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Tomorrow's Innovation: Changing R&D Model in Life Sciences

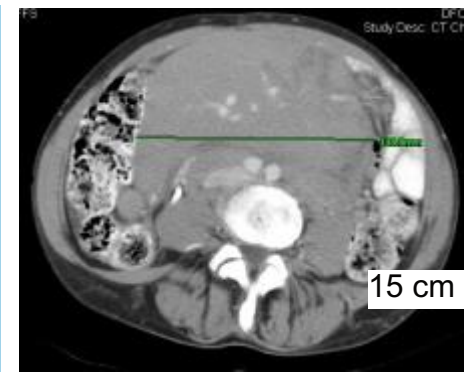
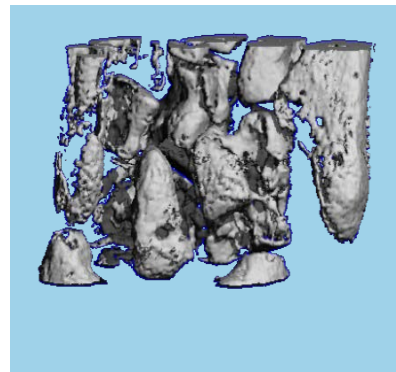
Jim Sullivan, Ph.D.

Vice President, Discovery



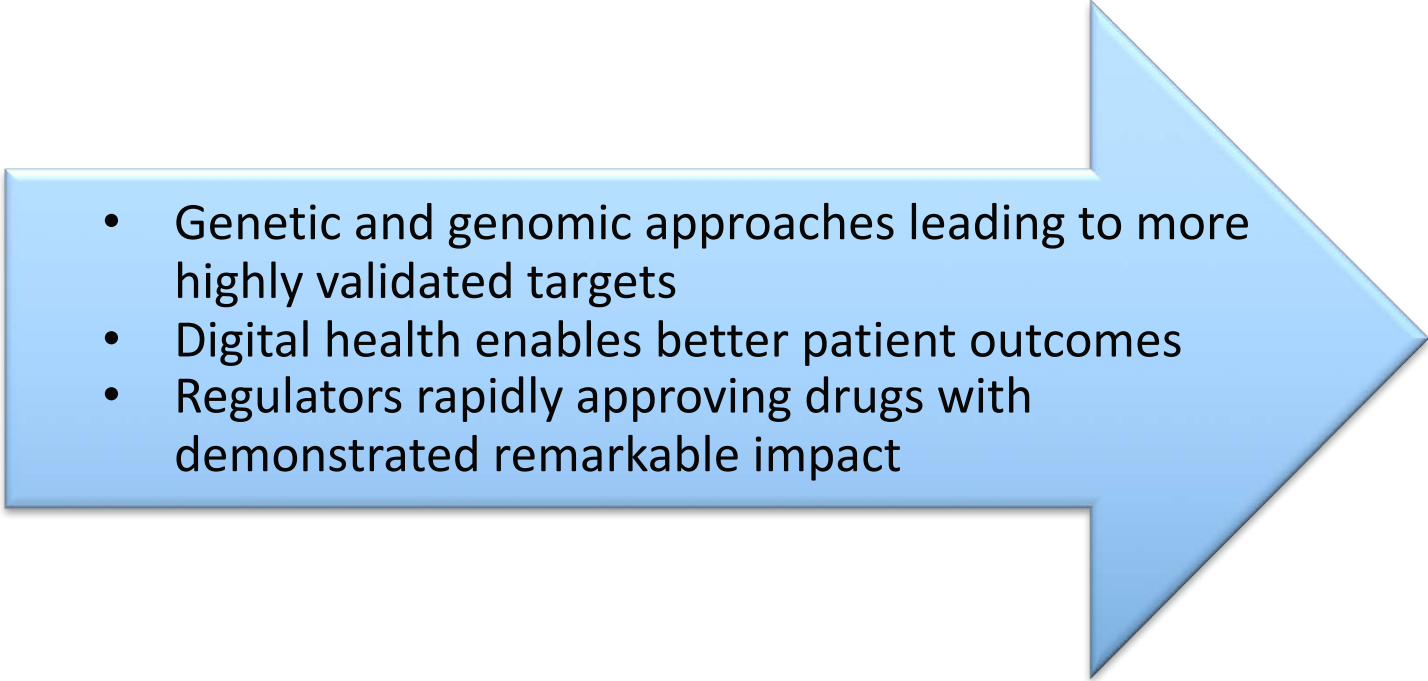
AbbVie's Discovery Mission: Focused on Remarkable Impact

Invent and deliver drugs that will have a *remarkable impact* on patients and *create significant value* for payers and physicians



Rapidly Changing Healthcare Environment: “The Patient Will See You Now”

Opportunities

- 
- Genetic and genomic approaches leading to more highly validated targets
 - Digital health enables better patient outcomes
 - Regulators rapidly approving drugs with demonstrated remarkable impact

Rapidly Changing Healthcare Environment: “The Patient Will See You Now”

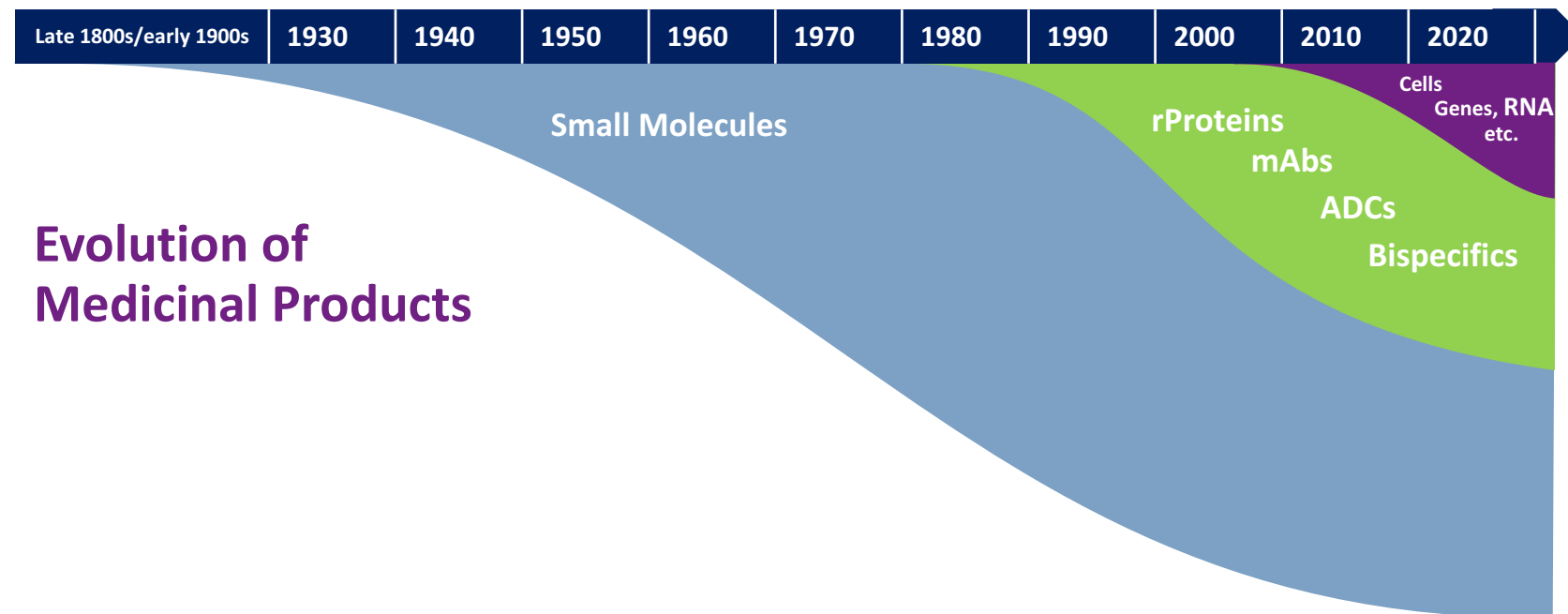
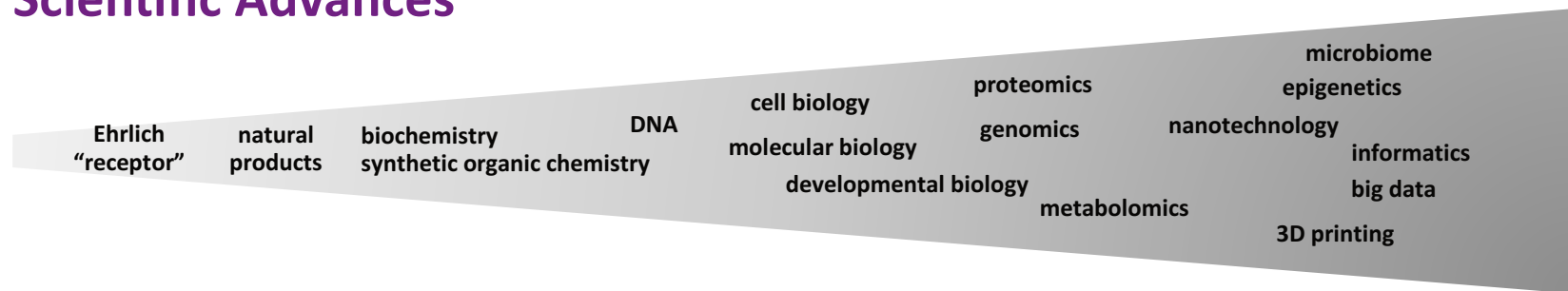
Challenges

- 
- payers demand more value for the same or less money
 - R&D costs increasing

Emerging Trends

A New Wave of Therapeutic Approaches is Emerging

Scientific Advances




Our Research Strategy

- Invest in and deliver science with transformational potential
- Build deep understanding of disease pathophysiology and pathway biology
- Translate understanding of disease biology into compelling clinical PoCs
- Augment our internal efforts with external innovation



Science with Transformational Potential

AbbVie has Pioneered the Field of BCL-2 Inhibition



NATURE · VOL 381 · 23 MAY 1996

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

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

nature
medicine

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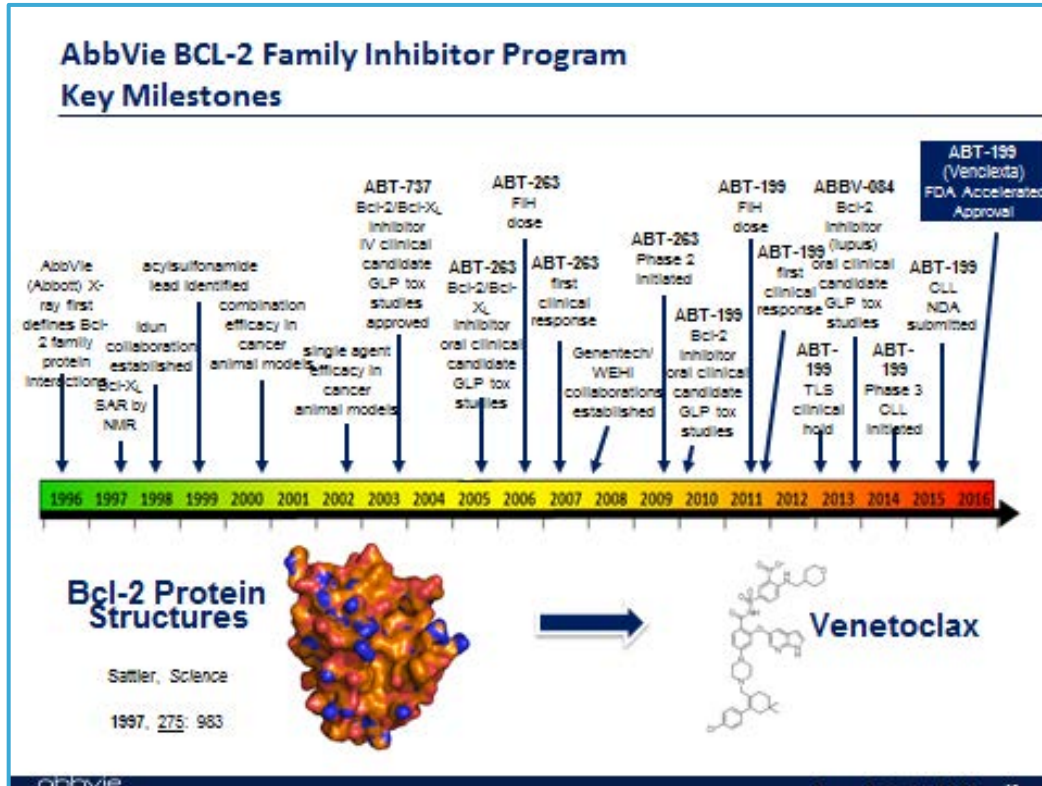
ABT-199, a potent and selective BCL-2 inhibitor, achieves antitumor activity while sparing platelets

Andrew J Souers¹, Joel D Levenson¹, Erwin R Boghaert¹, Scott L Ackler¹, Nathaniel D Catron¹, Jun Chen¹, Brian D Dayton¹, Hong Ding¹, Sari H Enschede¹, Wayne J Fairbrother², David C S Huang^{3,4}, Sarah G Hymowitz², Sha Jin¹, Seong Lin Khaw^{3,4}, Peter J Kovar¹, Lloyd T Lam¹, Jackie Lee², Heather L Maecker², Kennan C Marsh¹, Kylie D Mason³⁻⁵, Michael J Mitten¹, Paul M Nimmer¹, Anatol Oleksijew¹, Chang H Park¹, Cheol-Min Park^{3,7}, Darren C Phillips¹, Andrew W Roberts³⁻⁵, Deepak Sampath², John F Seymour^{4,6}, Morey L Smith¹, Gerard M Sullivan¹, Stephen K Tahir¹, Chris Tse¹, Michael D Wendt¹, Yu Xiao¹, John C Xue¹, Haichao Zhang¹, Rod A Humerickhouse¹, Saul H Rosenberg¹ & Steven W Elmore¹

Rationale

- Evades apoptosis (programmed cell death) – allowing cancer cells to develop
- Targets BCL-2 in order to help restore the process of apoptosis. Production of BCL-2 proteins is a key mechanism for preventing the apoptotic process from occurring

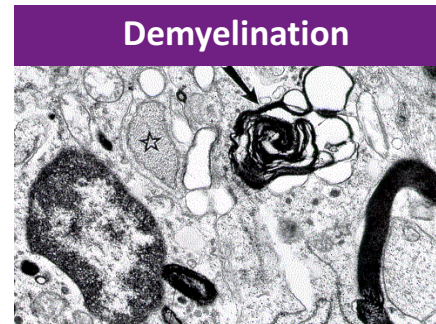
Transformational Science: Bcl-2 Inhibitors for the Treatment of Hematologic Cancers



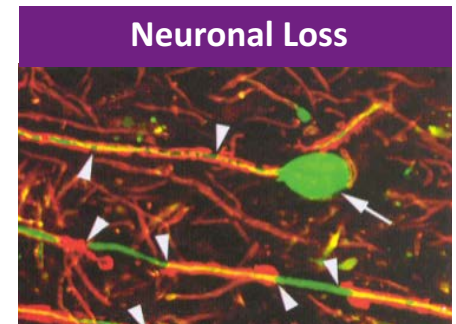
- Twenty year discovery and development journey
- Venetoclax binds selectively to BCL-2 proteins initiating a cascade of events leading to rapid cell death
- First drug to target the ability of cancer cells to evade apoptosis
- First drug targeting protein: protein interactions
- Multiple breakthrough therapy designations
- Approved in Europe and USA in 2016

Exploring New Areas with Transformational Potential Including...

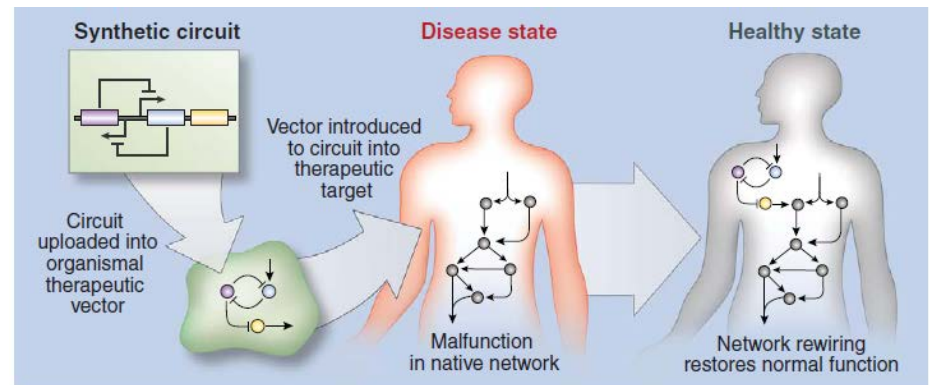
- T-cell receptors for oncology
- RGM biology for MS & spinal cord injury
- Biology of aging-Calico
- Leveraging bacteria as an expression system to deliver anti-inflammatory molecules to the GI tract
- Gene therapy



Demyelination



Neuronal Loss



That Will Allow Us to Deliver Remarkable Impact

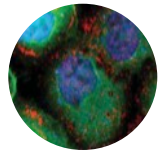
Immunology

- RA: Sustained remission
- Crohn's Disease: Improve remission rates and delay surgery
- Psoriasis: Greater efficacy (PASI scores) with oral molecules
- Build leadership in new areas



Oncology

- Deliver significant increases in overall survival in hematologic cancers and solid tumors



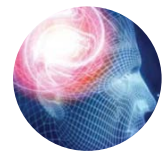
HCV and Liver Disease

- Develop pangenotypic next-generation HCV therapy with short-course therapy option
- Slow/reverse progression of fibrotic liver disease resulting from NASH



Neuroscience

- Alzheimer's Disease: Slow progression of disease
- Multiple Sclerosis: Reduce disability by targeting underlying neurodegeneration



Cystic Fibrosis

- Cystic Fibrosis: Significantly improve lung function in patients with F508del (~80% of patients)



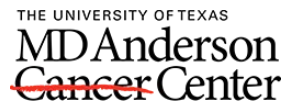
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EXTERNAL
COLLABORATIONS
AUGMENT OUR
INTERNAL RESEARCH



Multiple Models of Collaboration

Examples from the Last 18 Months



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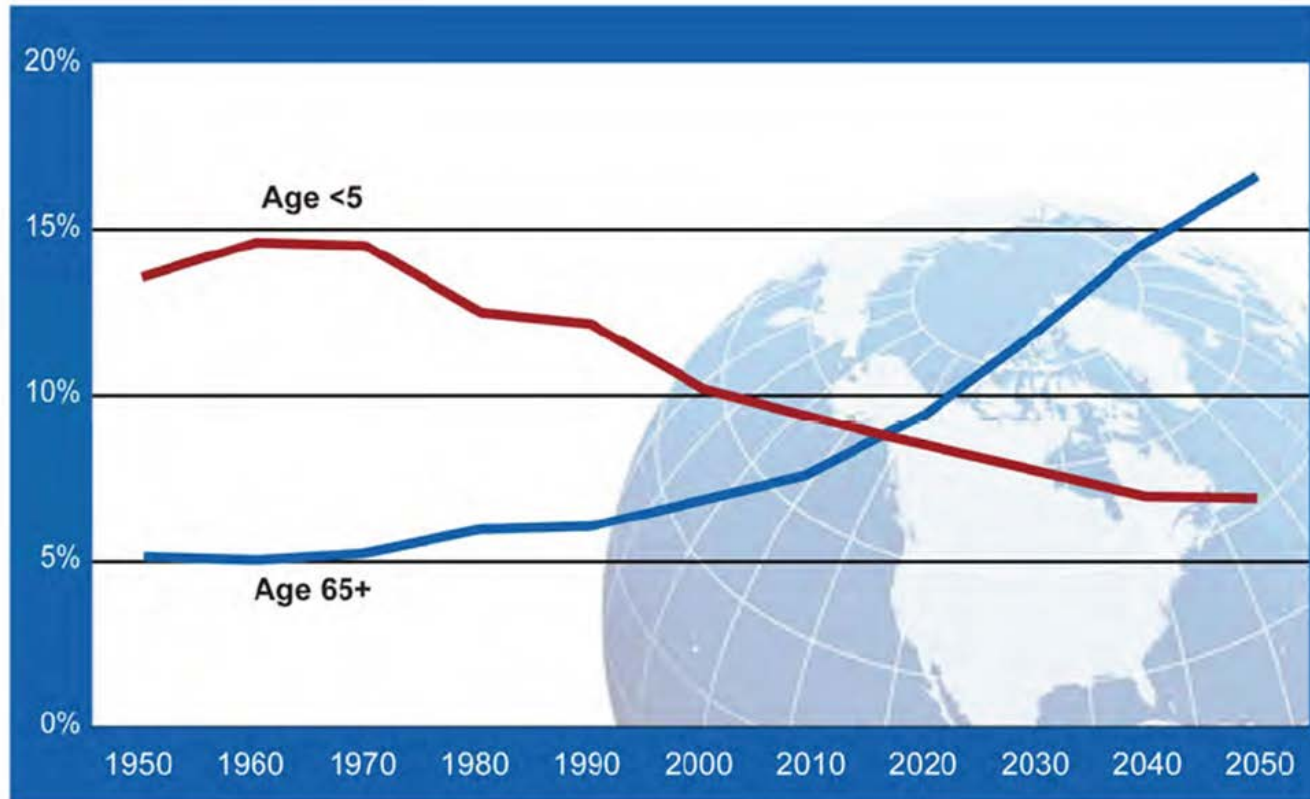
EXTERNAL
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Calico Collaboration



World Population Rapidly Aging

Children and Elderly as a Percentage of Global Population: 1950-2050



Source: United Nations. *World Population Prospects: The 2010 Revision*.
Available at: <http://esa.un.org/unpd/wpp>.

Impact on Society

- Will population aging be accompanied by a longer period of good health, or greater illness, disability and dependency?
- Are financial and health institutions prepared for the 21st century?



Dependency Ratios



Department for Work and Pensions

Tackling AGING



Photograph:
Dimitri Otis/Getty Images

Jeanne Louise Calment: February 21, 1875 - August 4, 1997

French Supercentenarian who had the longest confirmed human lifespan:
122 years, 164 days

- At age 85 (1960), she took up fencing
- Rode a bicycle until age 100

And yet....

- Smoked from age 21
- Diet rich in olive oil and chocolate (2.2.lb/week)



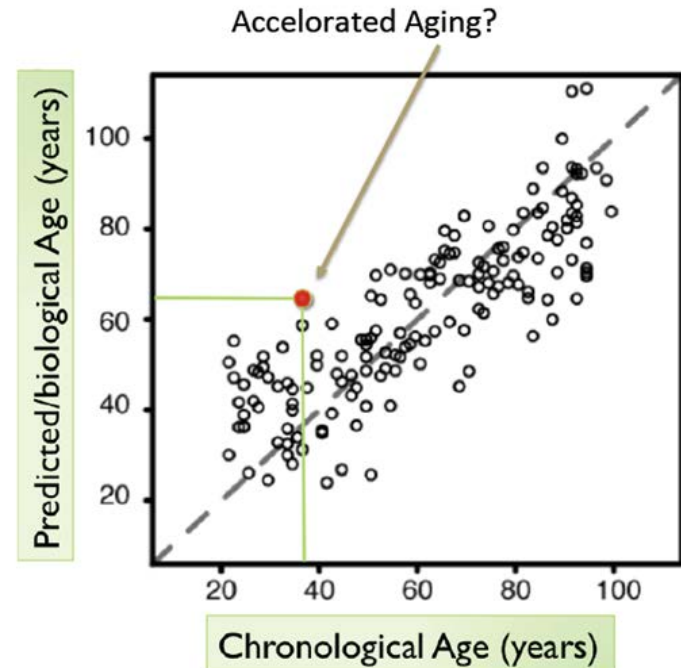
Humans Don't Age at the Same Rate

- Rate of biological aging is controlled by conserved genetic and biochemical pathways
- Increasing healthy lifespan by three years would be equivalent to curing all known cancers



Adapted from Cell 153, June 6, 2013

Measuring Biologic Age in Humans “The Super Cohort Project”



Calico and AbbVie Join Forces to Explore New Biology



Google's Calico, AbbVie forge deal against diseases of aging

BY RANDELL PIERSON
Wed Sep 3, 2014 3:35pm EDT

\$1.5 Billion Research Center Will Be Google's New Aging Tech Lab

Jason Oliva | September 17, 2014

FierceBiotech NEWS TOPICS ANALYSIS FEATU
THE BIOTECH INDUSTRY'S DAILY MONITOR

Topics: Partnering

UPDATED: AbbVie partners with Google's Calico on \$1.5B R&D operation focused on aging

September 3, 2014 | By John Carroll

TECH | 9/03/2014 @ 2:46PM | 4,240 Views

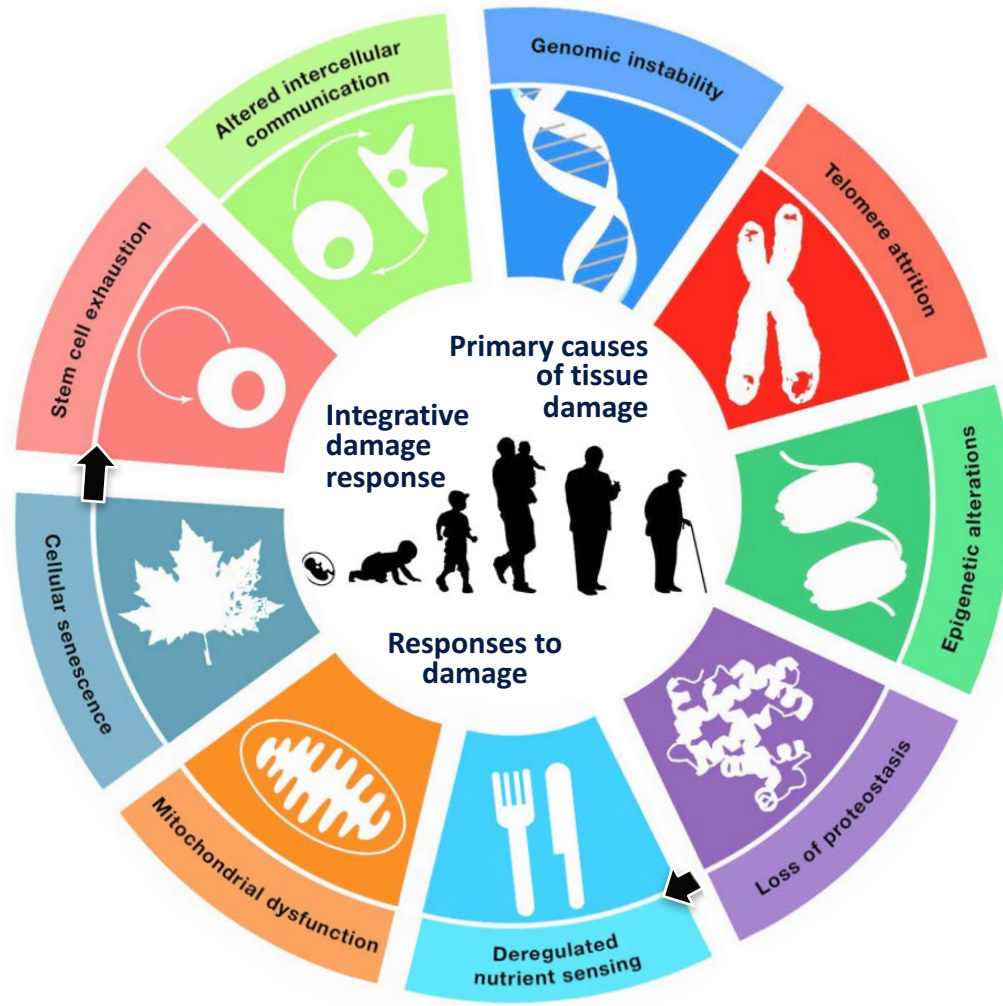
Google's Calico Joins AbbVie In 'Pivotal' Partnership To Develop Anti-Aging Drugs



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- AbbVie and Calico will combine their complementary strengths and co-invest to accelerate the availability of new therapies for age-related diseases
- 10 Year Collaboration

Unraveling The Biology of Aging: Areas of Focus



Adapted from *Cell* 153, June 6, 2013

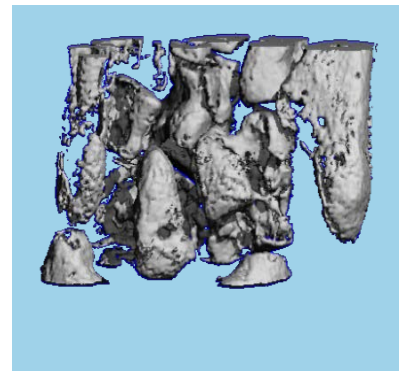
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THANK YOU

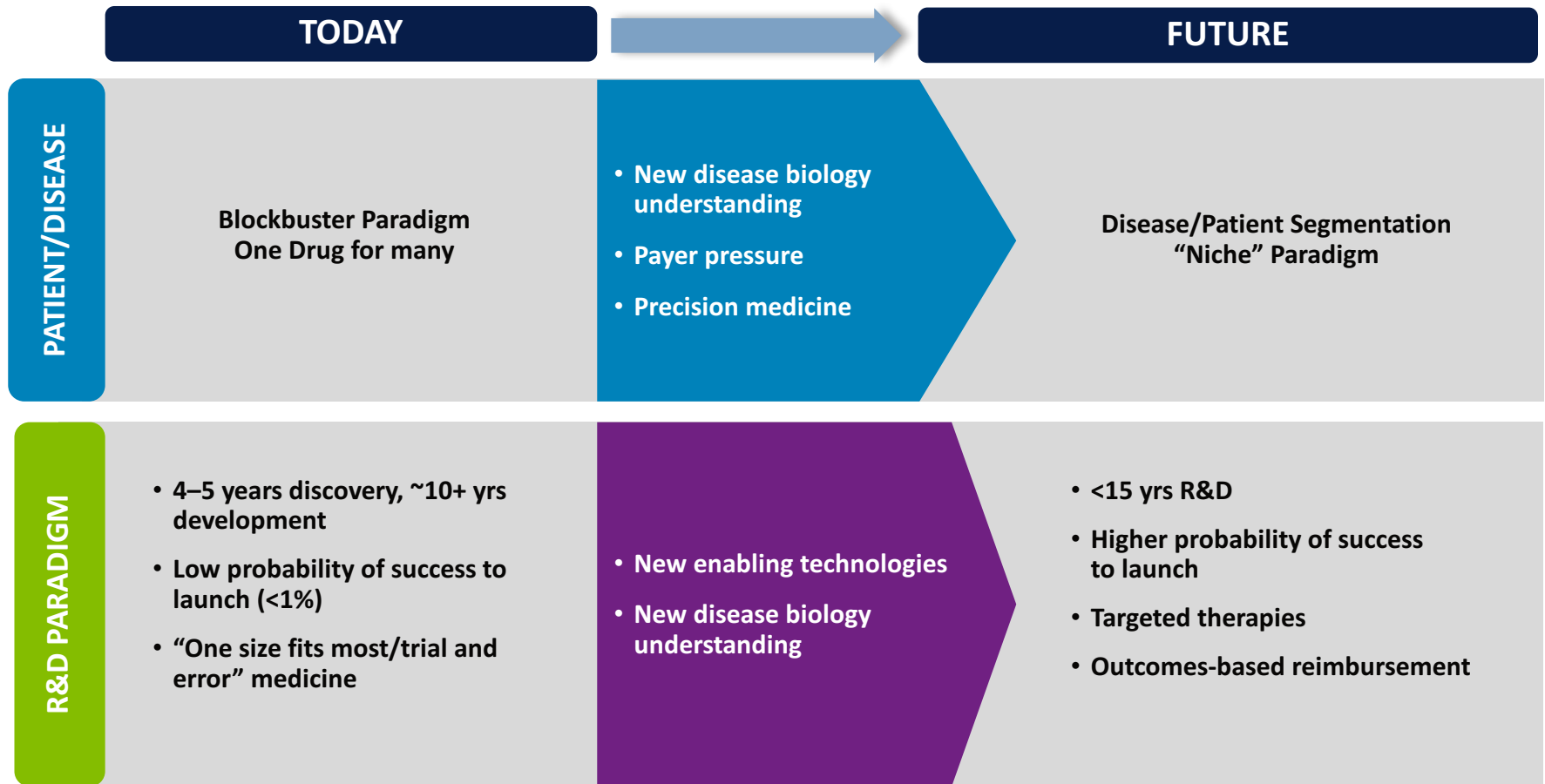


AbbVie's R&D Mission: To Discover New Medicines that have a Remarkable Impact for Patients and Families

Invent and deliver drugs that also create significant value for payers and physicians.

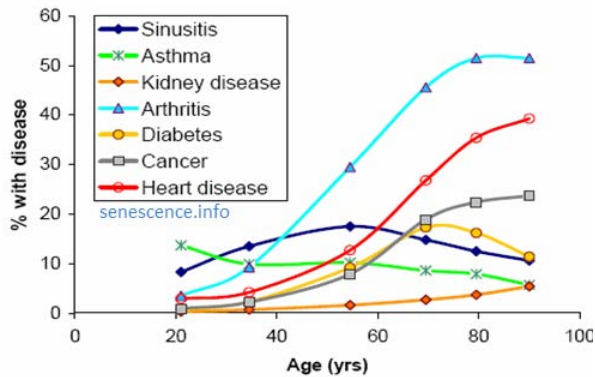


Executing our Mission in a Radically Different Healthcare Environment: “The Patient Will See You Now”

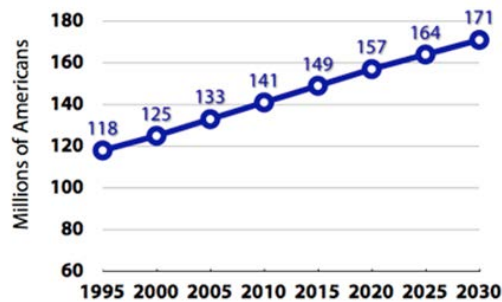


Aging: Primary Risk Factor For All Major Pathologies

Cardiovascular disease, cancers, neurodegenerative diseases (e.g., AD), skeletal and muscle degeneration and metabolic disorders

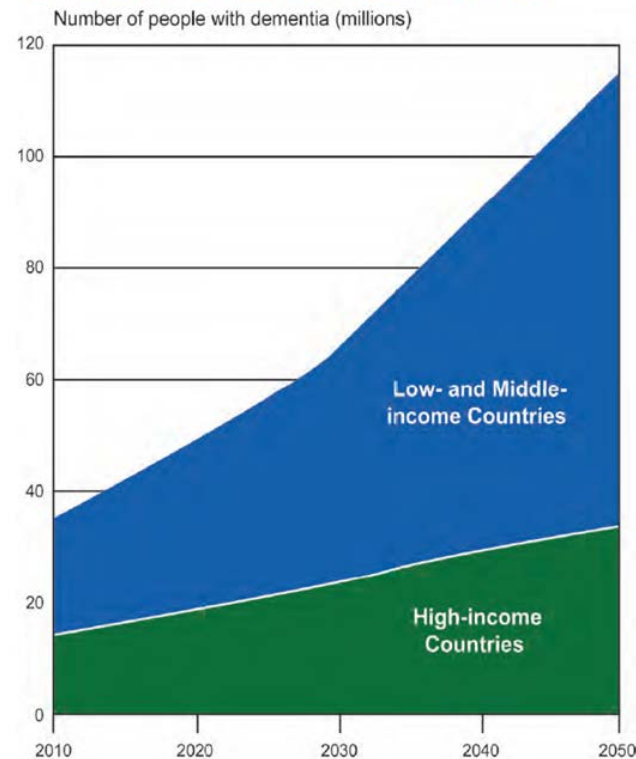


Prevalence of Chronic Disease in the U.S.



Source: Wu, Shin-Yi et al. 2000. Projection of Chronic Illness Prevalence and Cost Inflation. RAND Corporation.

The Growth of Numbers of People with Dementia in High- income Countries and Low- and Middle-income Countries: 2010-2050



Source: Alzheimer's Disease International, *World Alzheimer Report, 2010*. Available at: <http://www.alz.co.uk/research/files/WorldAlzheimerReport2010.pdf>.

Strategic Partnership in Human Genetics: Improving PoS by Identifying Targets with Strong Link to Human Disease

- **Exclusive partnership with GMI/WuXi NextCode**
 - Sequence the genomes of 45,000 volunteers across Ireland
 - Identify insights into disease pathway mechanisms
 - Discover new targets, identify biomarkers
- **Well-powered patient cohorts (6000) coupling WGS and rich clinical phenotype data in five disease indications**
- **Industry-leading informatics and analytical platform and expertise with proven track record**

