biologics to develop therapies that profoundly impact tumor cell fate

Example: Teliso-V

Teliso-V is a cMET-targeted ADC

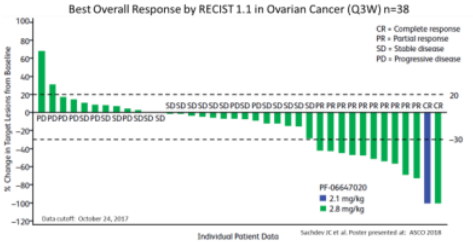
- Expressed in many tumor types: NSCLC, gastroesophageal adenocarcinoma, papillary renal cell carcinoma, ovarian, melanoma, etc.
- **Safety:** Well-tolerated in patients who have received multiple prior lines of therapy
- **Efficacy:** Promising Phase 1 clinical activity in monotherapy and combo with erlotinib in patients with an EGFR mutation
- **Potential for cPOC by 2020**
  - As monotherapy in NSCLC
  - Potential combination strategy with osimertinib in EGFR-mutant NSCLC



Example: ABBV-647

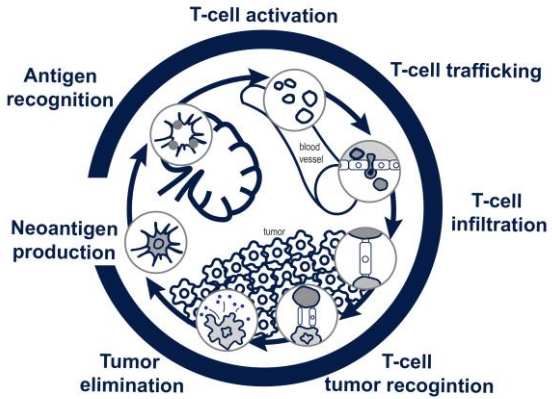
ABBV-647 is a PTK7-targeted ADC

- Expressed in many tumor types: Ovarian, NSCLC,TNBC, others
- **Safety:** Manageable side effects in Phase 1
- **Efficacy:** Promising Phase 1 clinical activity in heavily treated patients
- **Potential for cPOC by EOY 2021**:
  - As monotherapy in NSCLC and/or ovarian
  - Many lifecycle management options (e.g., I-O combos)



We have a growing I-O pipeline

Pursuing two broad areas in I-O



Cancer Immune Cycle

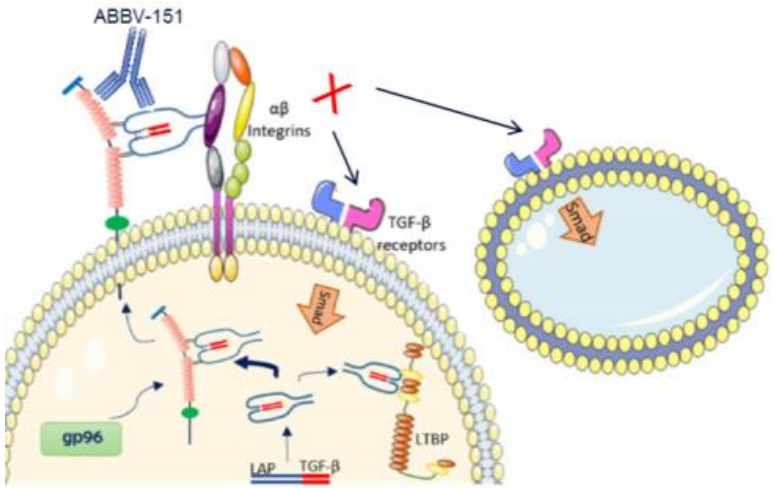
1. Modulation of Tumor Microenvironment

Program	MOA	Indication(s)
Triple I-O combo (ABBV-927+368+181)	CD40, OX40, PD-1	**NSCLC**
ABBV-151	GARP/TGF-β	**TNBC, bladder, pancreatic, HNSCC**
ABBV-368/TLR9 combo	OX40, TLR9, PD-1	**HNSCC**
TTX-030	CD39	**Solid tumors**
MAVU-104	ENPP1/STING	**Solid tumors**

2. Use Immune Cells as Antitumor Weapons

Program	MOA	Indication(s)
ABBV-184 T-cell redirection	TCR Peptide-CD3	**NSCLC**
ABBV-189 T-cell redirection	TCR Peptide-CD3	**NSCLC**
TNB-383B T-cell redirection	BCMA-CD3	**R/R multiple myeloma**
HPN-217 T-cell redirection	BCMA-CD3	**R/R multiple myeloma**
sCAR-T Next-gen cell therapy	Multiple targets	**Multiple**

ABBV-151 is a novel approach to disrupt the tumor microenvironment



- ABBV-151 targets GARP/TGF-β a key immune-suppressive pathway activated in tumors
- Helps disrupt suppressive tumor microenvironment – thought to profoundly enhance antitumor activity of PD-1
- Compelling/robust pre-clinical data
- Phase 1 in combination with ABBV-181 in multiple solid tumors: TNBC, pancreatic, bladder, HCC, HNSCC
- First patient was dosed in 1Q19: 47 days post IND clearance

T-cell redirection: Building a world-class CD3 portfolio

Why

CD3 bispecifics can lead to transformative efficacy comparable to that seen from cell therapies but without the accompanied complexity

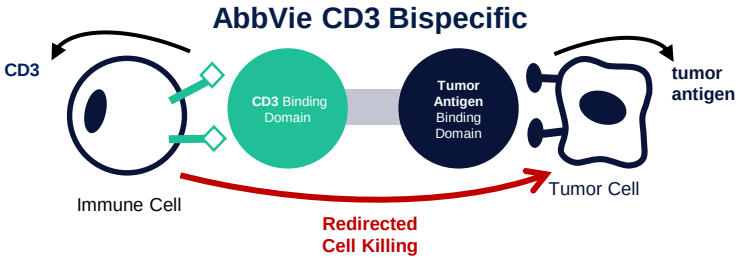
Goals

Develop a world class CD3 platform that enables first-in-class or best-in-class CD3 bispecifics to cPOC every year starting 2021 targeting both heme and solid tumors

Liabilities

Current generation CD3 bispecifics are limited to a restricted number of targets, efficacy only in heme malignancies, short half-life and inherent safety issues (cytokine release syndrome)

Our immune cell redirection platform interrogates multiple variables



Optimizing platforms for clinical success

Balancing validated vs less validated targets & tumors

1 Immune Cell Type

T-cell

ABBV-184
ABBV-189
TNB-383B
HPN217

TriNKET™

NK Cells

2 Immune Cell Binding Affinity

High

ABBV-184
ABBV-189
HPN217

TNB-383B

Low

3 Half-life

Longer

ABBV-184
ABBV-189

Shorter

4 Targets

Clinically validated

BCMA, CD38

Novel targets, novel technologies (TCRs)

More novel

5 Tumor Type

Clinically validated

Heme malignancies

Solid tumors

More novel

We have a compelling oncology pipeline

	Preclinical	Phase 1 / Phase 2	Phase 3 / Registrational	Submitted / Launched
Heme tumors	ABBV-467	ABBV-744 TNB-383B CLBR001/SWI019 HPN-217	VENCLEXTA (1L CLL, 1L AML, AML maintenance, R/R MM t(11;14), MDS) IMBRUVICA (1L CLL, R/R FL/MZL, R/R MCL, 1L MCL, 1L FL) Navitoclax (Myelofibrosis)	VENCLEXTA (1L CLL US) IMBRUVICA + Gazyva (1L CLL US)
Both	ABBV-184	ABBV-621 VENCLEXTA (ALL, solid tumors) ABBV-CX-2029		
Solid tumors	ABBV-637 ABBV-CLS-579 ABBV-189	Teliso-V ABBV-927 ABBV-321 ABBV-647 CCW702 ABBV-368 ABBV-155 ABBV-151 ABBV-011 ABBV-181 ABBV-165 TTX-030	Veliparib (1L ovarian, BRCA breast, NSCLC)	

MOA

- **I-O**
- **Apoptosis**
- **Tumor Targeting**

Immunology

Lisa Olson, Ph.D., Vice President Immunology Discovery

Evolution of AbbVie R&D

Existing and new capabilities

New capabilities:
Genetics and genomics;
innovation in clinical trials

Expansion of the pipeline

Oncology

Immunology

Neuroscience

Cystic Fibrosis

Calico

AbbVie's discovery portfolio
and pipeline snapshot

Leader in the field of immunology, pursuing breakthrough science and delivering best-in-class medicines

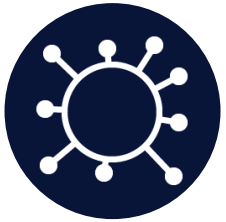
HUMIRA adalimumab destination you

Skyrizi risankizumab-rzaa

RINVOQ upadacitinib

3

approved immunology products worldwide



11

disease areas currently studied in clinical trials

94

ongoing clinical trials in over 50 countries

17

candidates in our late discovery portfolio

We stand on a strong foundation and are building our future beyond one brand with groundbreaking new medicines

Eliminate the burden for all those touched by immune-mediated diseases by advancing an industry-leading portfolio of transformational agents

Clinical goals:

Rheumatology: Rheumatoid arthritis and lupus

Achieve durable remission and halt disease progression

Dermatology: Psoriasis and atopic dermatitis

Achieve clear skin with durable response with an oral agent

Gastroenterology: Crohn's disease and ulcerative colitis

Improve clinical remission rates and induce mucosal healing

Fibrosis: Scleroderma, IPF

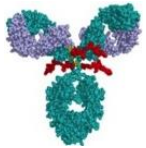
Achieve transformational efficacy by stopping fibrosis and reversing established extracellular matrix

Scientific goals:

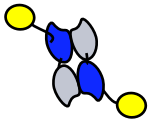
- Molecular understanding of disease pathology
- Identification of new pathways and targets from a convergence of molecular data and clinical response
- Patient stratification becoming a reality

Technological goals: Precise immunomodulation

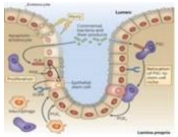
Specifically targeting immune dysfunction to deliver greater clinical efficacy and improved safety



Antibody-Drug Conjugates (ADCs)



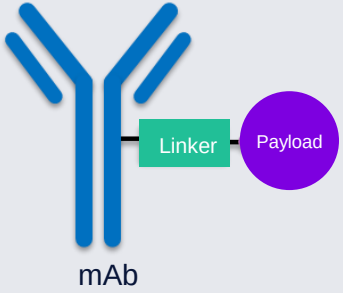
Targeted cytokines

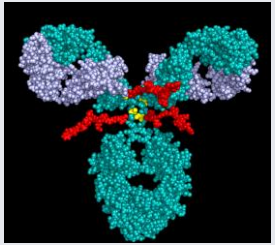


Local Delivery of Small Molecules

Targeted combinations

Utilization of the ADC technology for immune-mediated diseases required improvements in linker stability and payload potency

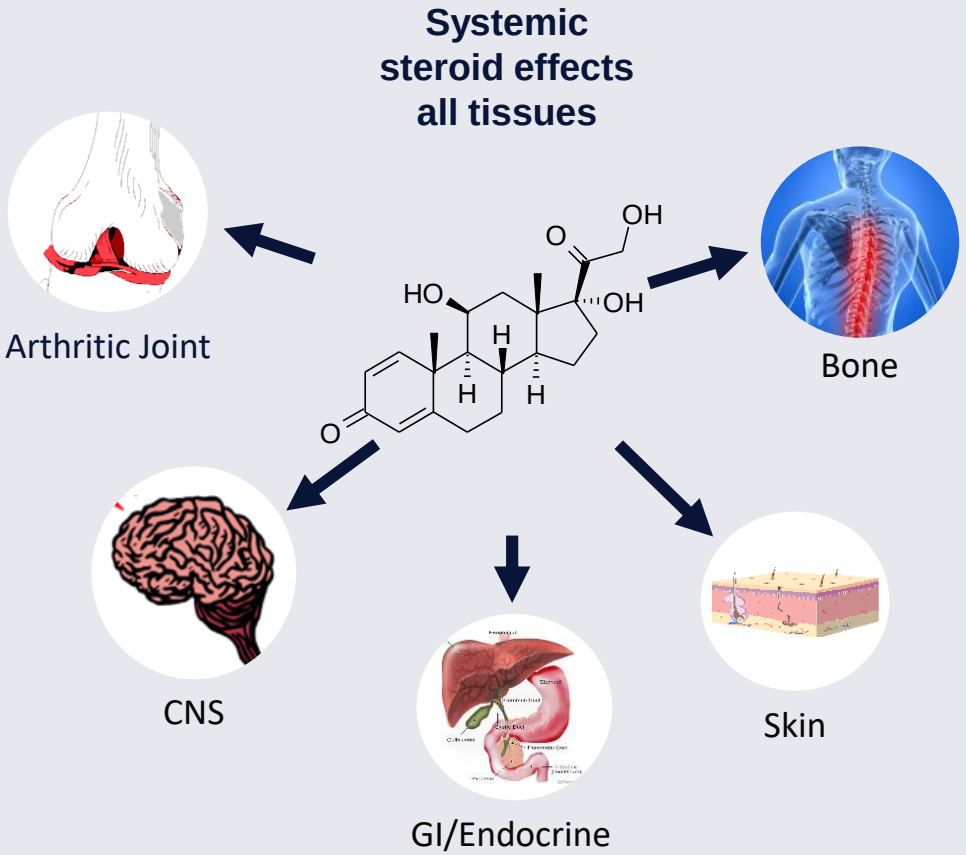




1	112	200
Monoclonal antibody	Linker combinations	Steroid payloads

Why combine anti-TNF and steroid into an ADC?

- Anti-TNF antibody and steroid therapies are very effective medicines and are used in many diseases including RA, IBD and psoriasis
- They are often used in combination but the use of steroids is limited to short duration or low doses due to severe side effects
- AbbVie discovered that anti-TNF mAB is internalized on activated immune cells through its binding to transmembrane TNF
- The anti-TNF ADC will direct the steroid payload directly to inflammatory cells



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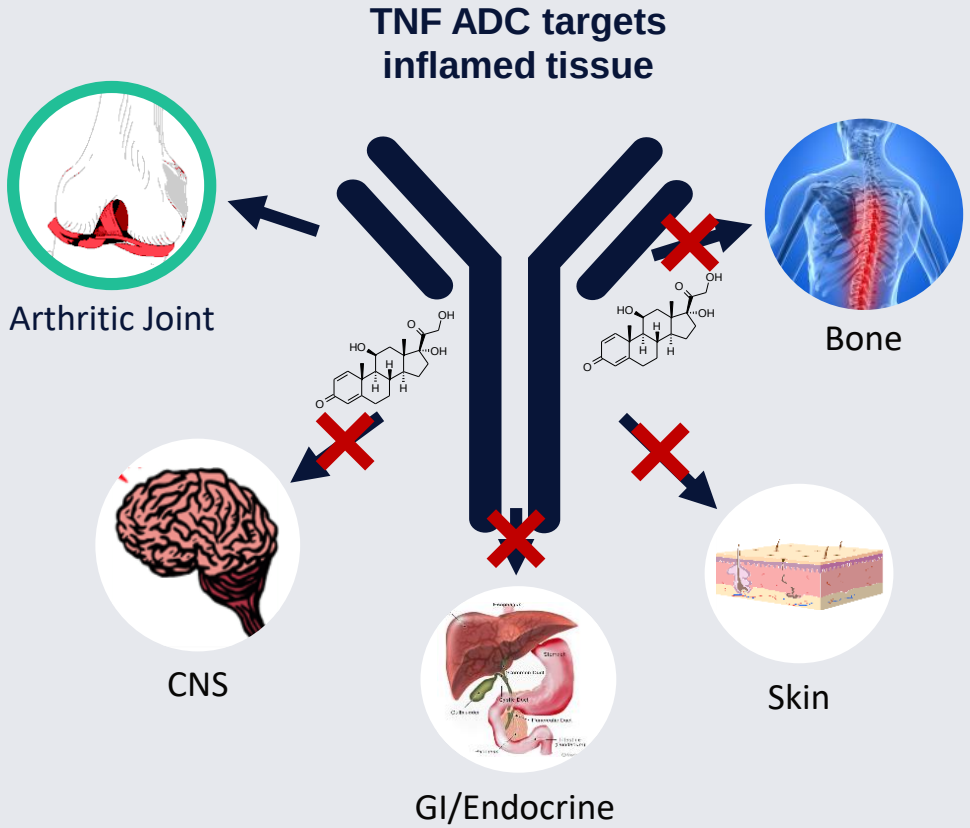
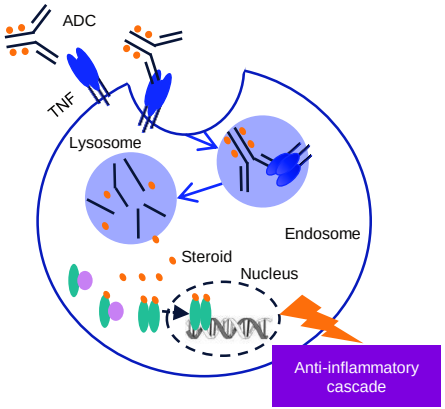


Anti-TNF-steroid ADC demonstrates targeted uptake, internalization and internal release of steroid in activated immune cells

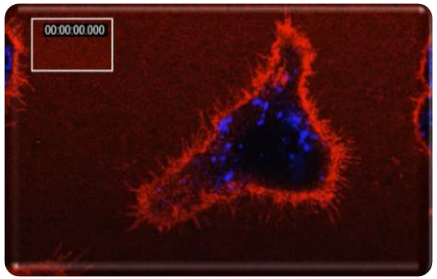
Hypothesis: Targeting activated immune cells with the anti-TNF-steroid ADC will demonstrate durable inhibition of inflammation with no steroid side effects

Targeted steroid release

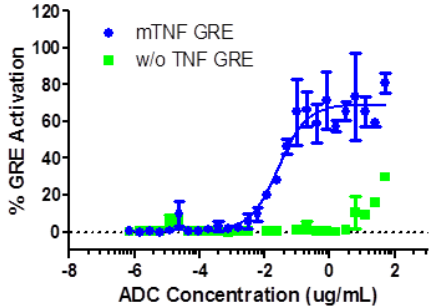


GRE, glucocorticoid responsive element; LPS, lipopolysaccharide; tmTNF, transmembrane TNF

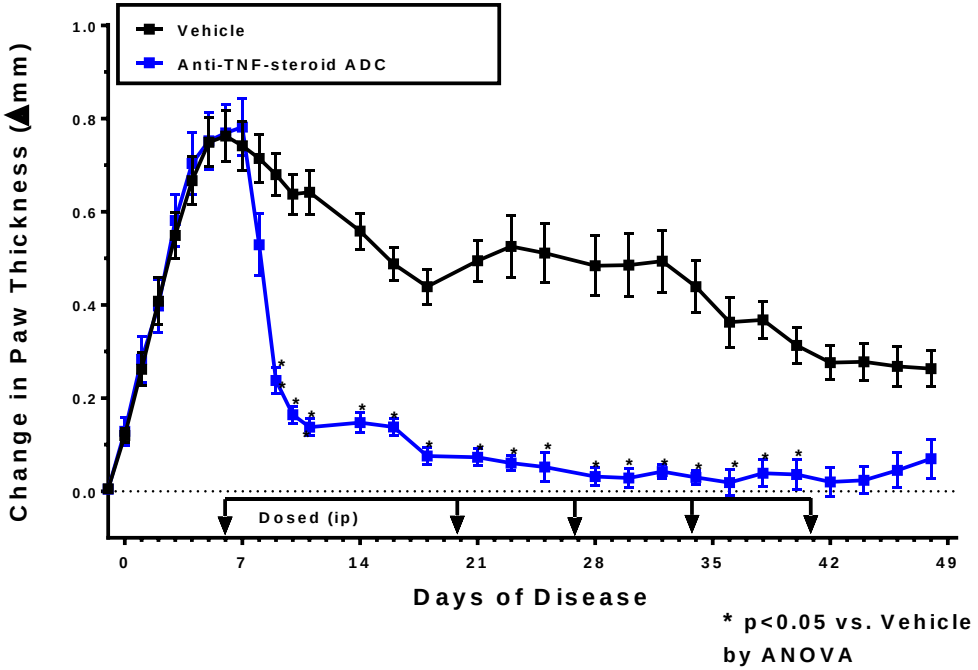
Double staining with anti-TNF and Lysotracker in LPS stimulated macrophages

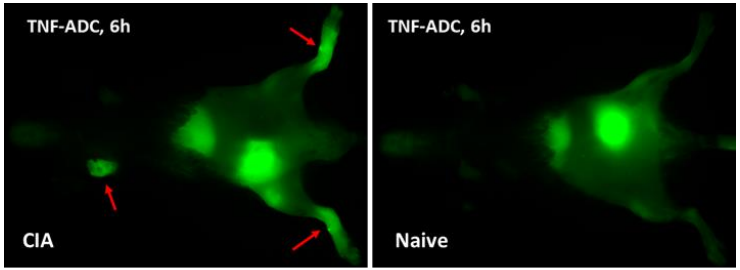


K562 GRE reporter assay

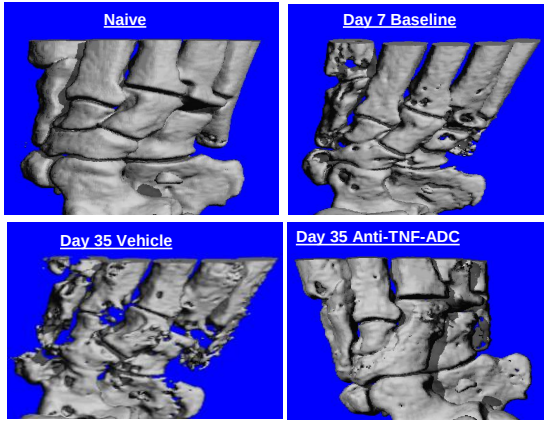


Repeat dosing of the TNF ADC reverses inflammation, maintains remission and restores bone to naïve levels in a mouse model of arthritis





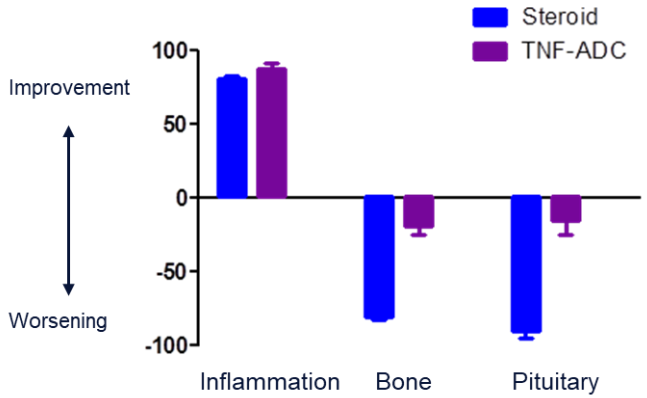
CIA vs. Naïve mice @ 6h post-dosing



Systemic glucocorticoid safety translated from preclinical species to humans

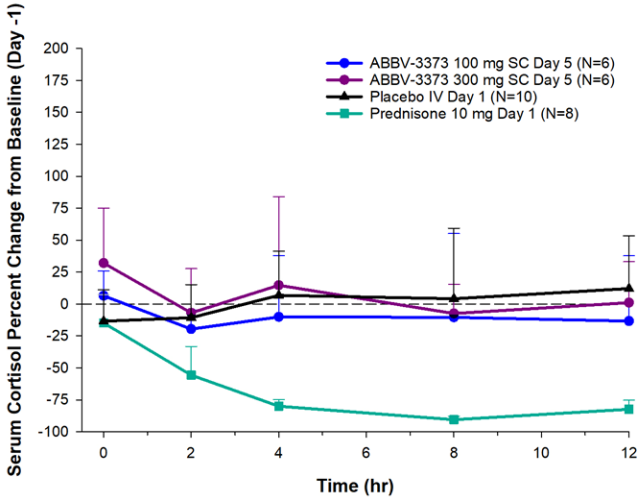
Preclinical

Anti-TNF ADC demonstrates comparable efficacy to high-dose steroid without side effects



Clinical

Systemic glucocorticoid safety: ABBV-3373 did not impact serum cortisol at 100 and 300 mg SC doses



AbbVie Data on File.

Mean+SD
Post-dose on **Day 1 or Day 5**
Time-matched % Change from Day -1 Baseline

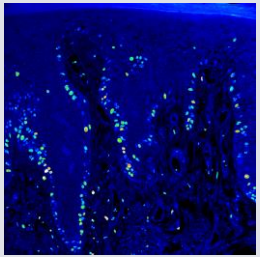
Advancing ABBV-3373 to clinical studies: Our goal is to achieve transformational efficacy in three disease areas, starting with RA

Rheumatology
RA, PsA & Others

Achieve durable remission and halt disease progression

Phase 2 readout in RA expected in 2020

Dermatology
Hidradenitis suppurativa

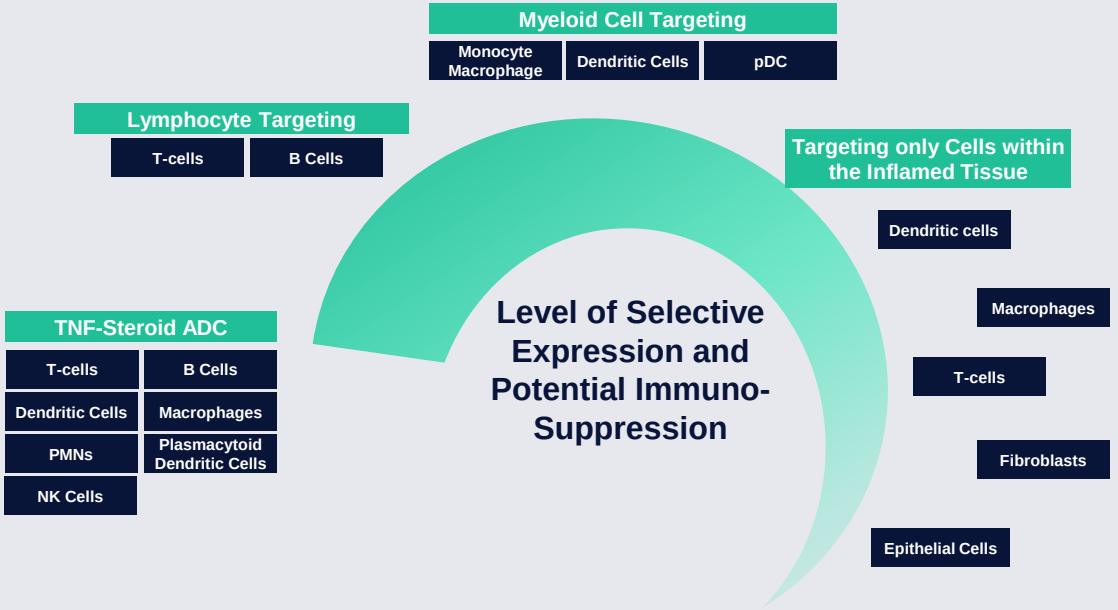


Achieve full skin clearance with durable response

Gastroenterology
Crohn's disease | Ulcerative colitis

Improve clinical remission rates and induce mucosal healing

Anchored by the success of the anti-TNF-steroid ADC, the next generation iADC platform strategy involves more selectively targeting pathogenic immune cells



ABBV-599 (combination of ABBV-105 and upadacitinib)

Designed to inhibit two distinct signaling pathways involved in the pathogenesis of immune-mediated inflammatory diseases

ABBV-105*

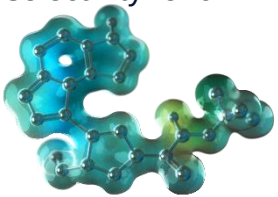
Inhibitor Bruton's tyrosine kinase (BTK)

Inhibits B-cell proliferation and Myeloid cell activation via FcR$_\gamma$

+

Upadacitinib

Janus kinase (JAK) inhibitor with greater selectivity for JAK1



Inhibits T-cell activation and multiple cytokine signalling molecules including IL6,& IFNγ

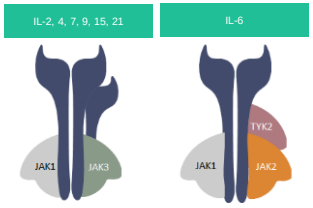
- Hypothesis: Inhibition of BTK and JAK signaling will result in superior efficacy for difficult-to-treat immune mediated diseases
- Currently in Phase 2 development for rheumatoid arthritis and lupus
- Entering Phase 2 in scleroderma

***ABBV-105 molecule not based on the actual molecular structure**

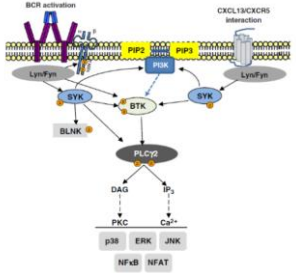
ABBV-599: JAK1/BTK in Phase 2 in RA

Hypothesis: Combining inhibitors of JAK1 and BTK will confer improved efficacy in autoimmune disease due to their independent and relevant mechanisms

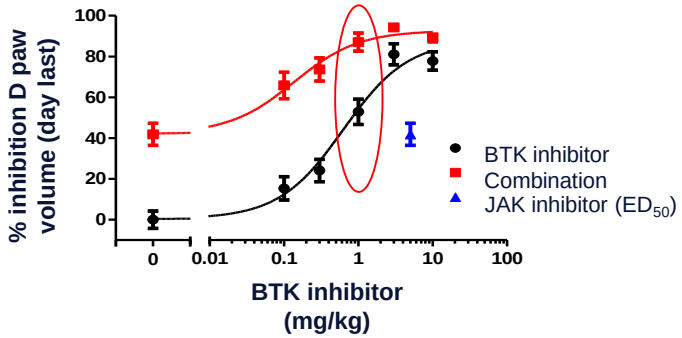
JAK1 inhibition blocks common γ-chain and IL-6 signaling



BTK inhibition impacts B-cell and myeloid cell populations



Combining JAK inhibition with BTK inhibition confers additive efficacy in rat CIA

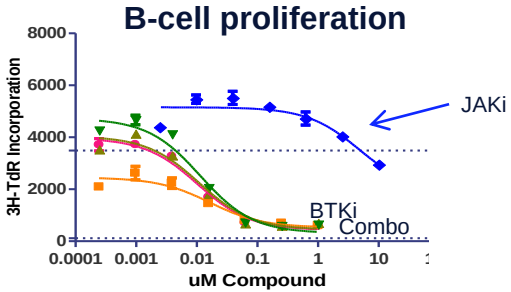


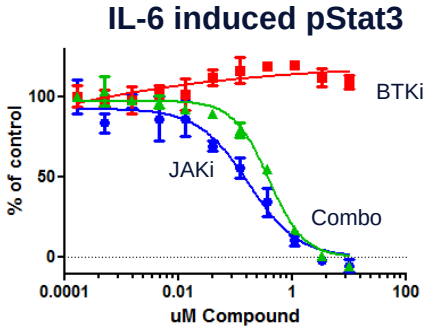
% inhibition of paw swelling

Combination	Mono	Combo
JAK + BTK	50	>80

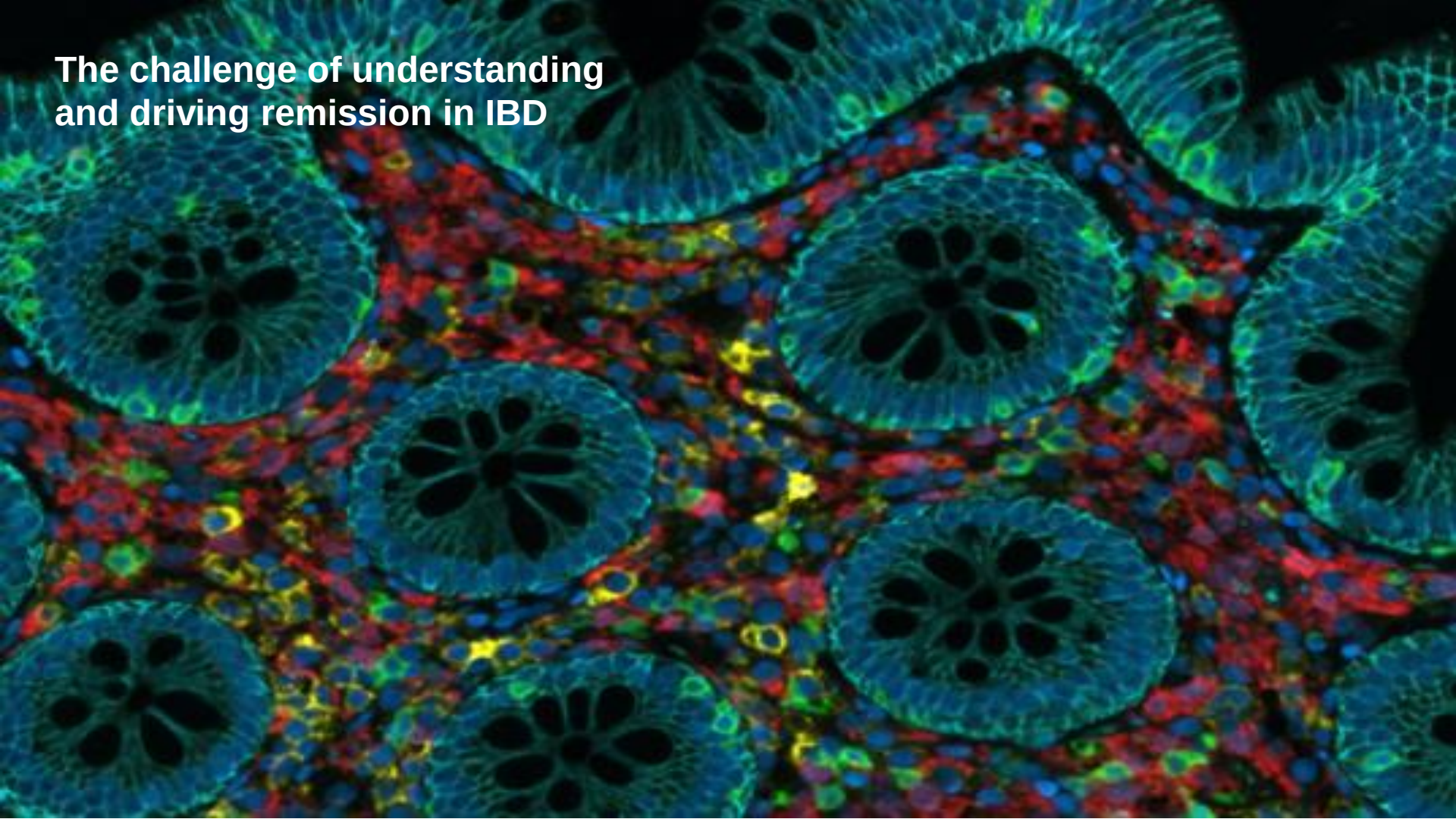
Phase 2 RA study will read out in 2020

JAK and BTK pathways do not overlap





The challenge of understanding and driving remission in IBD

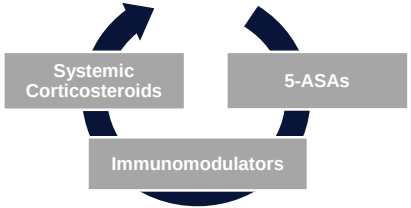


The best available IBD therapies leave significant room for improvement

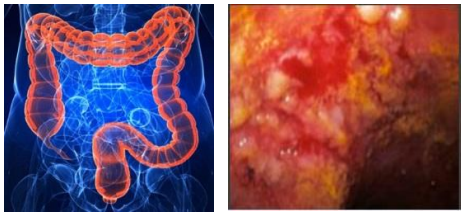
Failure to receive appropriate targeted treatment

Abdominal pain, frequent bowel movements and fatigue

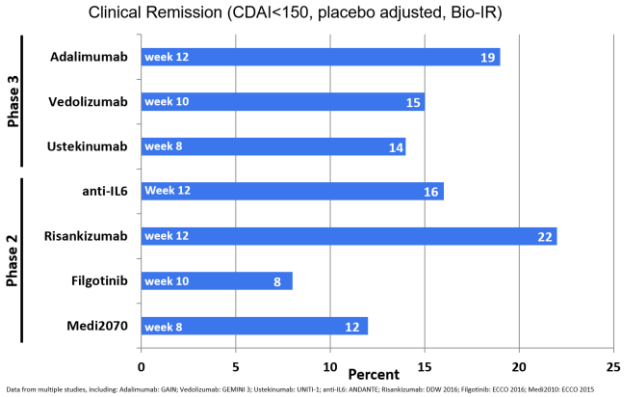
Cycling of conventional therapies



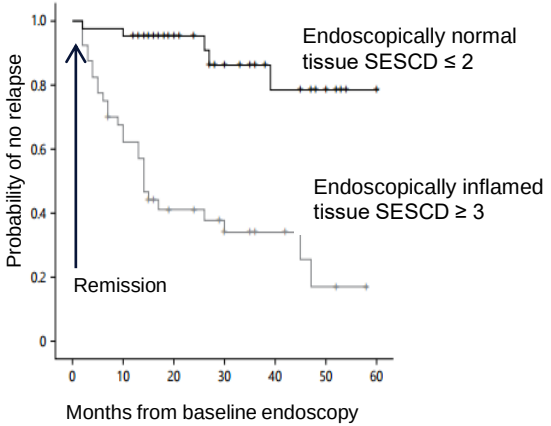
Damage Accumulates



Low levels of remission and endoscopic improvement

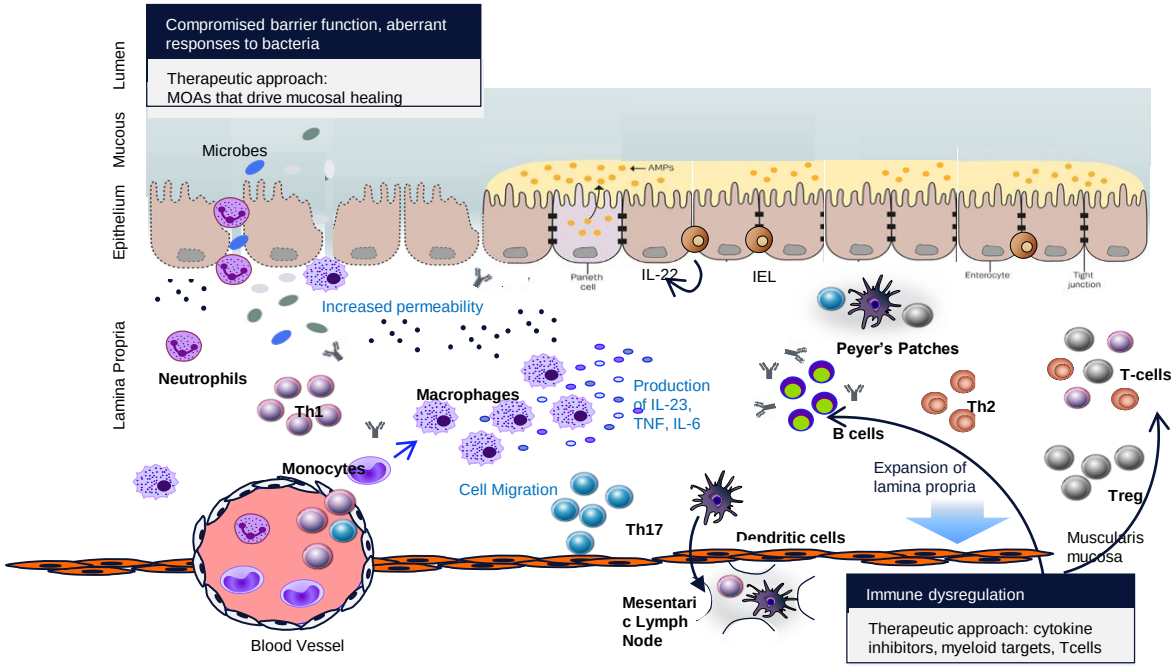


Improved outcomes demonstrated with Mucosal Healing



Naganuma, *Digestion* 93:55-71 (2016)

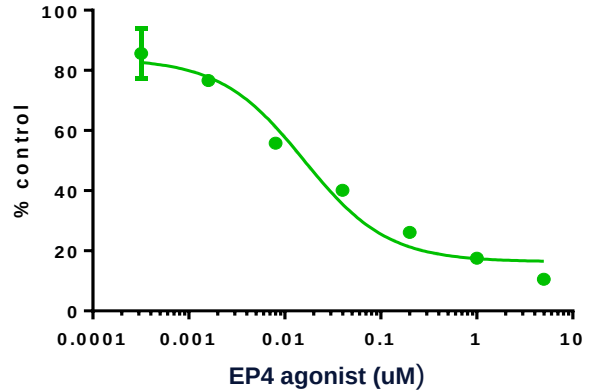
Our hypothesis: For transformational efficacy in IBD, both immune cell modulation and healing of the epithelial barrier are required



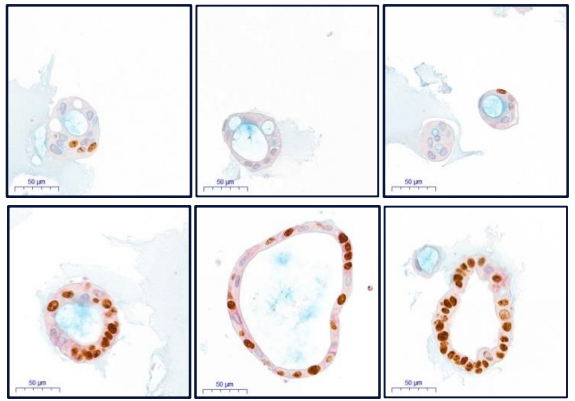
EP4 agonism will reduce inflammation and improve mucosal healing

- EP4 is a 7-transmembrane GPCR
  - One of four EP family members (EP1,2,3,4)
  - PGE2 is native agonist ligand
  - Highly expressed in colon

Human Whole Blood- LPS-induced TNF

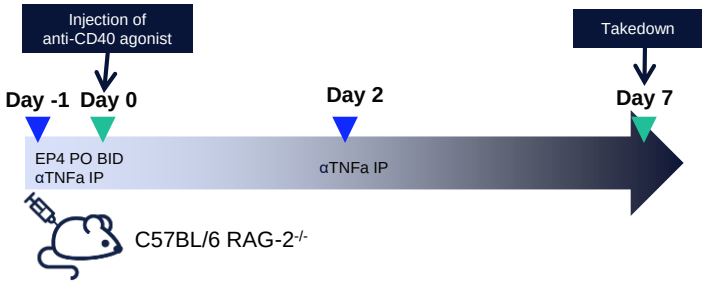


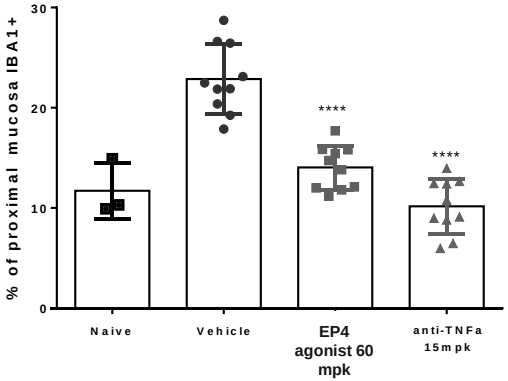
Human Organoids: Ki67 Histology



EP4 agonism reduces inflammation and protects the mucosa in murine models of colitis

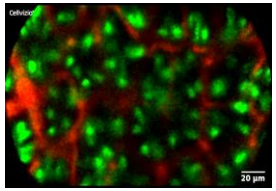
Anti-inflammatory



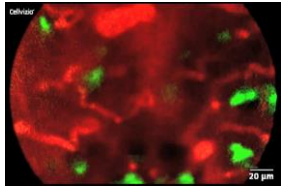


Mucosal Healing

Naive

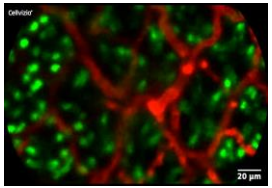


3% DSS Vehicle Control



- Moderate disease
- Significant vascular leakage, erosions, goblet cell loss
- Goblet cell morphology is altered

KAG-308 EP4 Agonist



- Minimal disease
- Vascular pattern intact, no leakage or erosions detected
- Goblet cells show normal distribution and morphology

Summary

- Immunology Discovery has invested deeply in understanding the molecular drivers of human immune-mediated diseases in the rheumatology, dermatology and gastroenterology areas
- Leveraging that knowledge, we have built a portfolio of assets that are focused upon delivering transformational efficacy
- Targeting activated immune cells with the anti-TNF–steroid ADC will demonstrate durable inhibition of inflammation with no steroid side effects
- Inhibition of two independent inflammatory pathways, JAK and BTK, will deliver increased levels of durable remission
- We believe that healing the mucosal barrier of the inflamed GI tract is an essential component of achieving higher levels of clinical remission in IBD
- EP4 agonism is one approach that demonstrates both anti-inflammatory and mucosal healing responses
- We’re exploring novel approaches that may take us into areas, such as lupus and scleroderma

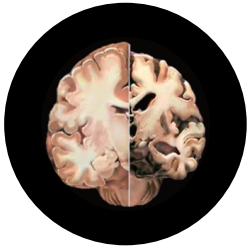
Neuroscience

Tom Hudson, M.D., Senior Vice President, R&D
and Chief Scientific Officer

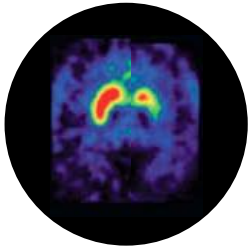
Why AbbVie is investing in neurodegenerative diseases

High unmet need

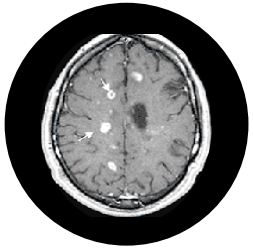
Alzheimer's disease



Parkinson's disease

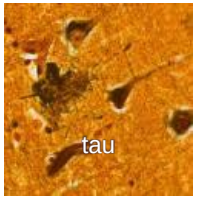


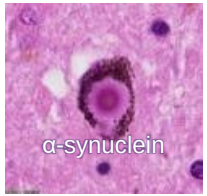
Multiple sclerosis



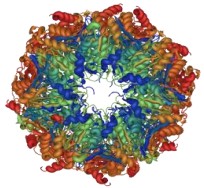
Increasing understanding in underlying biology

Pathological proteins

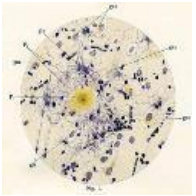




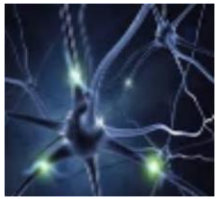
Proteostasis



Neuroinflammation



Neural protection



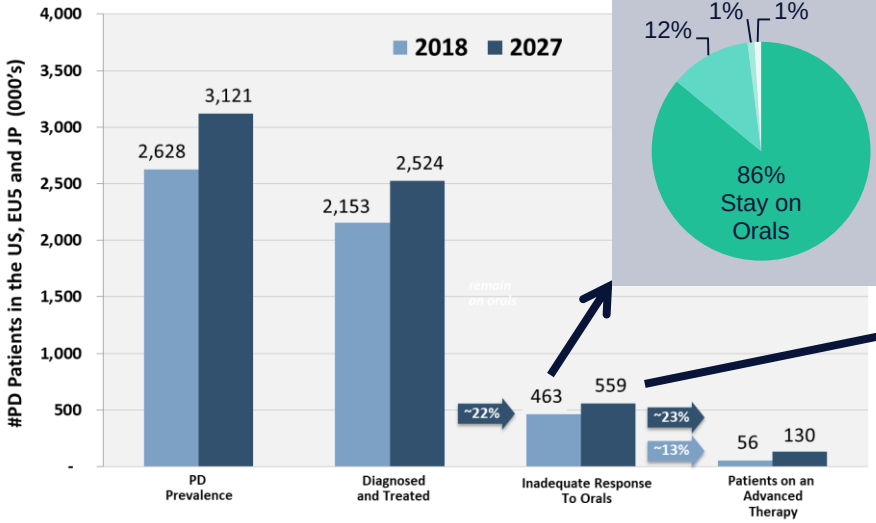
Our neuroscience pipeline is targeted to areas of continued unmet need

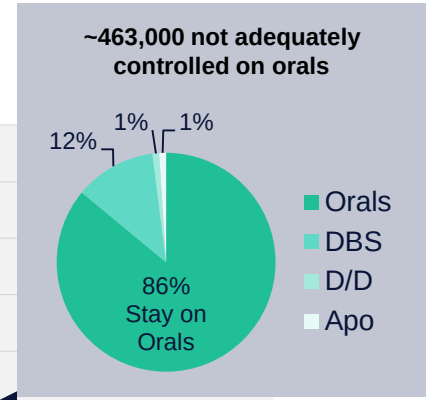
	Alzheimer's disease	Parkinson's disease	MS and others
Near-term opportunities		**Symptomatic Therapies** • **ABBV-951** (L-dopa and carbidopa prodrugs)	
Longer-term opportunities	**Disease Modifying Therapies** • **ABBV-8E12** (anti-tau) • **AL-002*** (TREM2) • **AL-003*** (CD33) • **Discovery programs**	**Disease Modifying Therapies** • **ABBV-0805** (anti-alpha synuclein) • **Discovery Programs**	**Neurorestorative Therapies** • **ABT-555** (anti-RGMA)

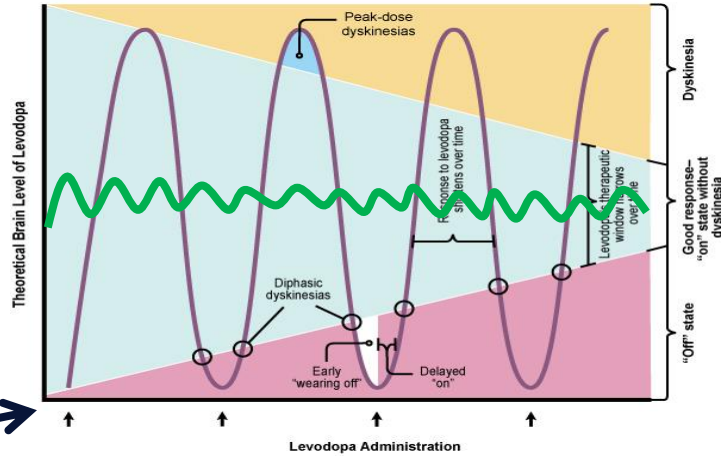
* upon agreement/option exercise

There is a need for an effective, non-surgical treatment option for advanced Parkinson's disease patients

Majority of advanced PD patients are inadequately controlled on oral therapy





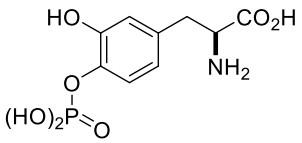


- With disease progression, gastric motility is impaired, making levodopa absorption from pills unpredictable
- With oral therapies, levodopa levels vary prominently: trough concentration leads to OFF time and peak concentrations lead to dyskinesia
- Providing a continuous, consistent and predictable amount of levodopa is key to controlling symptoms

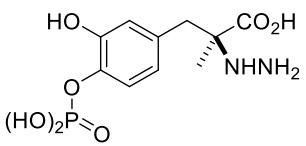
Our aspiration was to develop a way to provide continuous subcutaneous infusion of levodopa and carbidopa

AbbVie chemistry delivered innovative syntheses of both foslevodopa and foscarbidopa

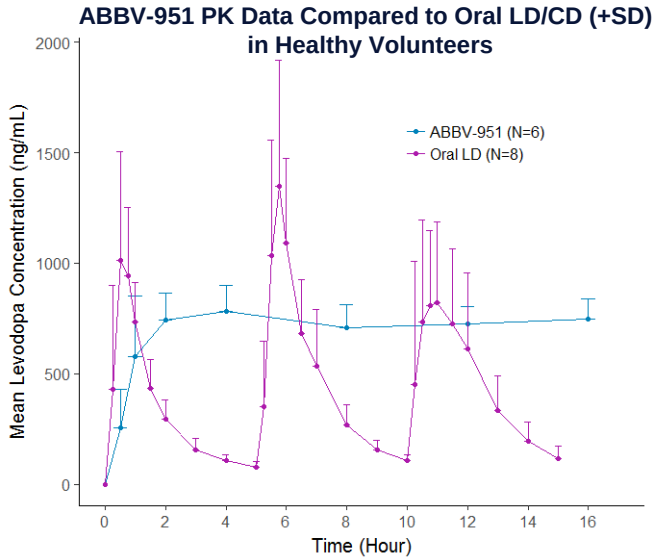
Foslevodopa



Foscarbidopa



Subcutaneous administration

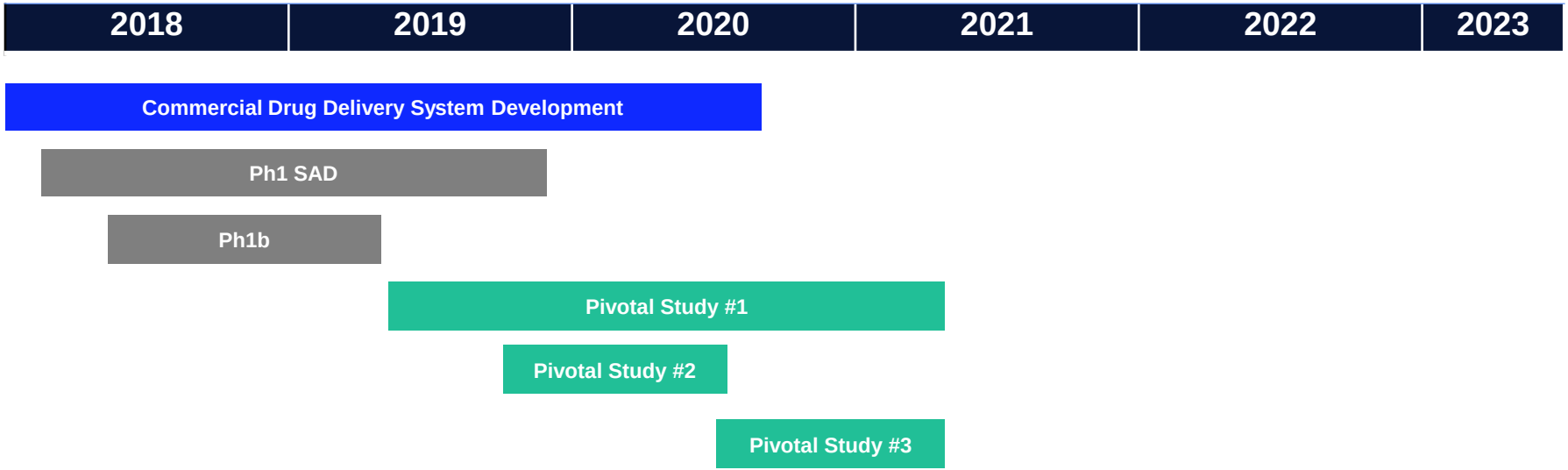


The synthesis of foslevodopa and foscarbidopa resulted in:

- A water-soluble prodrug that converts to levodopa in the subcutaneous space
- High prodrug solubility and concentration allowing lower dose volumes enabling subcutaneous delivery via a small pump
- The ability to individualize the dose
- Good tolerability in advanced PD patients

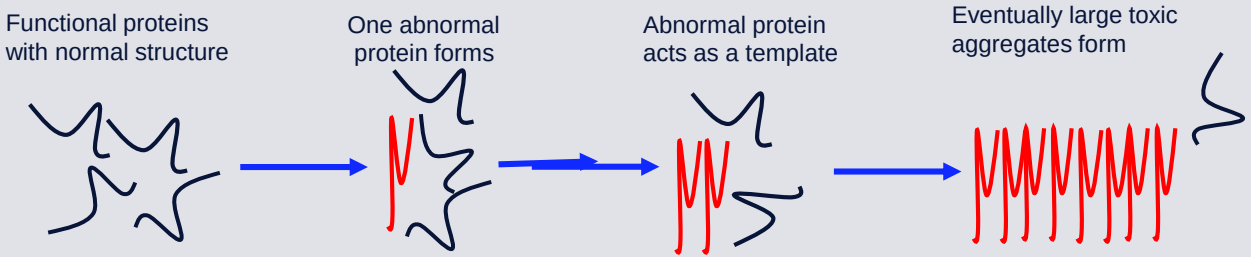
ABBV-951 demonstrated low plasma variability, potentially able to maintain levodopa exposure within a narrow therapeutic window. This is not possible with oral immediate release levodopa

ABBV-951 development program timeline: Program progressed directly from Phase 1 to Phase 3

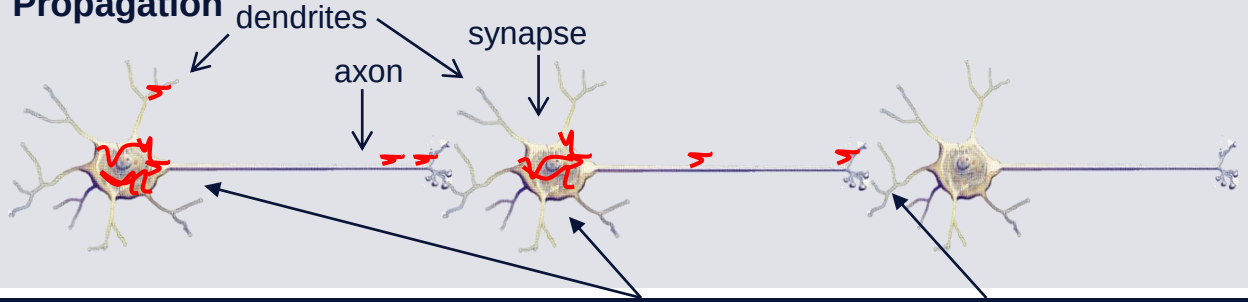


In many neurodegenerative diseases, protein aggregates form and spread through the brain from neuron to neuron, causing neuronal loss

Intra-cellular protein misfolding and aggregation



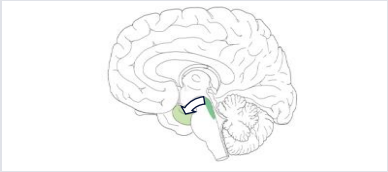
Propagation



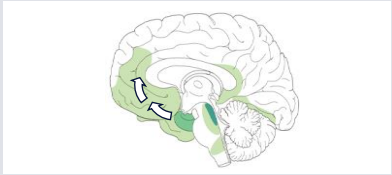
Therapeutic strategies: Prevent/remove aggregates, prevent propagation/uptake

Propagation correlates with neuronal loss and functional decline

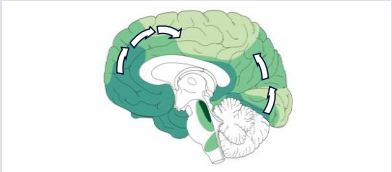
Stages I - II



Stages III - IV

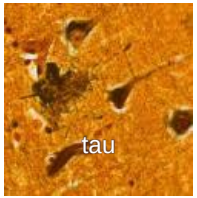


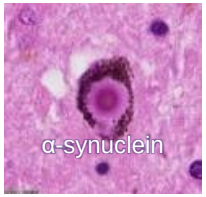
Stages V - VI



AbbVie's neuroscience pipeline is focused on processes that are strongly supported by genetic and mechanistic discoveries of the last decade

Pathological proteins

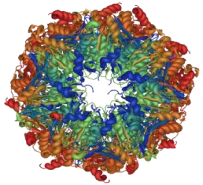




Tau:
- We are exploring multiple approaches for tau
- Our most advanced is ABBV-8E12, which is in Phase 2
- Other approaches include higher affinity Ab's that are selective for pathogenic/aggregated tau, AAV-delivery, degradation

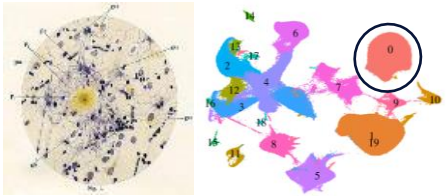
Anti-α-synuclein:
- ABBV-0805 antibody, binds fibrillar α-synuclein with nM affinity and high selectivity vs monomeric protein, currently in Phase 1 for PD
- Other approaches currently focused on selectivity to pathogenic α-syn

Proteostasis



Preclinical
- Failure of proteostasis leads to the formation of toxic protein aggregates
- Biology has provided a diversity of targets that have high preclinical in vivo validation
- Most advanced approach targets intracellular aggregates and facilitates rapid clearance

Neuroinflammation



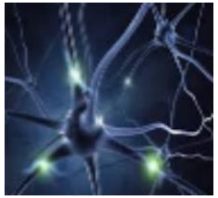
AL002: agonist mAb targeting TREM
- In Phase 1 for AD

AL003: antagonist mAb targeting CD33.
- In Phase 1 for AD

- ~1/3 GWAS hits associated with late onset Alzheimer's disease are expressed in microglia

Preclinical
- Single cell transcriptome analyses revealed novel pathology-associated microglia target genes in human Alzheimer's disease

Neural protection



Elezanumab: anti-RGMa mAb
- In Phase 2 for MS, SCI (2Q20) and stroke (Q2 2020)

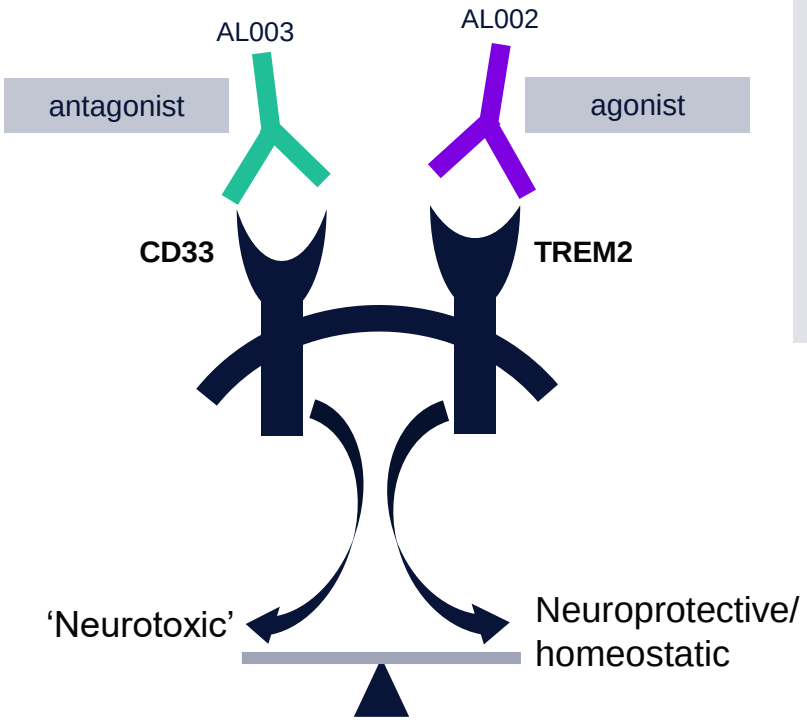
- RGMa blockade with monoclonal antibody elezanumab enhances repair and promotes functional recovery in numerous preclinical injury models

Alector collaboration testing antibodies to compelling neuroinflammation targets

CD33

- Receptor on the surface of microglia
- Human genetic variants associated with AD
- Activation converts microglia into a more neurotoxic form

AL002 and AL003 currently in Phase 1b trials for AD



TREM2

- Receptor on the surface of microglia
- Human genetic variants associated with AD
- Activation converts microglia into a more neuroprotective form

Cystic fibrosis

Tom Hudson, M.D., Senior Vice President, R&D
and Chief Scientific Officer

Cystic fibrosis: Rationale and status

- While recognizing that Vertex is the market leader, we believe that it is feasible to bring forward assets that will give meaningful benefits to CF patients

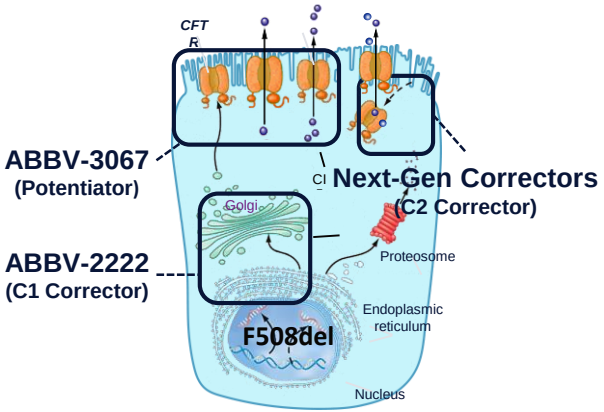
Vertex's Trikafta
- 20% of patients have an FEV1 improvement of 5% or less
- safety / tolerability liabilities: elevated liver enzymes, cataracts, DDI, GI

- Our data support the notion that the efficacy ceiling has not been met and safety/tolerability/dosing profiles can be improved
- We have preclinical data with AbbVie compounds that could achieve a transformational response (> 18% FEV1)

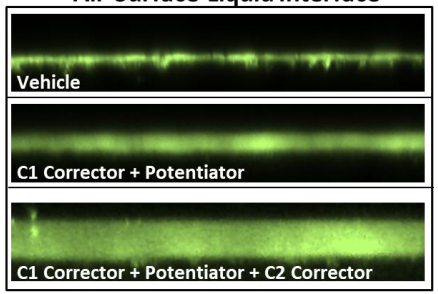
AbbVie Triplet
- C1 Corrector ABBV-2222: Best-in-class
- Two potentiators ABBV-3067 and ABBV-191
- C2 Corrector: ABBV-119 IND submission Q2 2020
- ABBV-2222+ ABBV-3067 doublet in Phase 2

- AbbVie is the only competitor with quality assets for all MOAs

AbbVie molecules



Air-Surface-Liquid Interface



AbbVie triplets show full restoration of fluid homeostasis

Calico

Tom Hudson, M.D., Senior Vice President, R&D
and Chief Scientific Officer

Calico and the AbbVie-Calico collaboration

- Founded in September 2013 by Google and Art Levinson (CEO)
- Launched unique, 10-year collaboration with AbbVie in September 2014
- In 2018, extended by 3 years to 2027, with significant funding enabling long-term view
- Mission: Increase understanding of the biology of aging and harness advanced technologies to bring therapies to market in aging-related diseases, including **neurodegeneration** and **oncology**
- Extensive external network of scientists and >30 sponsored research agreements with 22 leading Institutions that provide novel targets, additional resources, or capabilities for some collaboration programs

BROAD INSTITUTE · Buck · Penn University of Pennsylvania · qb3 ucb·ucsc·ucsf · The Jackson Laboratory · C4 Therapeutics · UCSF University of California San Francisco · Google

- AbbVie and Calico scientists partner throughout the drug discovery process
- AbbVie option triggers with Phase 2a data/clinical proof of concept

State of the collaboration

13 YEARS

Collaboration RUNWAY

400+ SCIENTISTS CLINICIANS

At ABBVIE and CALICO

44+ TARGETS

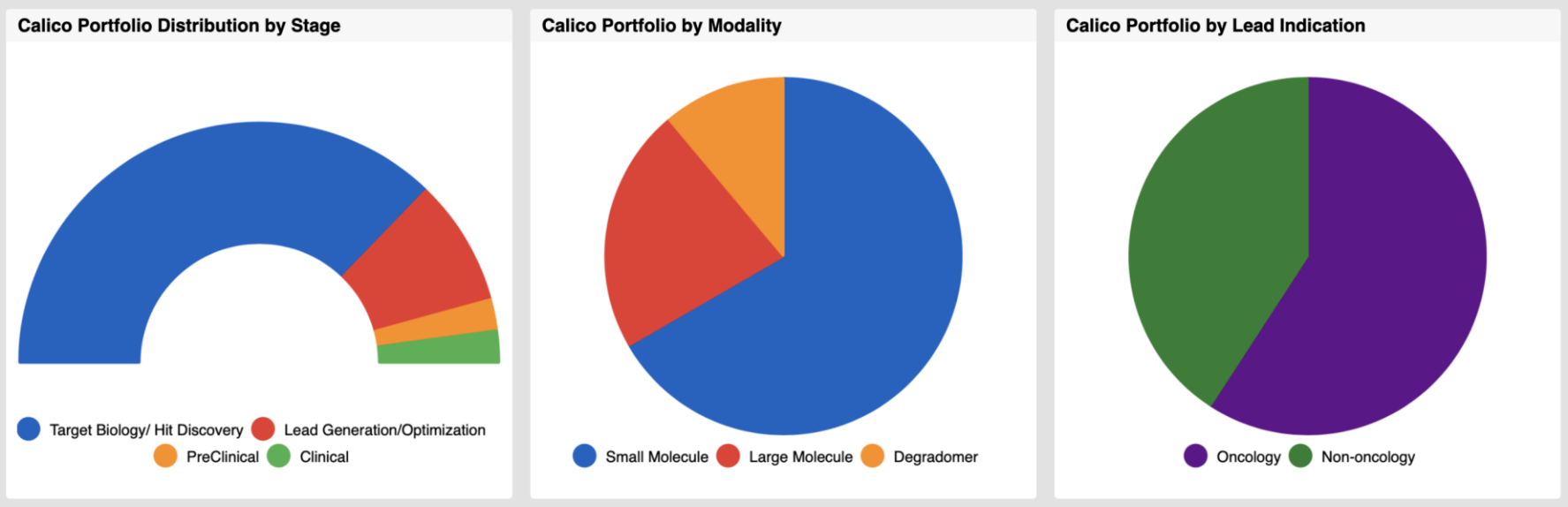
In the Joint PORTFOLIO

2 PROJECTS

In CLINICAL TRIALS by 2020

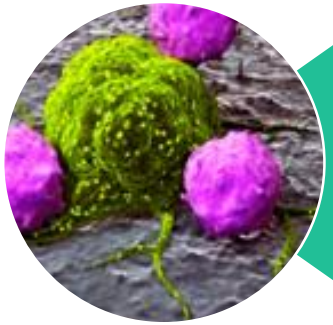
Collaboration metrics

The portfolio is split between oncology and neurodegeneration



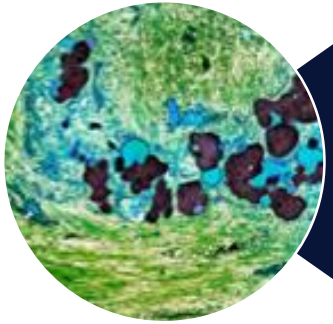
Current 26 Jan 2020

Portfolio snapshot (January 2020)



Oncology/I-O

- Target Biology/Hit Discovery: n=26
- Lead Generation/Optimization: n=1
- Preclinical: N=2
- Clinical: 1 program to Phase 1 FIH (2020)



Neurodegeneration

- Target Biology/Hit Discovery: n=13
- Lead Generation/Optimization: n=5
- Preclinical: N=1
- Clinical: 1 program to Phase 1 FIH (2020)

AbbVie’s discovery portfolio and pipeline snapshot

Mike Severino, M.D., Vice Chairman and President

AbbVie's discovery portfolio and clinical pipeline

As of February 7, 2020

Therapeutic Area	Early Target Portfolio			Late Discovery Portfolio			Clinical Development		
	Exploratory	Hit Generation	Lead Generation	Lead Optimization	Candidate Nomination & Selection	Pre-Clinical	Phase 1	Phase 2	Phase 3
Immunology	33	13	12	9	5	3	2	6	11
Oncology	45	26	20	10	10	7	18	3	13
Neuroscience	5	18	5	4			3	2	1
Other	1			2		4	1	2	1
Calico	8	6	2	5	2	2			


abbvie