

Photo Source: Medical News Today



REFLECTIONS ON 20 YEARS

Advances in Breast Cancer Diagnostics

from a breast cancer survivor and IVD marketer

Martha Townsend,
President, Market Ready Rx

AMDM Annual Meeting – Los Gatos , CA
October 4, 2019

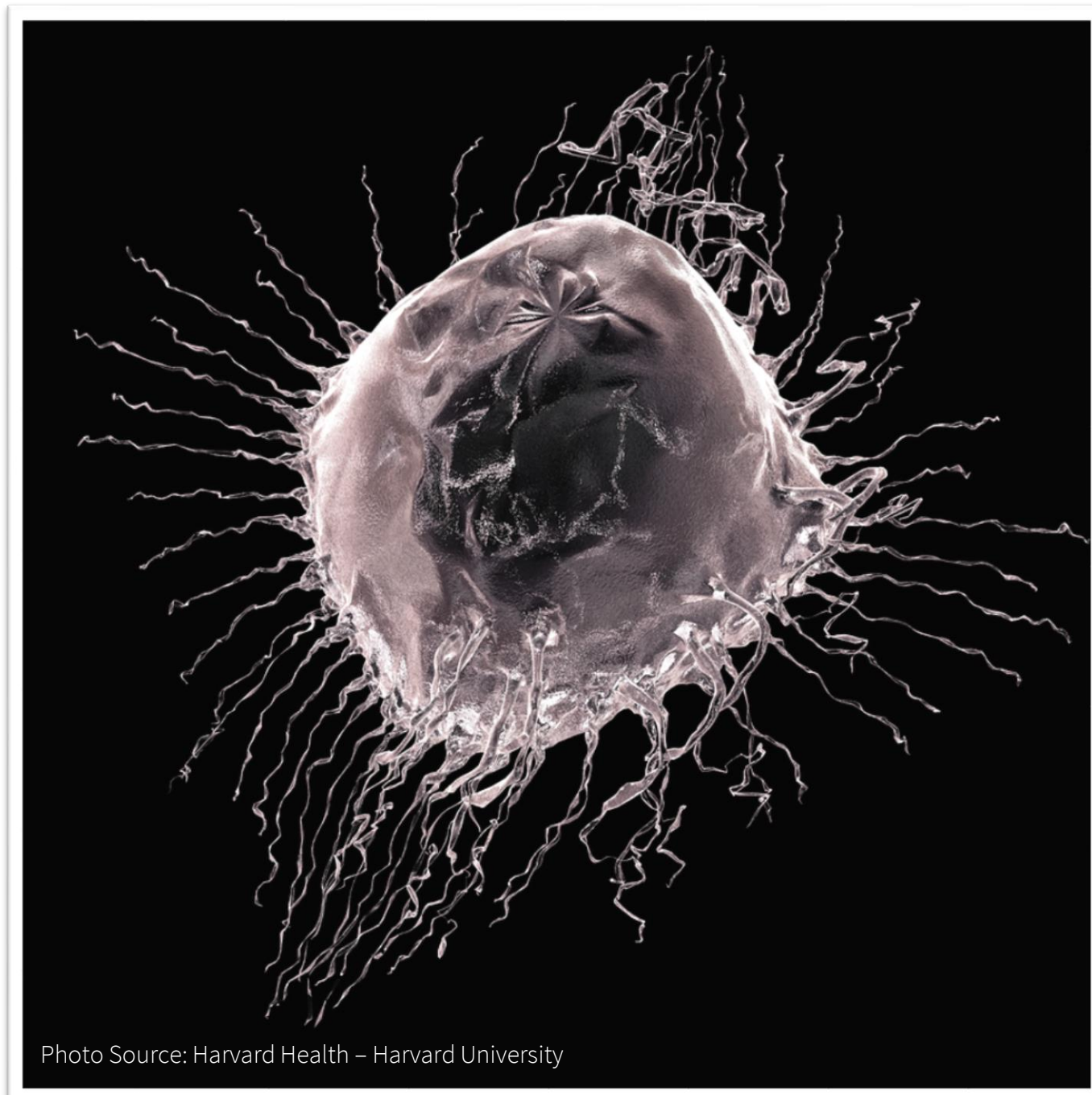


Photo Source: Harvard Health – Harvard University

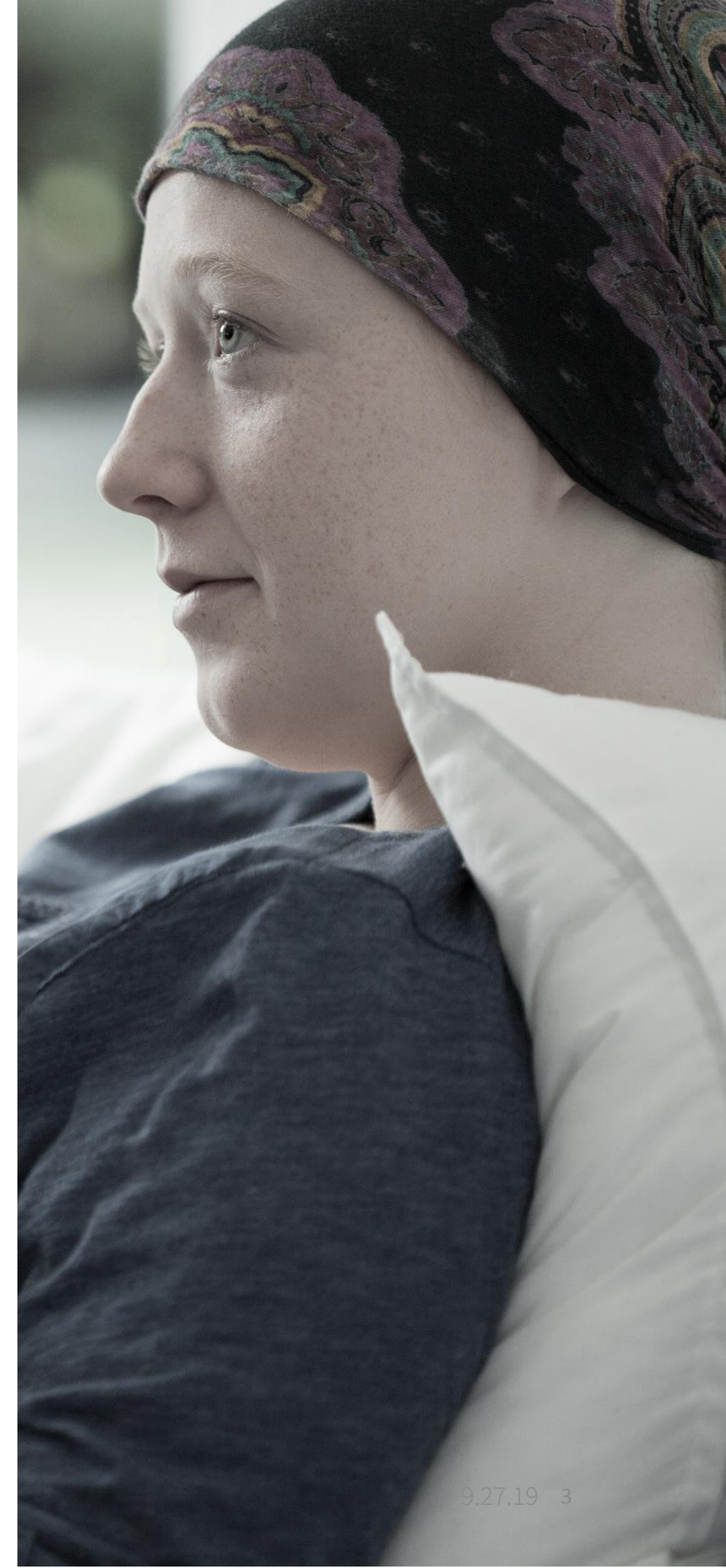
OVERVIEW

- The Evolution of Breast Cancer
- The Impact of Precision Medicine on Breast Cancer Diagnostics
- Breast Cancer Testing Industry Challenges & Opportunities
- The Future of Precision Diagnostics

BREAST CANCER

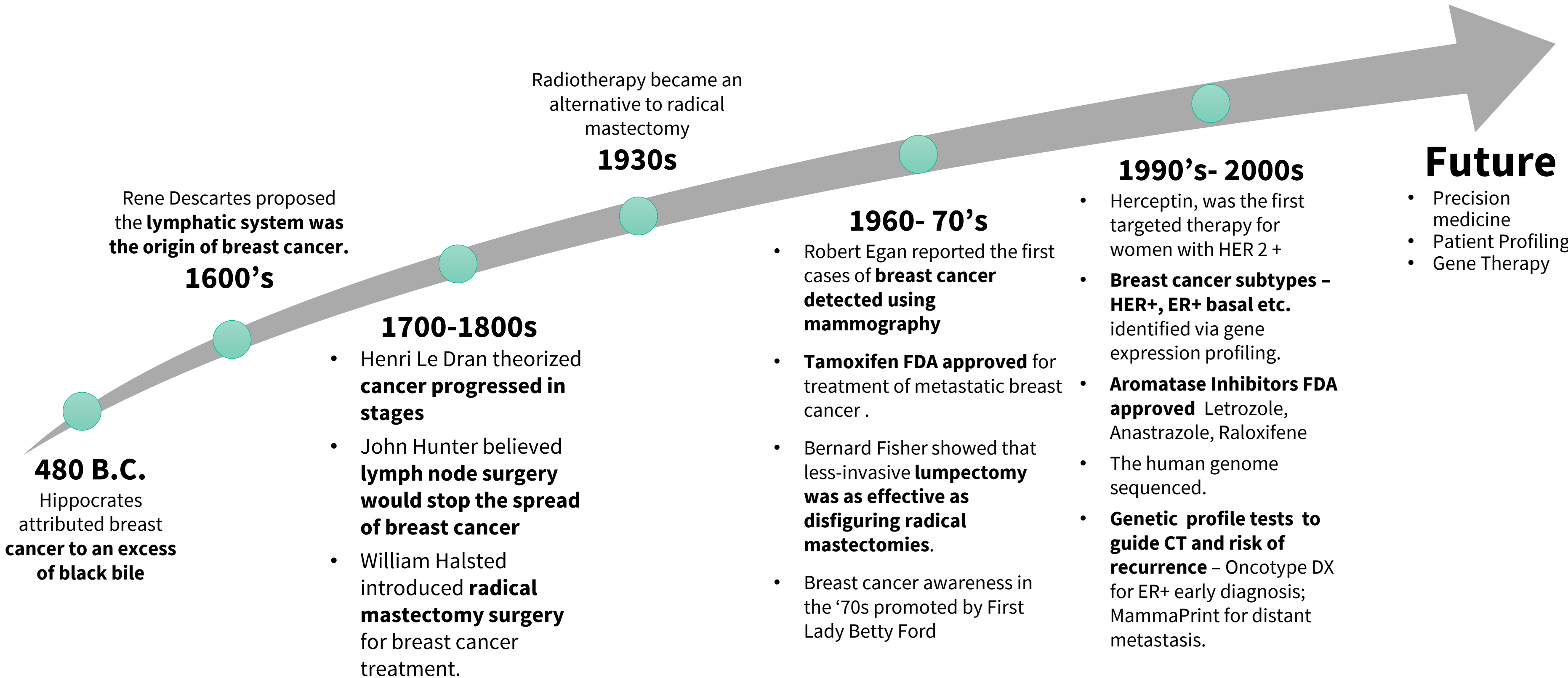
2012 GLOBAL SNAPSHOT

- Globally, **breast cancer** now represents **one in four of all cancers in women**
- **Nearly 1.7 million new breast cancer cases** were diagnosed
 - Breast cancer incidence has increased by more than 20 percent since 2008
 - Mortality has increased by 14 percent
- Breast cancer is the **second most common cancer** worldwide
 - Represents 12% of all new cancer cases
 - 25% of all cancers in women.
- In 140 of 184 countries **globally breast cancer is the most frequently diagnosed cancer among women**





THE EVOLUTION OF BREAST CANCER



Breast Cancer Evolution

460 BC – Today

Breast Cancer Advances

1950's



1970's



1990's

DIAGNOSIS

- Palpable tumor
- Screening mammography
- Two-view screening mammography followed
- Mammography screening SOC¹
- Standardized BI-RADS² Reports

TREATMENT

- Radical Mastectomy Surgery
- Radiation
- Radical Mastectomy
- Lumpectomy surgery SOC¹
- Radiation Therapy
- Introduction of Adjuvant Chemotherapy after Surgery
- Lumpectomy Surgeries +Radiation SOC¹
- Adjuvant Radiation +Chemo after Surgery
- HER2 for Herceptin responders

US DEATHS /YEAR

32 in 100,000

32 in 100,000

Drops to 26.6 in 100,000 by 1999

¹Standard of Care

² Breast Imaging Reporting and Data System

BREAST CANCER

Today

DIAGNOSIS

- Screening mammography Standard of Care
- 3D Mammography for Dense Breasts

TREATMENT

- Radiation Therapy
- Surgery – Lumpectomy / Mastectomy
- Adjuvant CT + Surgery
- ImmunoTherapy PD-L1 for Triple Negative BC

PERSONALIZED DIAGNOSTICS

- Personalized biomarker driven treatments using IHC, FISH, and PCR

US DEATHS PER YEAR

Drops to 20.1 in 100,000 by 2016

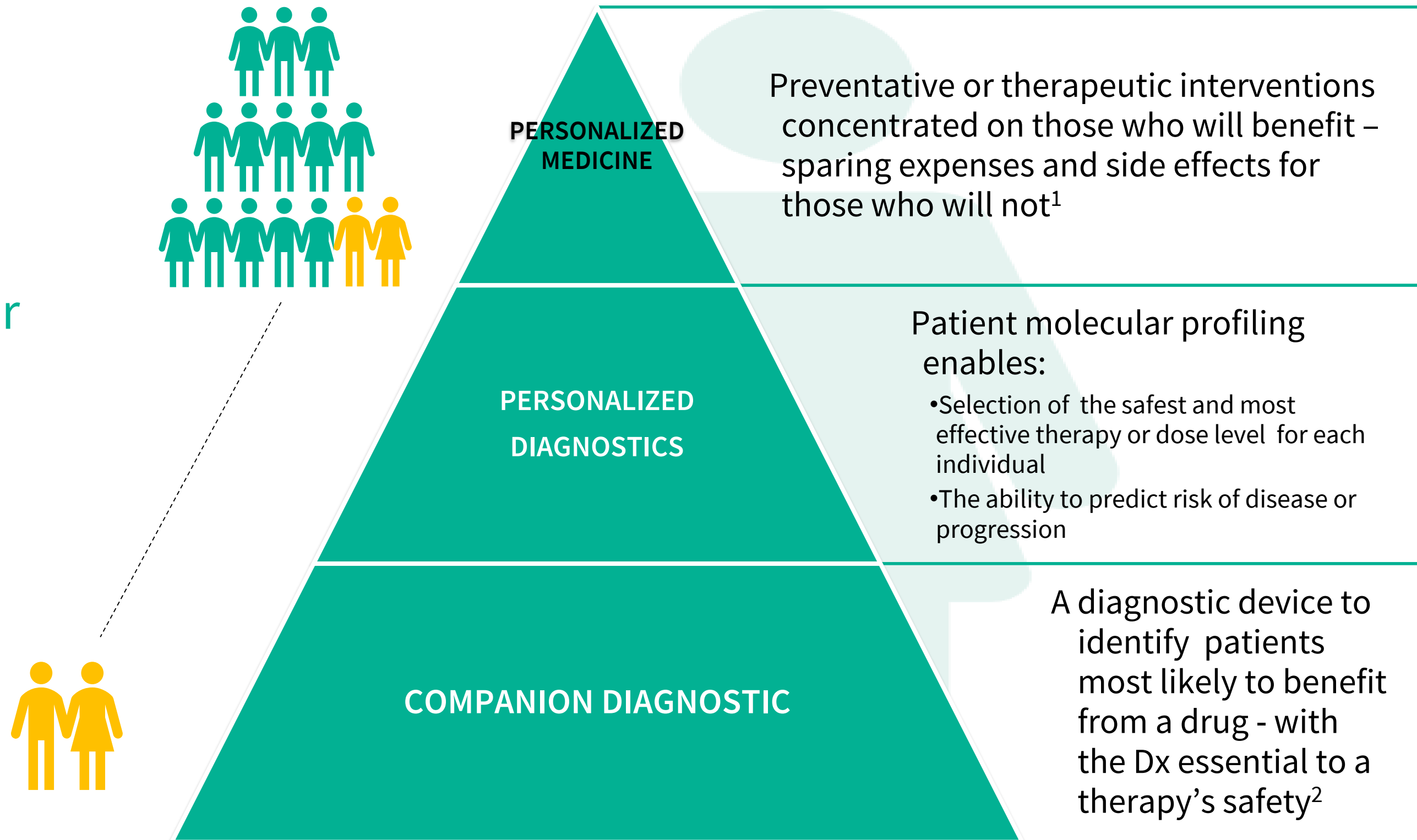


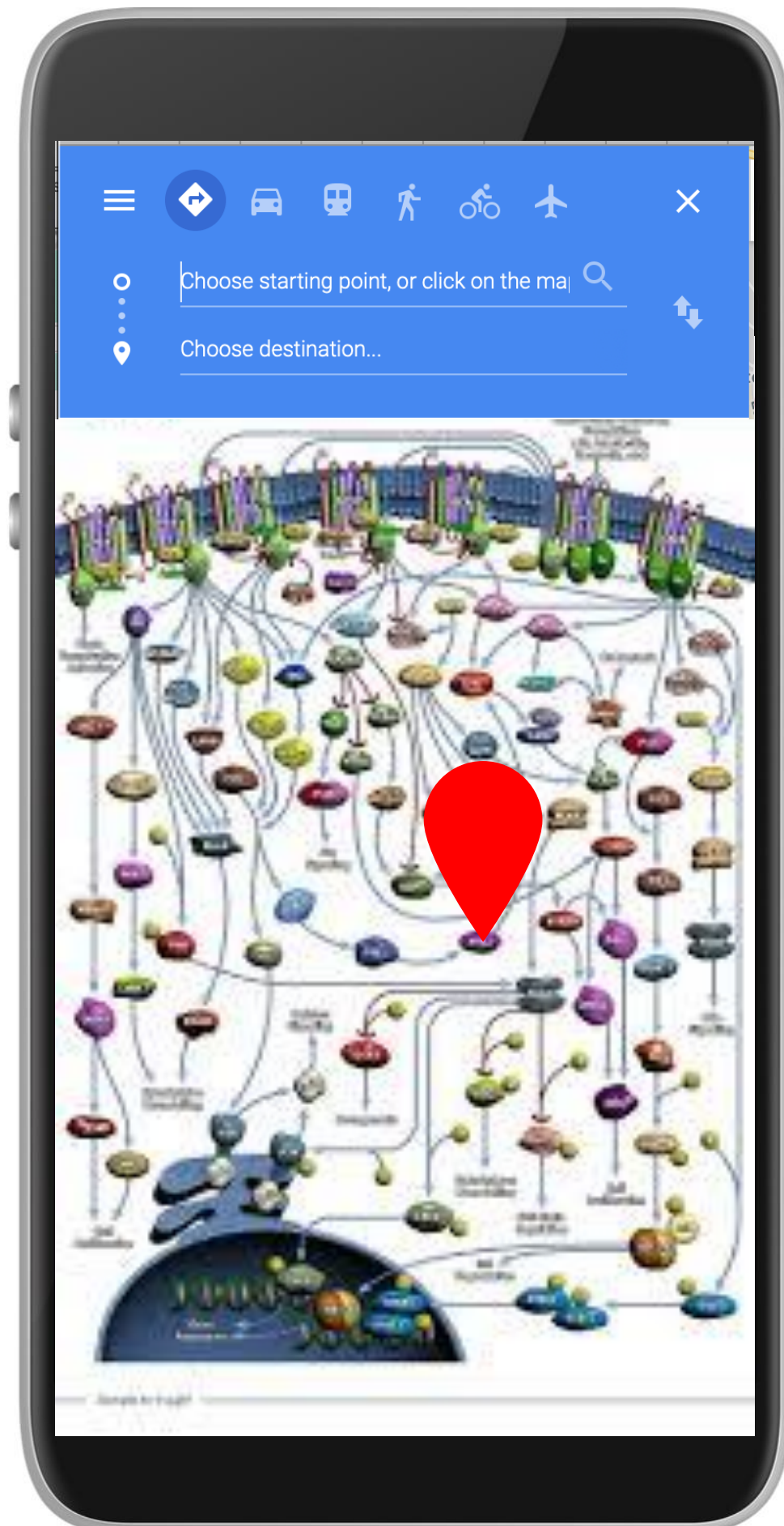
The background of the slide is a complex digital visualization. It features a wireframe model of a human head and torso, rendered in a light blue/white color. This model is superimposed on a dark background filled with vertical columns of binary code (0s and 1s) and horizontal lines of varying lengths, creating a data-centric aesthetic. The overall color palette is dominated by dark greys, blacks, and light blues/whites.

THE IMPACT OF PRECISION MEDICINE ON DIAGNOSTICS

DEFINING PERSONALIZE DIAGNOSTICS

Patients are profiled to identify proper dosing or to determine likelihood of treatment response.



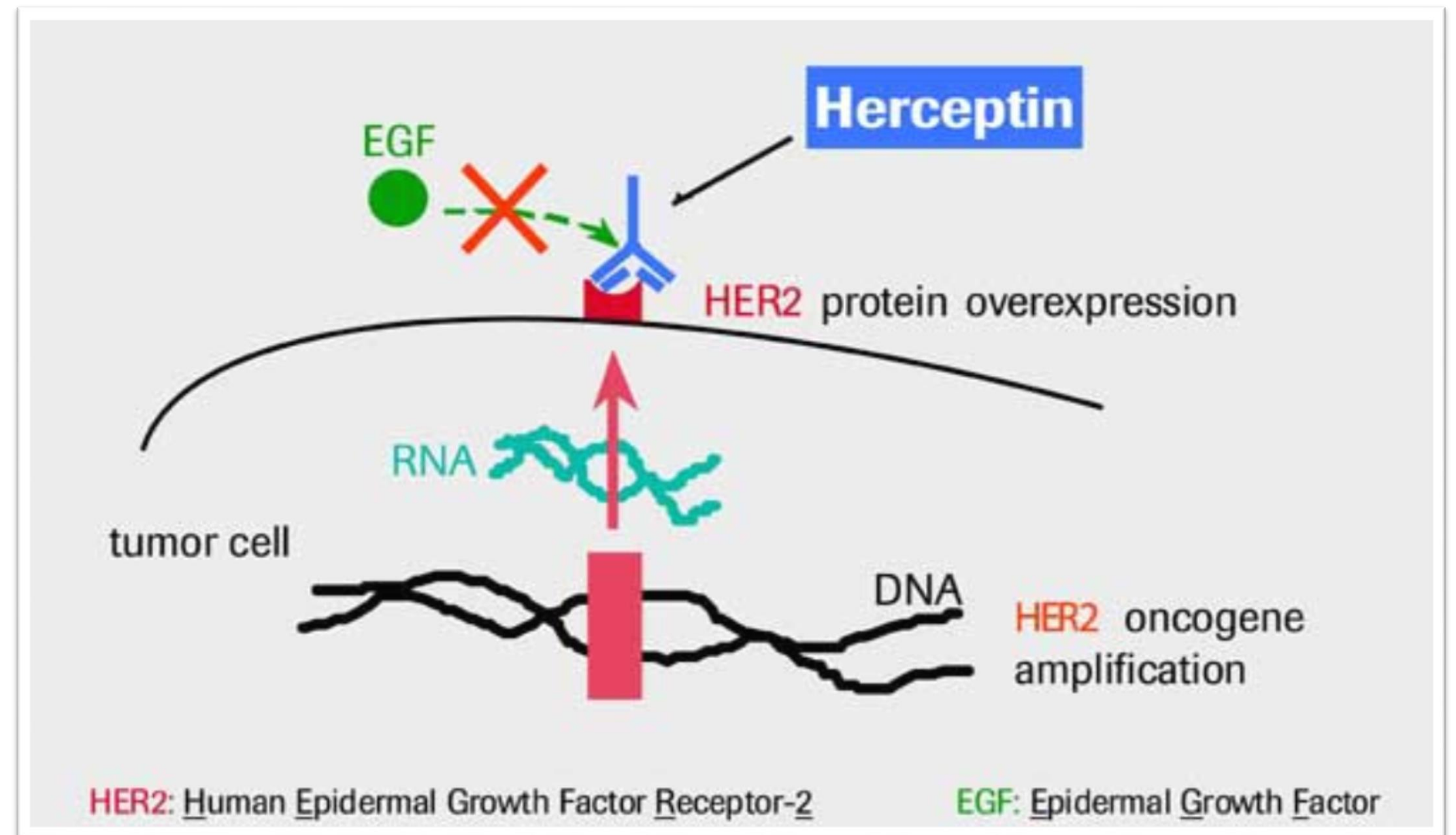


BREAST CANCER IS A COMPLEX DISEASE

....with multiple pathways and no
Google Maps to guide us

HER2 TARGETING IMPORTANCE

The HER2 Discovery enabled us to identify responders and non responders with one Biomarker



SCREENING & EARLY DETECTION

GENETIC TESTING – BRCA 1/2

DIAGNOSTIC TEST

PRIMARY SCREENING

- Screening and early detection BRCA 1/2 mutation carriers show increase risk of the individual developing breast cancer along with age, ethnicity, family history & lifecycle

BRCA 1 / 2
Mutation
Clinical &
Family History

- FDA approved for BRCA 1-2 , HER2-Metastatic BC
- FDA approved for BRCA 1-2 , HER2-Metastatic BC

EARLY STAGE GENOMIC PROFILE TESTS

RISK & RECURRENCE TESTS



GENOMIC HEALTH

Dx TEST INDICATION

- Predicts chemotherapy benefit with a 1-21 score
- Risk of early recurrence

TREATMENT INFORMED BY Dx

- Chemotherapy

AGENDIA

- Mammamprint defines Low Risk” or “High Risk” of developing metastases within the first 10 years after diagnosis

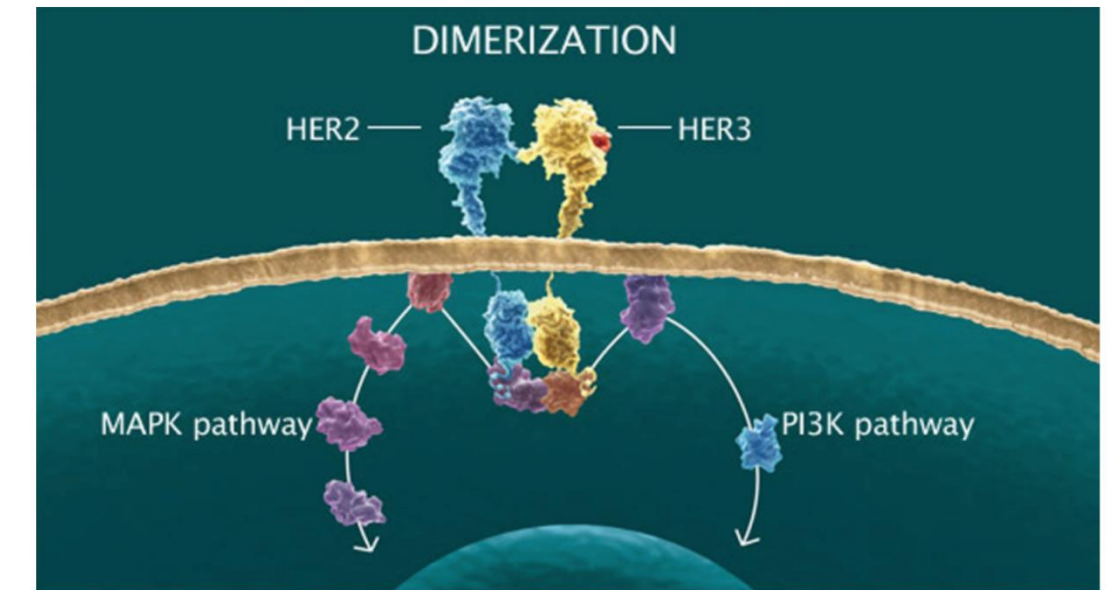
- None

BIOETHERANOSTICS

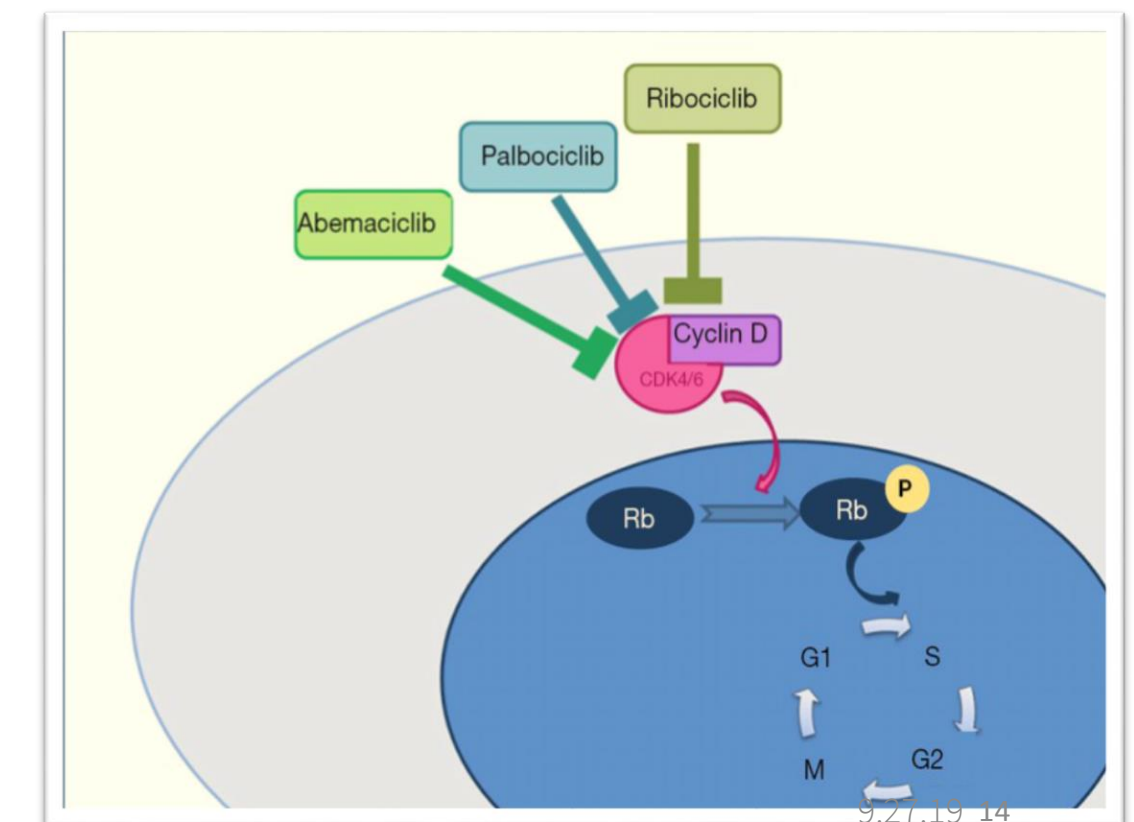
- CLEAR ID Predicts likelihood of benefit from extended endocrine therapy or AI
- Prognostic for risk of late distant recurrence
- Aromatase Inhibitors

METASTATIC BREAST CANCER TREATMENT WITH CORRESPONDING TEST

DRUG & CLASS	INDICATION	IVD / CDX TEST
Biologic Antibodies <ul style="list-style-type: none"> Trastuzumab (Herceptin) Pertuzumab (Perjeta) 	<ul style="list-style-type: none"> Herceptin FDA approved for HER2+ metastatic or adjuvant BC Perjeta FDA approved for HER2+ Metastatic BC in combo with Herceptin & docetaxel AND Early BC in combo with Herceptin & CT 	HER2 + Immunohistochemistry (IHC) or HER2 + In Situ Hybridization (ISH)
Tyrosine Kinase Inhibitors <ul style="list-style-type: none"> Neratinib (Nerlynx) lapatinib (Tykerb) tucanitib 	<ul style="list-style-type: none"> Nerlynx- FDA approved for metastatic BC In clinical studies for metastatic BC, FDA approved for early BC In clinical studies for metastatic BC 	HER2 + IHC or HER2 + ISH
CDK 4, 6 Inhibitors <ul style="list-style-type: none"> Abemaciclib (Verzenio) Palbociclib (Ibrance) Ribociclib (Kisqali) 	<ul style="list-style-type: none"> Verzenio- FDA approved for metastatic BC Ibrance and Kisqali - FDA approved for metastatic BC in combination with AI 	ER+, PR+ (Hormone +) IHC, HER2 - IHC or HER2 - ISH
PARP Inhibitors <ul style="list-style-type: none"> olaparib (Lynparza) talozoparib (Talzenna) 	<ul style="list-style-type: none"> FDA approved for BRCA1-2 , HER2- Metastatic BC 	BRCA1-2 Genetic Mutation & HER2 - IHC or HER2 - ISH
PIK3 Kinase Inhibitors <ul style="list-style-type: none"> alpelisib (Pigray) 	<ul style="list-style-type: none"> FDA approved May 2019 in advanced or metastatic BC following endocrine based regimen 	PIK3CA Genetic Mutation ER+, PR+ (Hormone +) IHC HER2 - IHC or HER2 - ISH



As seen in preclinical models: PERJETA targets a different subdomain on the HER2 receptor than Herceptin does, allowing the combination to provide a dual blockade of HER2-driven signaling pathways.^{1,10,11}



PD-L1 EXPRESSION FOR IMMUNOTHERAPY IN TRIPLE NEGATIVE BC

METASTATIC TRIPLE NEGATIVE BC

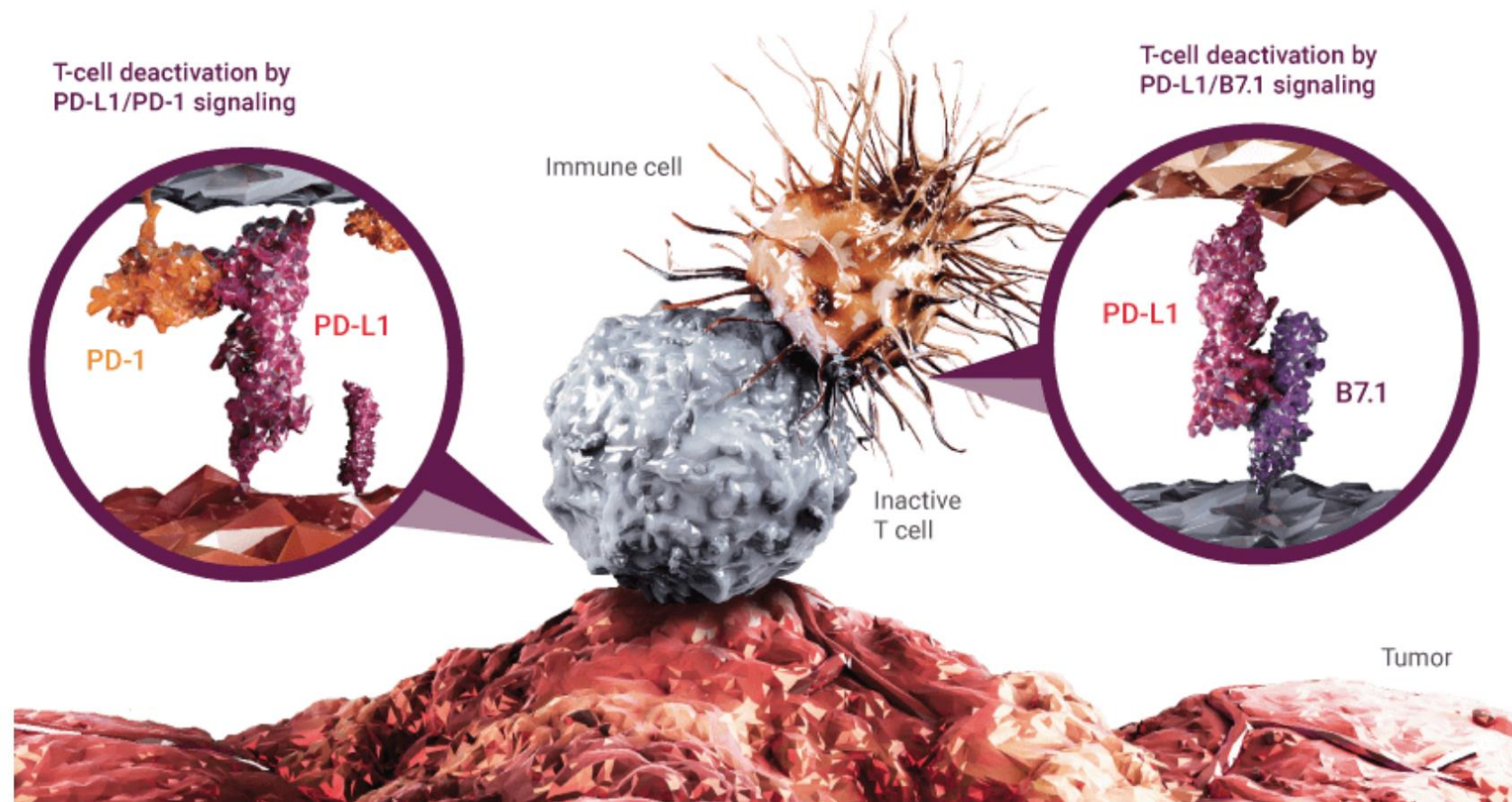
TECENTRIQ for adult patients with unresectable locally advanced or metastatic triple-negative breast cancer

Diagnostic Test

HER2 –
ER,PR –
≥1%
PD-L1
Expression

atezolizumab
(TECENTRIQ)

FDA **approved** in locally advanced or metastatic triple-negative breast cancer (TNBC) BC in combination with paclitaxel protein bound



Binding of the ligand PD-L1 to its inhibitory receptors PD-1 and B7.1 on T cells can suppress cytotoxic T-cell activity

BREAST CANCER

IVD PRODUCT LANDSCAPE

IVD/ CE
Systems

IHC

ER, PR, HER2, PD-L1

Roche-Ventana, Leica, Agilent-Dako

ISH

HER2

Abbott Molecular, Roche-Ventana, Leica, Agilent-Dako, BioCare

Molecular

Oncomine Breast of DNA
For research Use Only

Thermo Fisher



BREAST CANCER

COMMERCIAL LAB SERVICES LANDSCAPE

Commercial Labs	Recurrence Gene Profile	Oncotype Dx, Mammaprint, ClearID
		Genomic Health, Agendia, Biotheranostics resp.
	NGS	MammaSeq, Foundation Act <i>(studies underway)</i>
		Magee Womens HUPP, Foundation Medicine
	Molecular	BC Proteomic Signatures <i>(studies underway)</i>
		Max Planck Institute of Biochemistry, Germany
	Screening	BRCA 1/ 2
		Myriad Genomics



The background of the slide features a pattern of interlocking puzzle pieces. Most pieces are white, but one piece in the upper right quadrant is dark grey. A solid dark grey horizontal band spans the width of the slide, positioned in the middle. The title text is centered within this band.

BREAST CANCER DIAGNOSTICS INDUSTRY CHALLENGES & OPPORTUNITIES

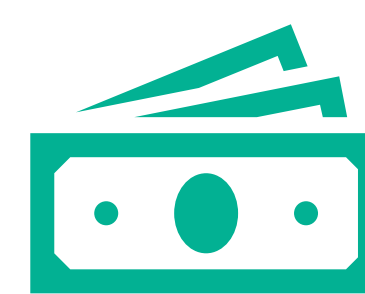
INDUSTRY CHALLENGES



Multiple stakeholders
influence diagnostic
development



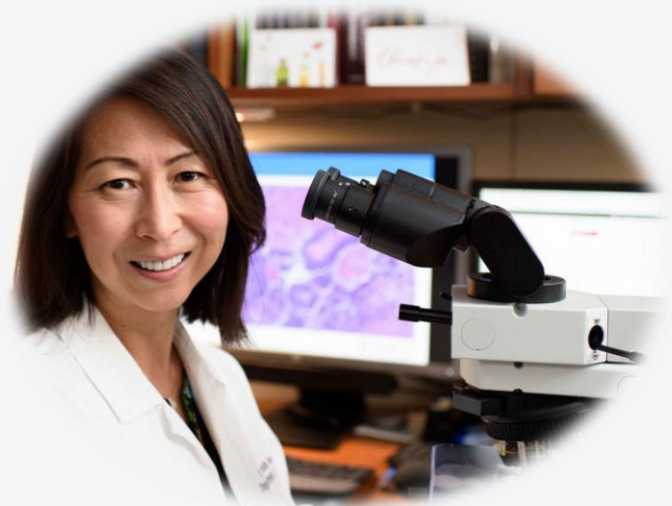
Multiple modalities
being developed to
achieve the same
endpoint



Reimbursement
challenges for new
molecular advanced
diagnostics

MULTIPLE STAKEHOLDERS INFLUENCE DIAGNOSTIC TEST DEVELOPMENT

Different Stakeholders Have Different Needs & Priorities



BREAST PATHOLOGIST

- Clear Test Interpretation
- Solid clinical data for BC
- Streamlined test workflow



ONCOLOGIST

- Understandable Report
- Test results align with clinical experience for confidence Rx decision
- Rapid turnaround time



PHARMA RX PARTNERS

- Reimbursement of Test
- Rapid turnaround time to accelerate Rx script
- Ease of Oncologist ordering of Rx

MULTIPLE STAKEHOLDERS INFLUENCE DIAGNOSTIC TEST DEVELOPMENT

Different Institutions Have Different Needs & Priorities



ACADEMIC HOSPITAL LAB

- High quality results
- Clear supporting clinical data Dx to Rx efficacy



CANCER CENTER

- High quality results
- First to market access to test



COMMUNITY HOSPITAL

- Easy to interpret
- Reimbursable
- Easy to integrate with minimal training



COMMERCIAL REFERENCE LAB

- Competitive Price
- First to market access to test
- Easy to integrate test in high volume lab workflow
- Robust and reproducible

FACTORS INFLUENCING ADOPTION

TESTING CHOICE

Source: Kathryn Becker – World CDx Conference 9.11.19 Boston, MA

GENETIC INFORMATION

- Type of information required (DNA, rna)
- Amount of information (spot mutations, whole genome)

Determines the technology platform choice

ACCESS TO TESTING (LOCATION)

- Patient Loss to follow-up
- Costs
- Ease of Report Interpretation
- Turnaround time

Drives Selection of Lab

SPECIMEN TYPES

- Specimen type and volume of sample
- Ease of specimen collection & transport

Dictates clinical adoption of test

BREAST CANCER IS COMPLEX

TYPES OF BREAST CANCER	US % OF BREAST CANCER	
Lobular Carcinoma In Situ (LCIS)	Pre-cancerous	High risk of invasive breast cancer
Ductal Carcinoma In Situ (DCIS)	20%	Non Invasive
Invasive ductal Carcinoma (IDC) <i>Multiple subtypes</i>	80%	Invasive – spread to surrounding breast tissue
Inflammatory Breast Cancer (IBC)	1%	
Metastatic Breast Cancer (Stage IV)	6-10%	De novo metastasis to brain, bones, lung



BC TUMOR BOARDS

The complexity of breast cancer has driven a need for multi-disciplinary decision treatment decisions and the addition of Genomic tumor boards due to the multiple Diagnostic modalities

- DCIS Stage 2, Grade 2
- Her2 +, ER-, PR-
- OncotypeDx 6 Score
- NGS Variants



FISH
NGS
IHC
PCR

- Radiation Therapy
- Hormone Rx or
Aromatase Inhibitor Rx

US REIMBURSEMENT CHALLENGES FOR ADVANCED DIAGNOSTICS

Different Codes with Payment Variation

EVOLVING TESTING LANDSCAPE

- More biomarkers
- More labs offering advanced Dx tests (NGS, etc.)
- Clinical utility data needs to be developed
- Reimbursement bodies need to catch up

EACH PRODUCT HAS DIFFERENT COVERAGE

- Each product has different Coverage, Coding and payment rates depending on practice setting
- Public vs. Private payors have different requirements for evaluation

ADVANCED Dx REIMBURSEMENT IS COMPLEX

- Medicare is Medical Evidence
- Private is Medical Necessity
- MOL Dx evaluation group manages policy across most US states

CPT CODING COMPLEX

- Mol Path Tier 1 and 2
- MAAA for LDT - Oncotype Dx
- Genomic Sequencing (GSP)- 2 codes for > 50 panels , 5-50 genes
- Proprietary Lab Code (PLA)- New codes 2017 for Foundation and Oncomine specific to sole source marketed to multiple labs
- Other Mics

Mutations/ Technologies	IHC	ISH	PCR	Diagnostic (Dx) Sequencing
Single Nucleotide Polymorphism (SNP) Point Mutations	-	-	++	++
Insertion and Deletion (Indel) Duplications	-	-	++	++
Copy Number Variation (CNV)	+	++	+	+
Translocation/ Fusion	+	++	+	+
Gene Expression ^b	+	+	++	+
Protein Expression ^c	++	-	-	-

MULTIPLE MODALITIES ARE BEING DEVELOPED FOR SAME ENDPOINT

**TODAY...NO SINGLE TECHNOLOGY
CAN PROVIDE A COMPLETE
BIOMARKER PROFILE**

- Physicians are seeking **ANY opportunity to identify a treatment for their patients** by mining biomarkers tied to relevant therapy options
- Each technology has unique characteristics to address physician needs:
 - Sensitivity, specificity
 - Diagnostic yield
 - Turn around time
 - Cost
 - Coverage, coding, payment
 - Patient request



THE FUTURE OF BREAST CANCER DIAGNOSTICS

PRECISION DIAGNOSTICS EVOLVES BEYOND THE LAB

PATIENTS ARE DRIVING THE FUTURE OF PERSONALIZED MEDICINE

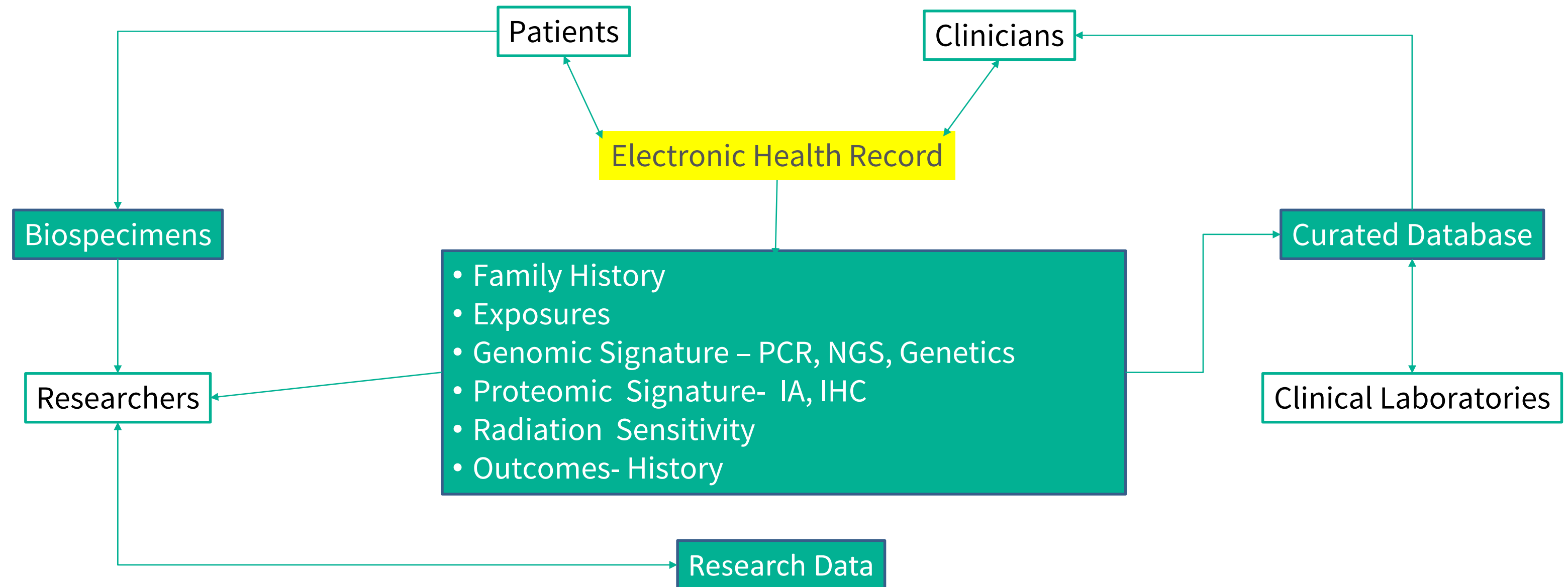


78% of Patients expect providers to make personalized recommendations based on information that is specific to the patients individual needs

Source: MM&M What patients want from HCPs December 2018 <https://www.mmm-online.com/home/channel/data-analytics/infographic-what-patients-want-from-hcps/>

THE FUTURE OF PRECISION DX

**EMR IS GAME CHANGING – ENABLES CURATED BIOINFORMATICS
DATA FOR INDIVIDUAL PATIENT TREATMENT PLANS**



CELL & GENE THERAPY CLINICAL TRIALS

CURRENT TRIALS INVOLVING ADVANCED THERAPIES

GENE THERAPY

TOTAL: 362
Phase I: 120
Phase II: 210
Phase III: 32

GENE MODIFIED CELL THERAPY

TOTAL: 362
Phase I: 158
Phase II: 188
Phase III: 16

CELL THERAPY

TOTAL: 263
Phase I: 53
Phase II: 177
Phase III: 33

TISSUE ENGINEERING

TOTAL: 41
Phase I: 10
Phase II: 20
Phase III: 11

Source: Steve Anderson, SVP Covance – World CDx Conference 9.11.19 Boston, MA

Per clinicaltrials.gov 81 Breast Cancer gene therapy studies are currently recruiting

THE FUTURE OF BREAST CANCER

INDIVIDUAL PATIENT PROFILE

- Genomic BC signature
 - BRCA 1/2
- Proteomic Signature
- Metabolomic Profile
- Gene Therapy options
- Tx Options



CONTACT INFO

HOW TO GET IN TOUCH

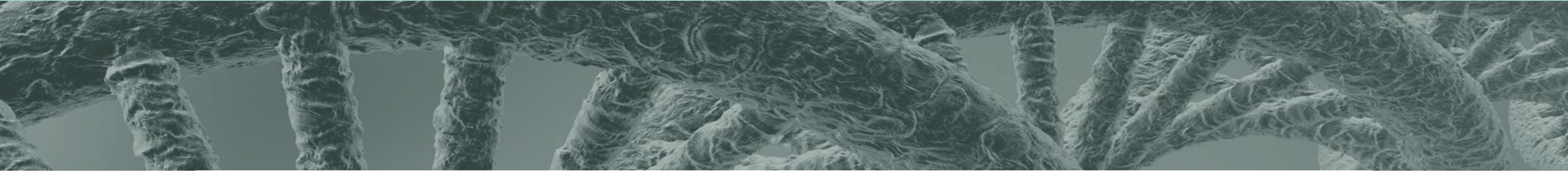


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Market Ready Rx brings real-world industry experience to marketers around the world. We create and execute global commercial launches to help our clients become market-ready.

Market Ready Rx Brings Personalized
Diagnostics To Market.