

AVALON HEALTHCARE SOLUTIONS **LAB INSIGHTS FORUM**

October 19, 2021





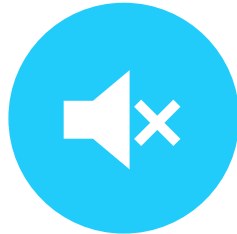
OVERVIEW & INTRODUCTIONS

Barry Davis, Chief Growth Officer, Avalon

Before we start



This meeting is being recorded



We will be **MUTING** everyone except the presenter to make sure the AUDIO is clean and clear



Q&A will be done by using the “**Questions**” feature

Agenda

OVERVIEW AND INTRODUCTIONS

Barry Davis, Chief Growth Officer, Avalon

THE LATEST ON THE NO SURPRISES ACT

Julie Barnes, Principal, Maverick Health Policy

WHAT'S COMING—DISRUPTIVE DIAGNOSTICS AND WHY YOU SHOULD CARE

Rob Epstein, M.D., M.S., Chief Executive Officer, Epstein Health

IMPROVING CARE AND REDUCING COSTS BY MANAGING LAB SERVICES

Fireside Chat With Mark Werner & Sherry Mullies of Blue Cross and Blue Shield of North Carolina and Moderated by Martha Owens Perry

CLOSING REMARKS

Bill Kerr, M.D., Chief Executive Officer, Avalon



THE LATEST ON THE NO SURPRISES ACT

Julie Barnes, Principal, Maverick Health Policy

No Surprises Act - Basics

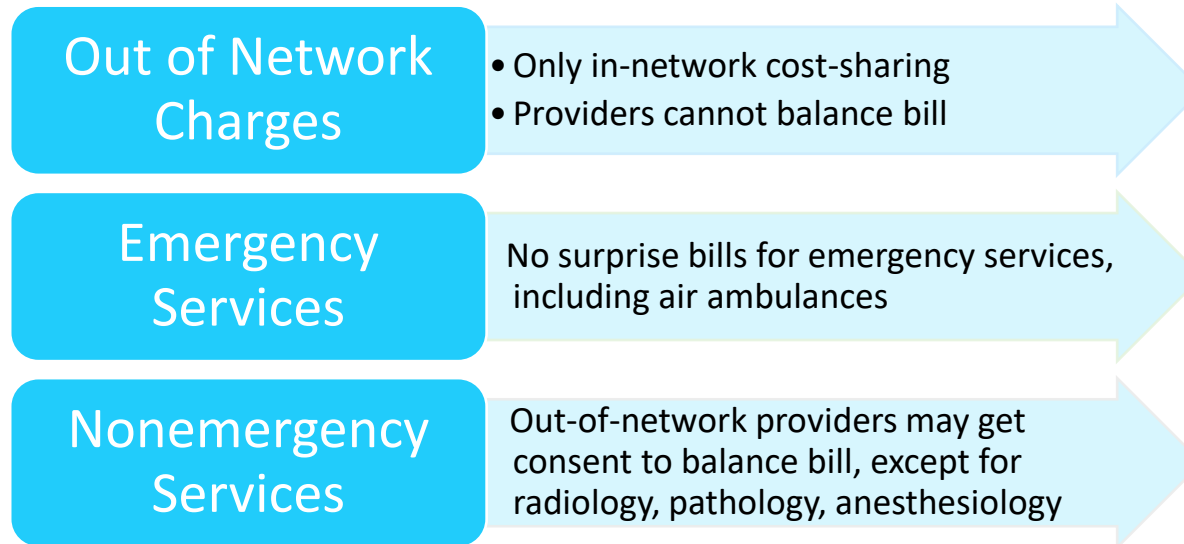
When: Starting January 1, 2022 – phasing in the rest

What: Holds patients harmless from big surprise medical bills.

No balance billing—patients pay in-network cost-sharing or consent otherwise.

New arbitration process will settle fights about reimbursement.

Price transparency mandates for health plans and providers.



Enforcement for hospitals: CMPs of up to \$10,000

No Surprises Act – Implementing Rules (so far, more to come):



July 1, 2021, Interim Final Rule

August 20, 2021, FAQs

Sept. 10, 2021, Proposed Rule

Sept. 30, 2021, Interim Final Rule

No Surprises Act – Rule #1

July 1st
Interim
Final Rule

NO MORE BALANCE BILLING

- Bans surprise billing for all ER services.
- Bans OON charges for OON care (e.g., labs or anesthesiologist) at in-network facility.

NO MORE SURPRISES

- Consent process – patients can agree to be balance billed for OON charges for non-ER services.
- Notice rules – providers and plans must tell patients about protections.

NARROWS \$\$: Creates a formula to determine the total amount paid to a provider – the “qualifying payment amount”

No Surprises Act– Rule #3

Sept. 30th
Interim
Final Rule

New Website:
www.cms.gov/nosurprises

Independent Dispute Resolution (IDR)

- Payers median contracted rate is the default

New Uninsured Patient Rules

- Good faith estimates
- Dispute resolution process

External review expanded

- Includes No Surprises Act-related disputes

COMING NEXT YEAR: No Surprises Act Price Transparency Mandates

Good Faith Estimates and Advance EOB

Consumers can
request information
about coverage
BEFORE services are
provided

Price Comparison Tool

Consumer-facing tool
must be available online
showing price
comparisons across
providers

Provider Directories

Update in-network
provider directories
at least every 90
days

No Surprises Act



Takeaways

- Hospitals have a short period of time to prepare their billing departments for these changes by 2022.
- Network adequacy / health professional staffing agencies pose bigger issues now.
- Health plans have a big advantage in rate-setting and contract negotiation because their in-network rate is the default.



WHAT'S COMING— DISRUPTIVE DIAGNOSTICS AND WHY YOU SHOULD CARE

Rob Epstein, M.D., M.S.,
Chief Executive Officer, Epstein Health

Disruptive Diagnostics and Why You Should Care

OCTOBER 19, 2021

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Disclosures

Grant/Research Support: *Taiho Oncology, Radius Health, Merck, Halozyme, G1 Therapeutics, Takeda*

Speaker's Bureau: *None*

Consultant: *Janssen, Taiho Oncology, Merck, Otsuka, G1 Therapeutics, Halozyme, TriAxia Healthcare, Medocity, Pierian Dx, Health Catalyst Capital, Vestar Capital Partners, Casdin Capital, Health Rhythms*

Board of Directors currently: *Illumina, Veracyte, Fate Therapeutics,*
previously: *Proteus Digital, Decipher Bio, OnQity, Aveo, Mindstrong Health)*

Why Should You Care About Upcoming Tests?

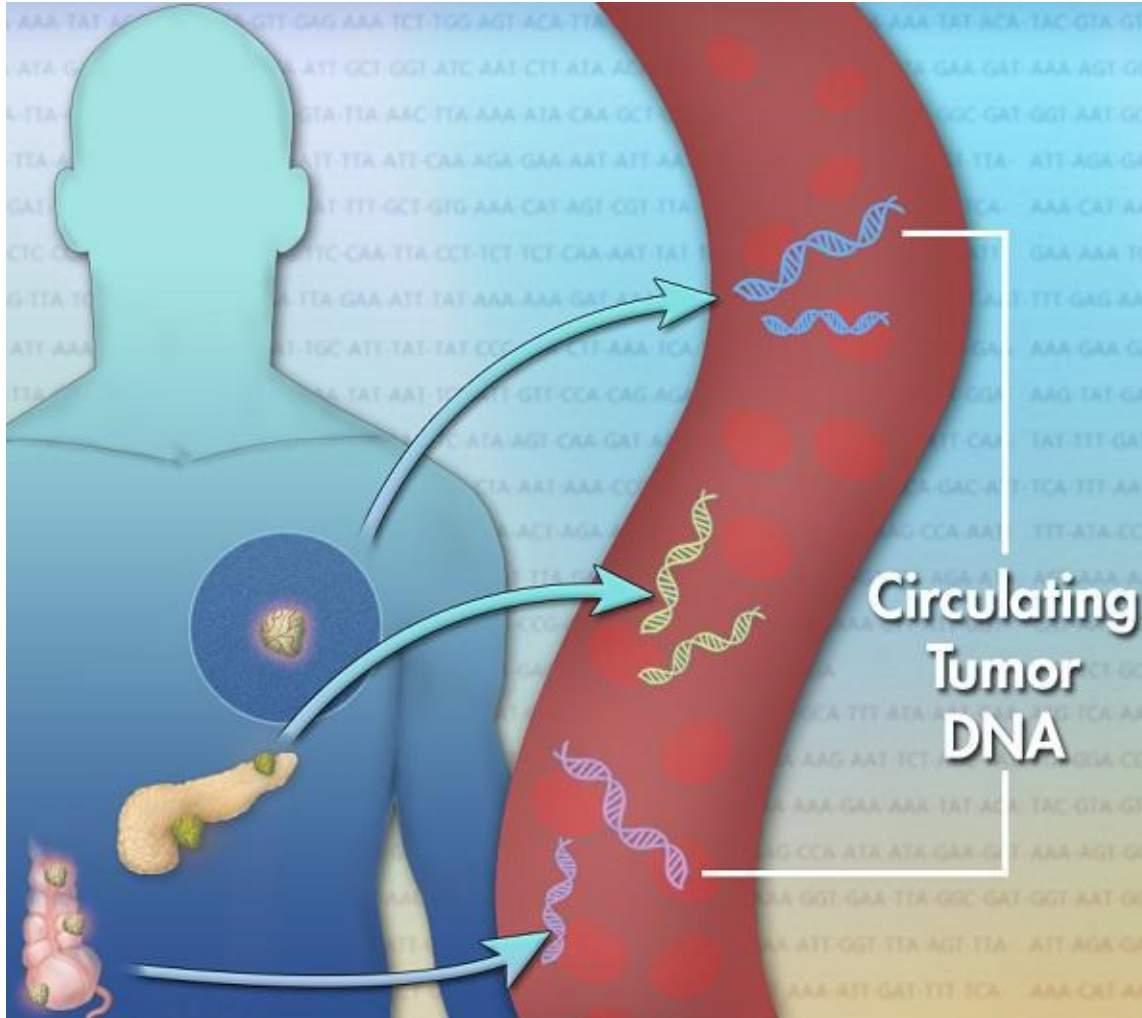
1. Pipeline of diagnostic tests never as robust as today —
2. Current crop of disruptive diagnostics are poised to
 - Help identify CURES rather than maintenance treatments for chronic diseases
 - Keep ahead of mutating cancers by earlier detection and treatment selection
 - Reduce wasted procedures/costs/risk by better detecting and prognosticating
3. Entering a confusing marketplace
 - MDs too busy to learn all the new sciences — opportunity for errors
 - Technology assessment complicated
 - Evidence of clinical utility often missing

Key Drivers of the Diagnostic Pipeline?

3 areas for today's discussion

1. **Science** evolving to favor development of novel diagnostics
2. **Drug pipeline** contains products that require diagnostics
3. **Rare disease** research continues dramatic upswing

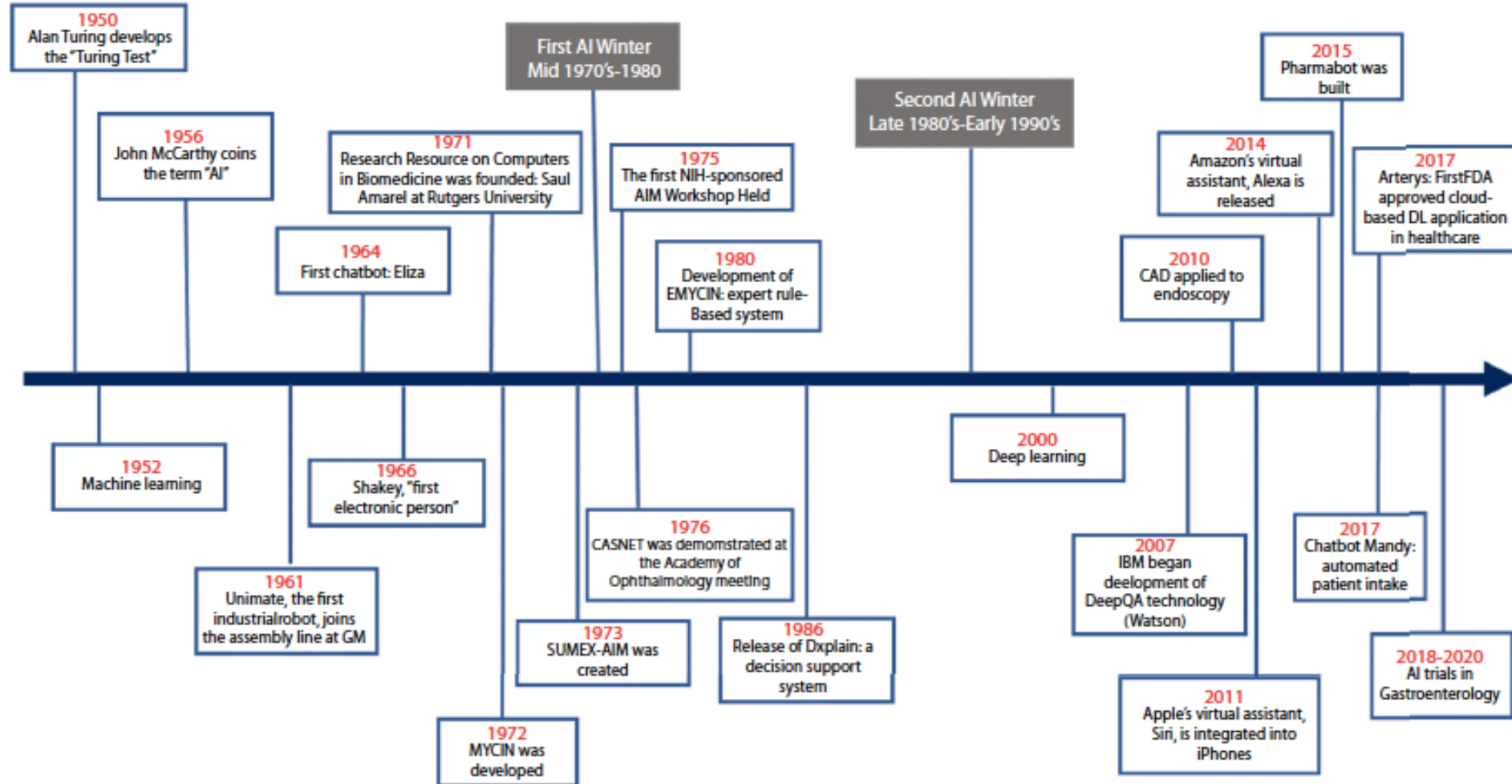
Science: Genomic Sequencing Has Uncovered Surprises



“Discordant noninvasive prenatal testing results in a patient subsequently diagnosed with metastatic disease”

Source: <https://pubmed.ncbi.nlm.nih.gov/23559449/>

Sciences of AI and Machine Learning Inform Development of Diagnostics



Source: [https://www.giejournal.org/article/S0016-5107\(20\)34466-7/pdf](https://www.giejournal.org/article/S0016-5107(20)34466-7/pdf)

AI Came to Standard Imaging Interpretation

Rise of Digital Radiology

CT scans

- ▶ Were 50-100 slices 5 years ago - today 100,000 slices
- ▶ Still have same 5 minutes to look at all that and interpret
- ▶ AI helping to flag abnormalities

Standard X-rays

- ▶ Especially useful in rural hospitals where no radiologists at night

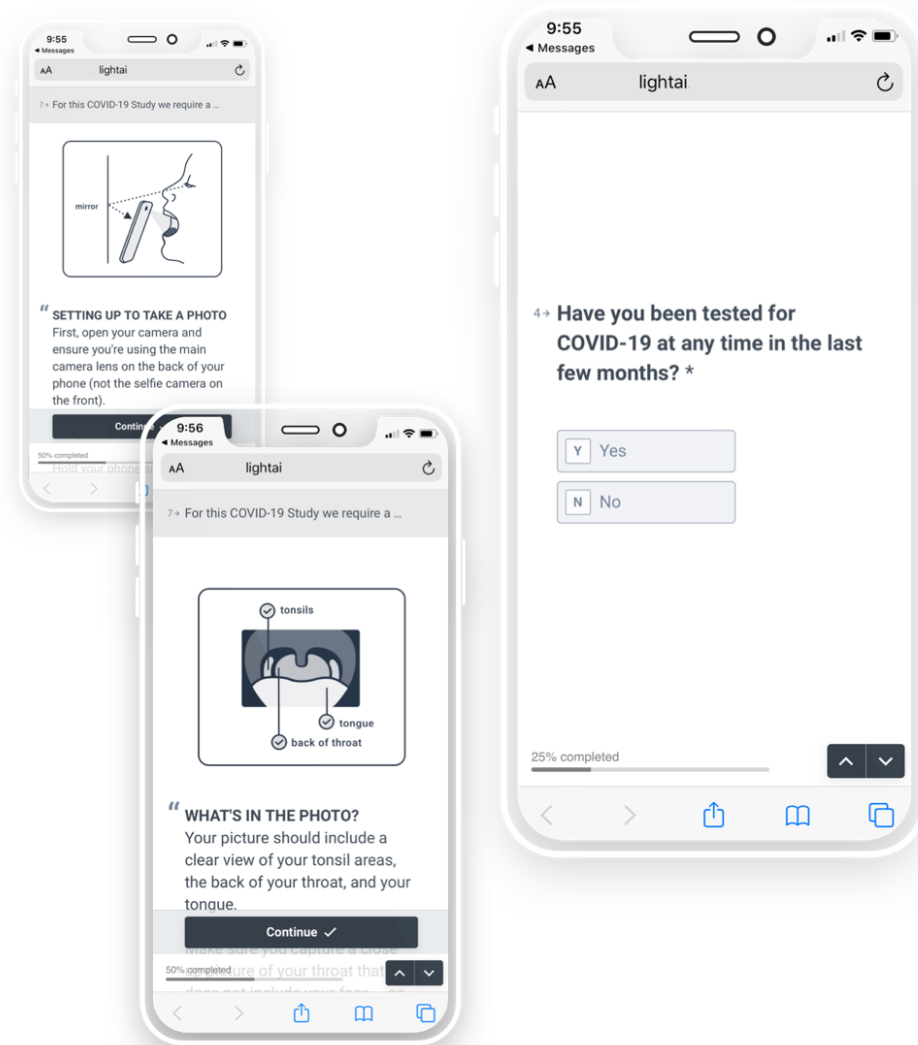
AI/Machine Learning Came to Pathology

Promise of Digital Pathology



Source: <https://www.leicabiosystems.com/knowledge-pathway/what-is-digital-pathology/>

AI Is Being Trained to Interpret Cell Phone Images of Throat — to Detect COVID-19 Infection



Source: <https://light.ai/technology/>

Science Really Moving Along!

Recipients of 2020 Nobel Prize for Chemistry



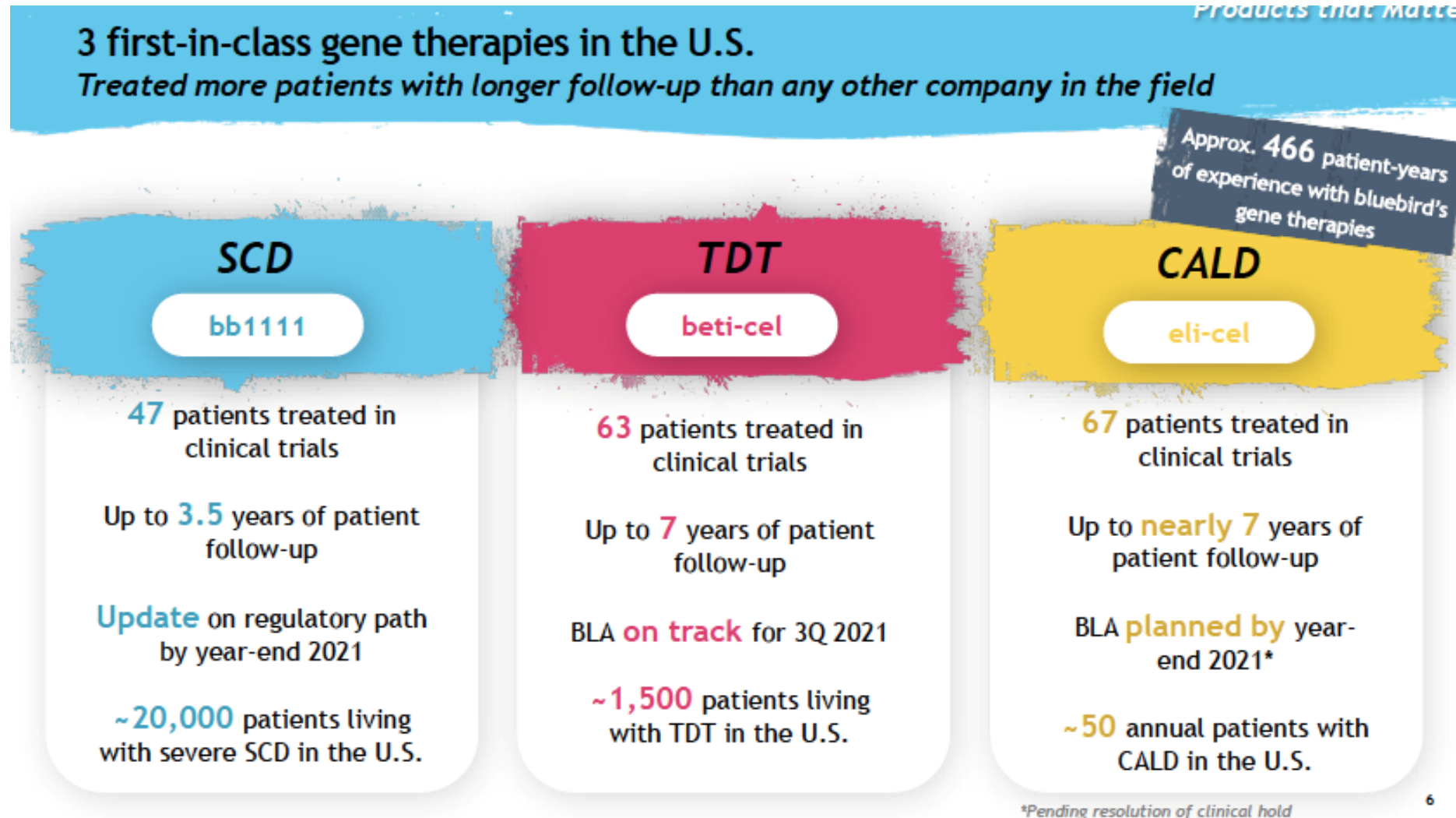
Emmanuelle Charpentier



Jennifer Doudna

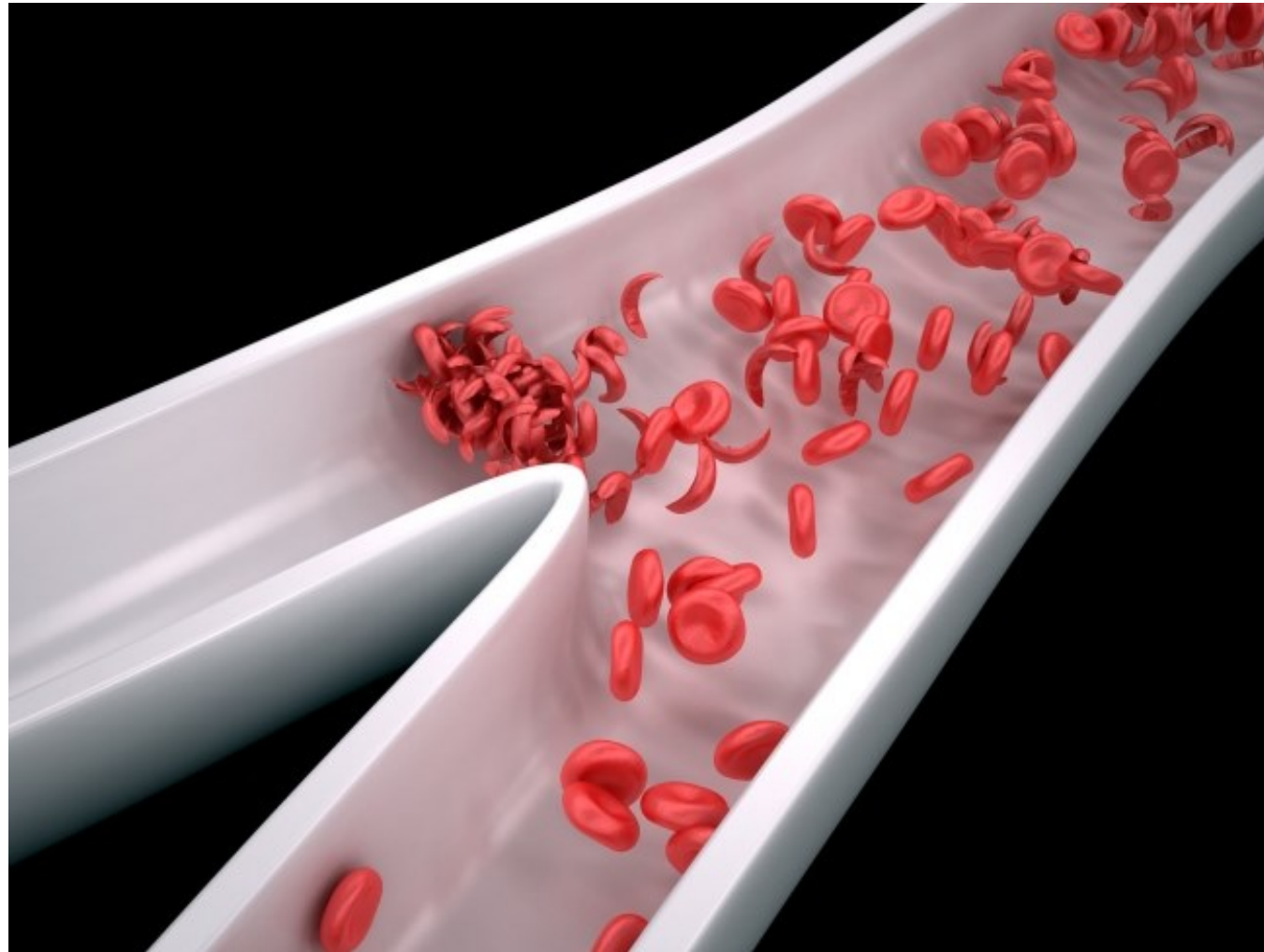
CRISPR Technology — which enables gene editing!

Near-term Gene Therapies Needing Diagnostics....



Source: <https://investor.bluebirdbio.com/static-files/a6ba7865-f65f-4216-8efd-400917a90a40>

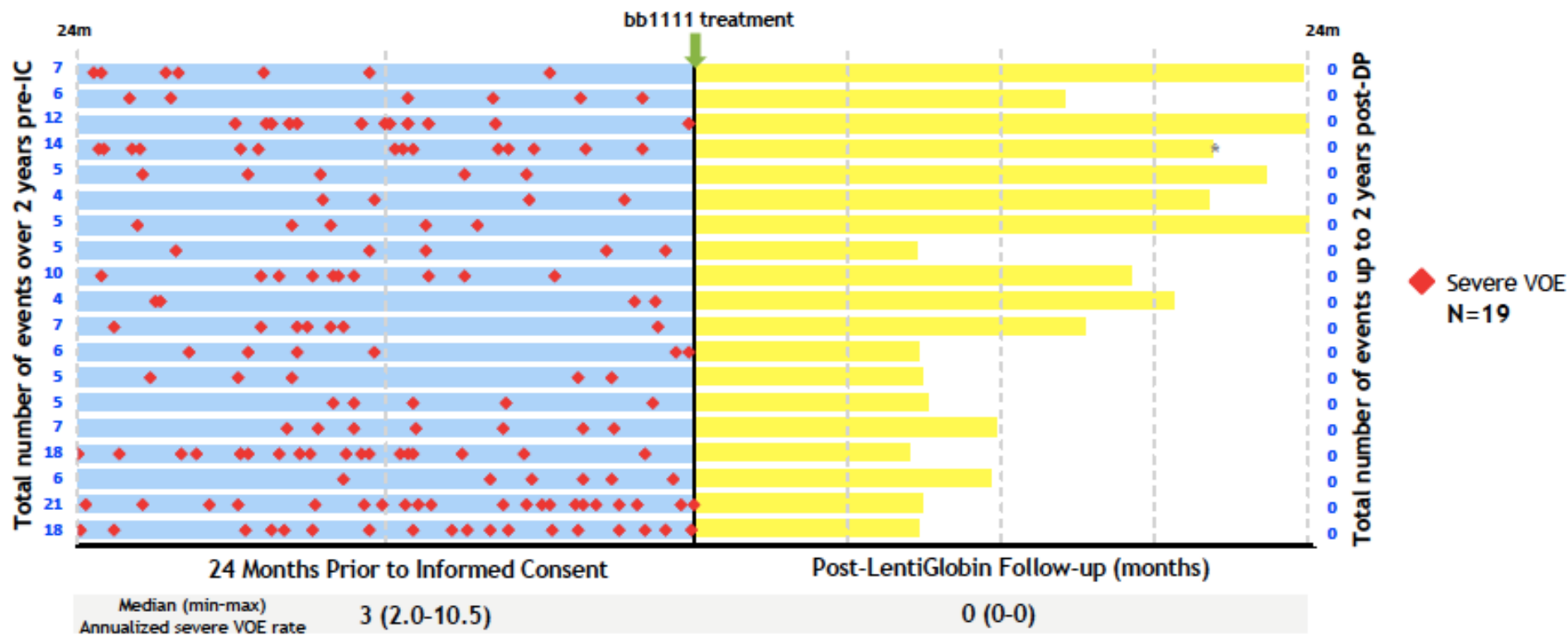
Sickled Red Blood Cells Clog Circulation



Source: <https://www.practicalpainmanagement.com/pain/other/trial-shows-l-glutamine-leads-fewer-instances-sickle-cell-related-pain>

No Severe Sick Cell Occlusive Events Post-gene Treatment!

SCD: Unparalleled efficacy with complete resolution of severe VOs post-bb1111 treatment in HGB-206 Group C clinical study



¹Protocol sVOEs are shown; Patients with ≥ 4 sVOE at baseline before IC and with ≥ 6 months of follow-up post-DP infusion are included. A severe VOE is as an event with no medically determined cause other than a vaso-occlusion, requiring a ≥ 24 -hour hospital or emergency room observation unit visit or at least 2 visits to a day unit or ER over 72 hours with both visits requiring intravenous treatment for the following: acute episodes of pain, acute chest syndrome, acute hepatic sequestration, and acute splenic sequestration; ²HbA_{1c} stabilizes within 6 months; ³One death, unlikely related to LentiGlobin, > 18 months post treatment in a patient with significant baseline SCD-related cardiopulmonary disease.
⁴Note: In the last dataset, one patient had a non-serious VOC expression at Day 107. This event is recorded as an investigator reported VOE but does not meet the definition of a protocol VOE.
⁵DP, drug product; ER, emergency room; IC, informed consent; max, maximum; min, minimum; sVOEs, severe VOEs; VOE, vaso-occlusive event; VOC, vaso-occlusive crises.

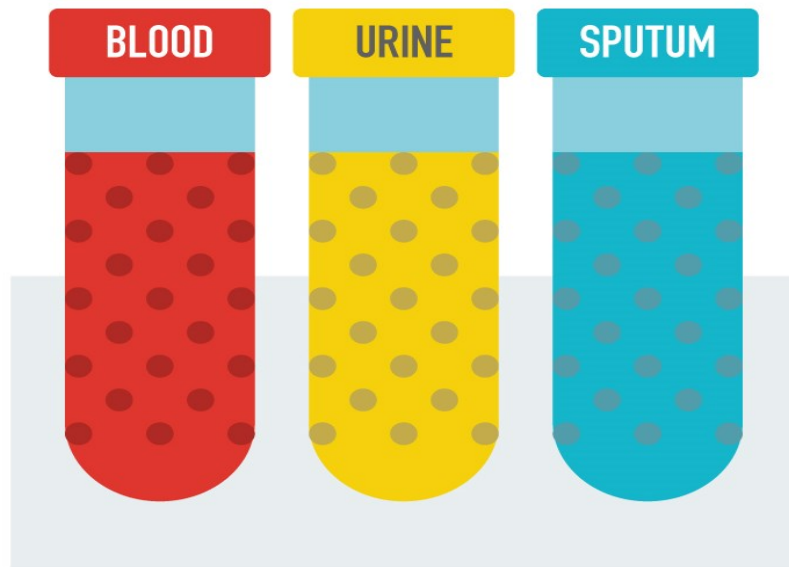
Data as of 20 August 2020 ⁸

1. Science...

1st area for discussion

LIQUID BIOPSY

A new, noninvasive technique that can detect disease biomarkers in:



- Guardant Health
- Roche
- Neo Genomics
- Qiagen
- ArcherDX
- Bio-Techne
- Resolution Bioscience
- Personal Genome Diagnostics
- Laboratory for Advanced Medicine (LAM)
- Lucence Diagnostics
- Foundation Medicine Inc
- Biocept
- Sysmex Inostics Inc.
- Veridex LLC (Janssen Diagnostics)
- Biodesix
- Pathway Genomics
- Exact Sciences
- Angle Plc
- GRAIL Inc.
- NuProbe
- OncoCell MDx Inc
- Merck
- AmoyDx

Source: <https://prevention.cancer.gov/news-and-events/infographics/liquid-biopsy-new>

Liquid Biopsy Enables Precision Medicine

Providing multiple advantages

Minimally invasive¹

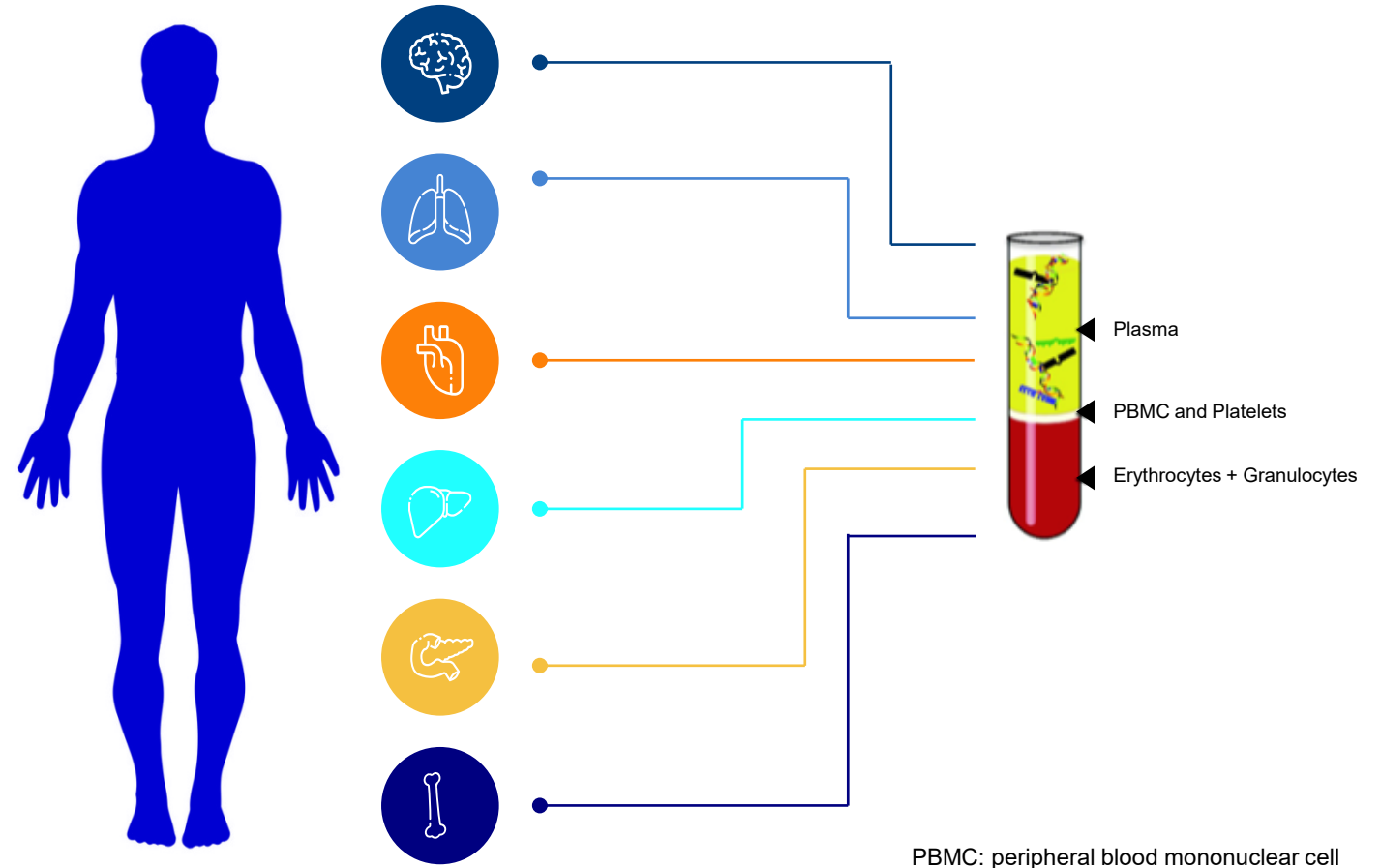
More information about cancer heterogeneity (temporal and spatial)^{1,2}

Enables repeat sampling

(e.g. monitoring progression and/or resistance)¹

Less expensive than tissue biopsies¹

Faster sample preparation than tissue biopsies¹



1. Saarenheimo J, Eigeliene N, Andersen H, et al. The Value of Liquid Biopsies for Guiding Therapy Decisions in Non-small Cell Lung Cancer. *Front. Oncol.* 2019 Mar 5;9:129.

2. Rapisuwon S, Vietsch EE, Wellstein A. Circulating biomarkers to monitor cancer progression and treatment. *Comput Struct Biotechnol J.* 2016 Jun 1;14:211-22.

Liquid Biopsy Market Landscape

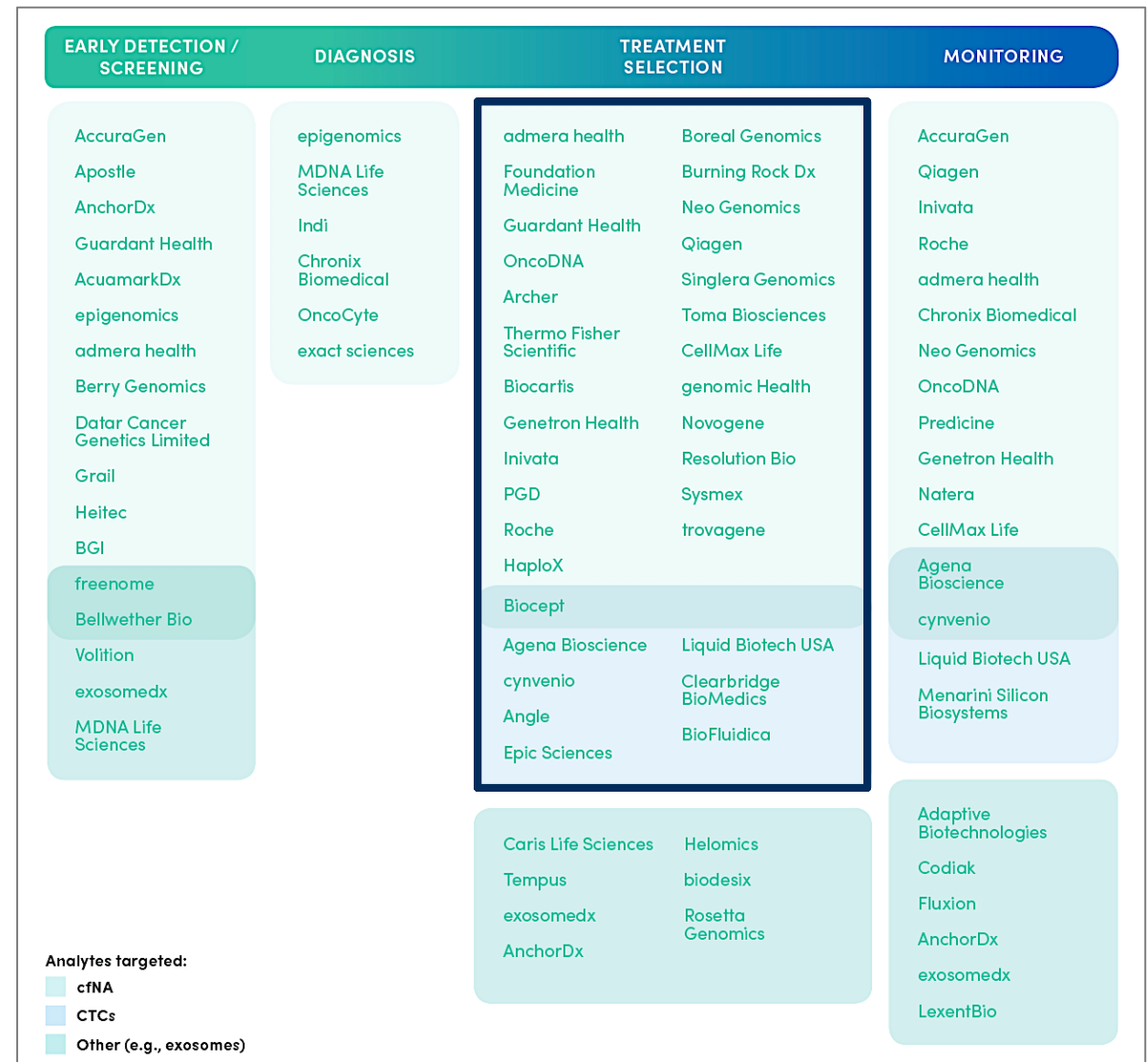
Treatment selection most popular application

Liquid Biopsy Applications & Market Players



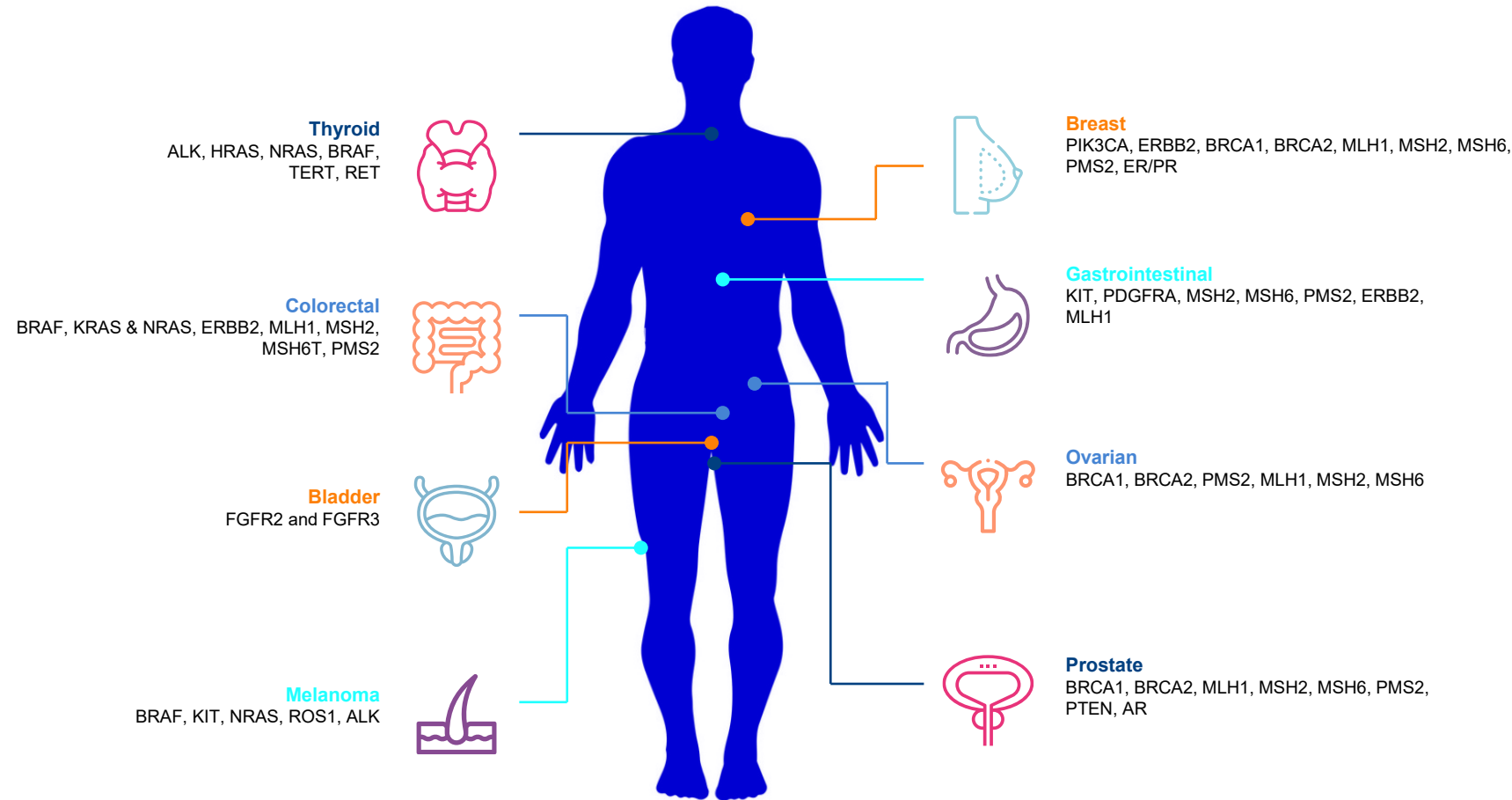
With more than 80 companies competing in the liquid biopsy market, the treatment selection application is the most popular.

Liquid Biopsy Market Report and Stakeholder Toolkit. Decibio. 2019.
<https://www.decibio.com/resources-library/white-papers/liquid-biopsy-stakeholder-toolkit/>



A Growing List of Biomarkers/Diagnostics

Biomarkers in US guidelines and drug labels for highly prevalent tumors¹⁻³



Solid tumors (pan-cancer)

NTRK

TMB

MSI

Sources: 1. <https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications> (accessed on December 21st, 2020); 2. www.nccn.org (accessed on April 1st, 2020); 3 – Courtesy of PierianDx CGW knowledgebase, as of March 1st /2020.

Diagnostic Biomarker Segmentation for Top Solid Cancers

Expansion of diagnostic biomarkers presents opportunity for Precision Medicine

Nearly all major cancers have witnessed increasing biomarker-based segmentation over the past two decades

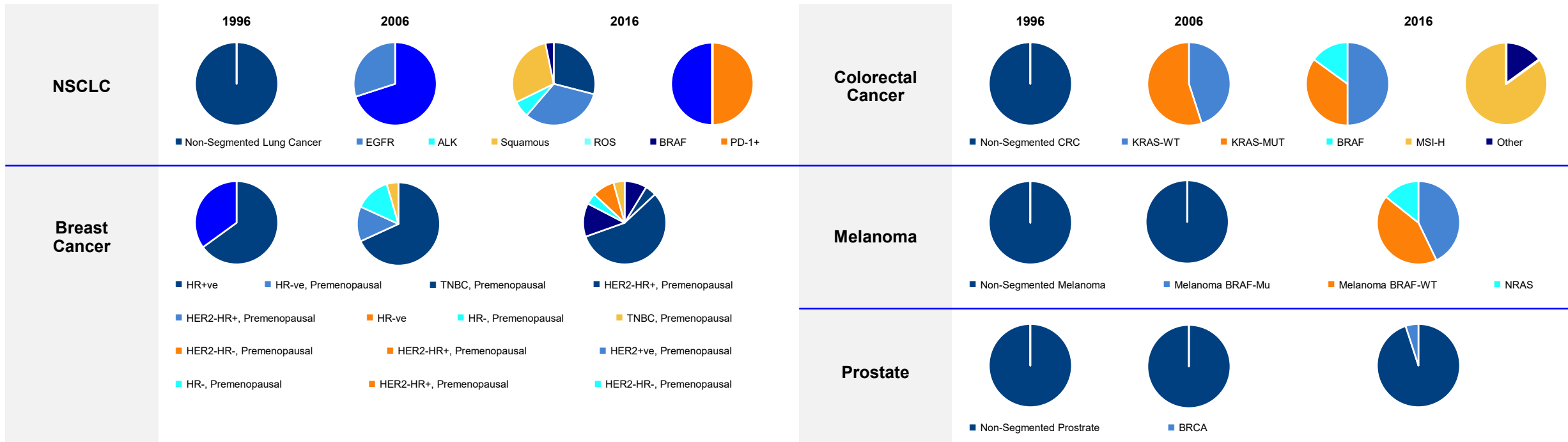


Chart adapted from: Decibio: 2019 Liquid Biopsy Market Report – Stakeholder Toolkit: <https://www.decibio.com/resources-library/white-papers/liquid-biopsy-stakeholder-toolkit/>

Note: Breast Cancer chart sequence contains multiple duplications in the key.

Tumor Heterogeneity Presents a Challenge

Liquid biopsy (ctDNA) can help address sampling bias

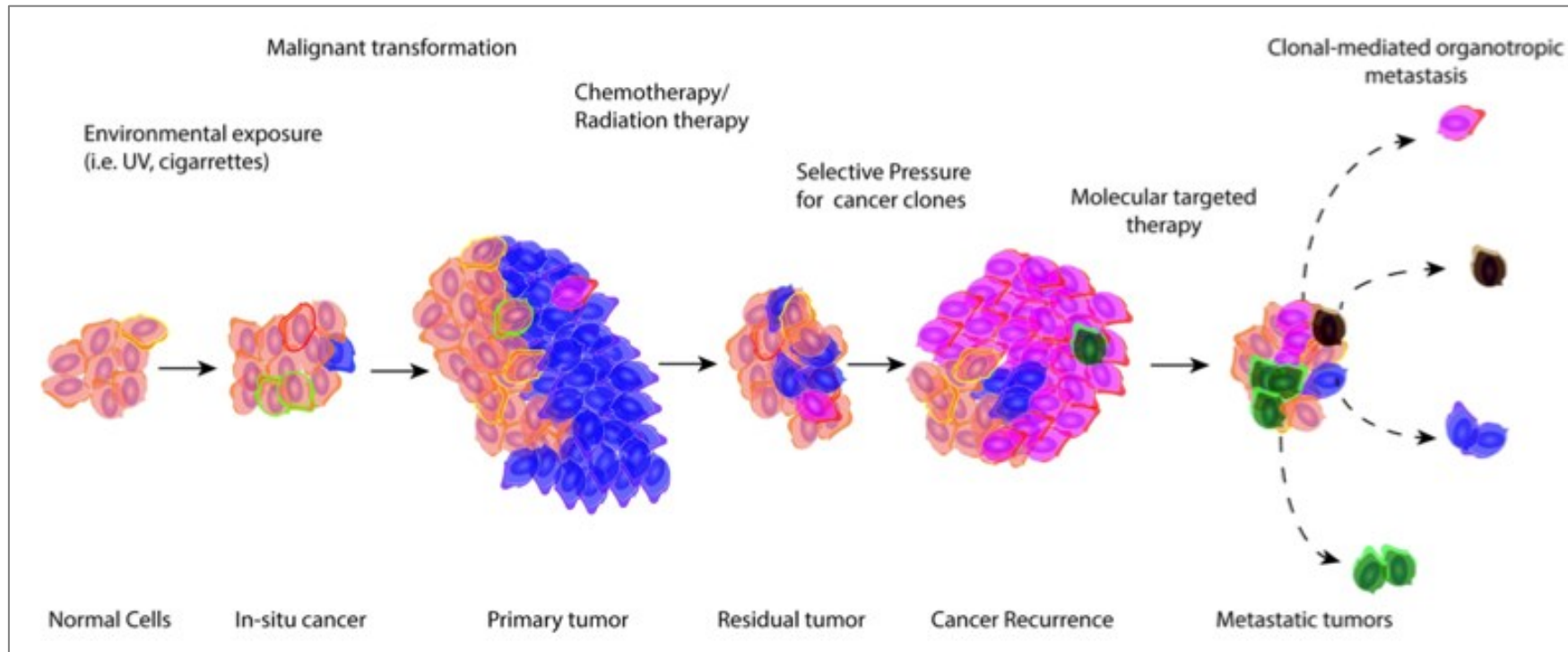


Image: Reference 1, Figure 2.

Each tumor clone may harbor a genomic variant sensitive to a specific therapy

ctDNA from blood can represent clones from a single primary tumor, as well as multiple metastatic sites

1. Rapisuwon S, Vietsch EE, Wellstein A. Circulating biomarkers to monitor cancer progression and treatment. Comput Struct Biotechnol J. 2016 Jun 1;14:211-22. doi: 10.1016/j.csbj.2016.05.004. PMID: 27358717; PMCID: PMC4913179.

How Far Along Are These Companies? Straddling These 3 Areas in 2021...

1. Science side – still **developing** final versions of their tests
 - Using AI and machine learning – to uncover the best set of signals (e.g., methylation) that improves the test characteristics
 - Setting the specificity very high – few false positives (98-99%)
 - Doing what they can to have reasonable sensitivity (50+%)
 - Weeding out indolent disease – watchful waiting
2. **Conducting** analytical and clinical validation studies in the intended populations (e.g., low prevalence for cancer)
3. **Conducting** clinical utility studies

Recent Data from ASCO 2021

Study to evaluate the sensitivity and specificity of test to identify colorectal cancer in blood (fragments, methylation patterns, etc.)

- ▶ Using a classifier previously developed on >600 patients
- ▶ Sample of 434 patients with known CRC and 271 matched controls

RESULTS

- ▶ Sensitivity of 91% (88% for Stage I-II cancers)
- ▶ Specificity of 94% (255/271 patients)

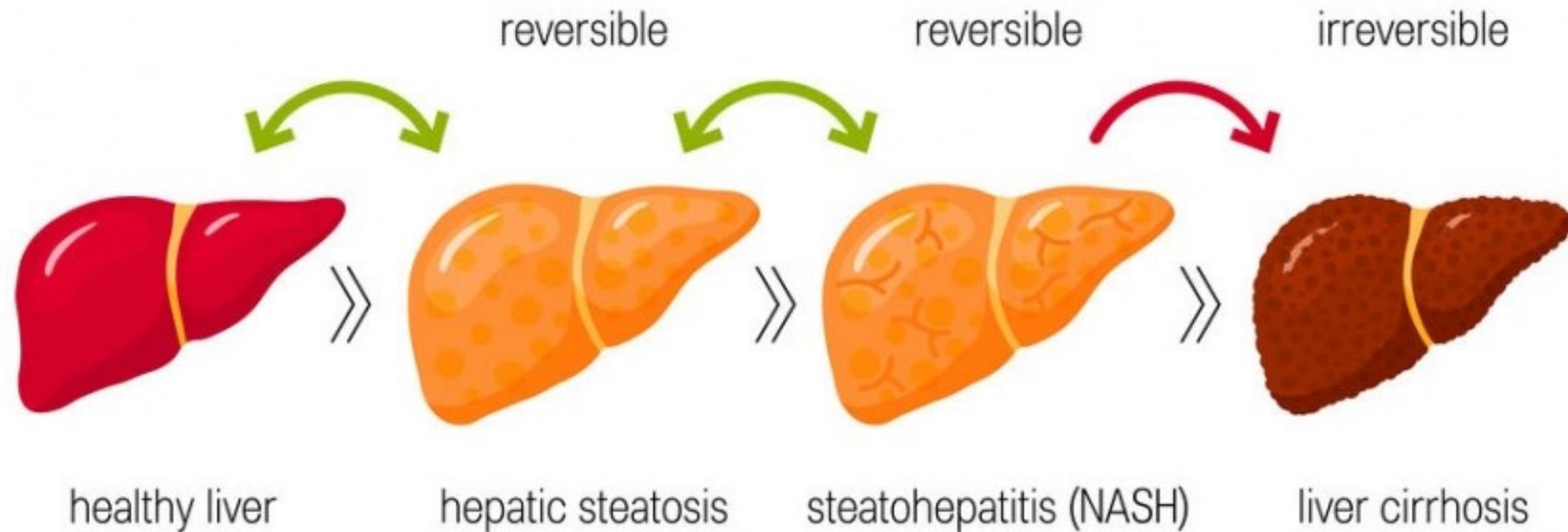
CONCLUDING Enrollment of a 10,000-patient registration study in low prevalence population this fall

NASH – Non-alcoholic Steatohepatitis

140 Drugs in Pipeline, 5 in Phase 3

Fatty liver 20% of USA adults, NASH 5% of USA = 17MM

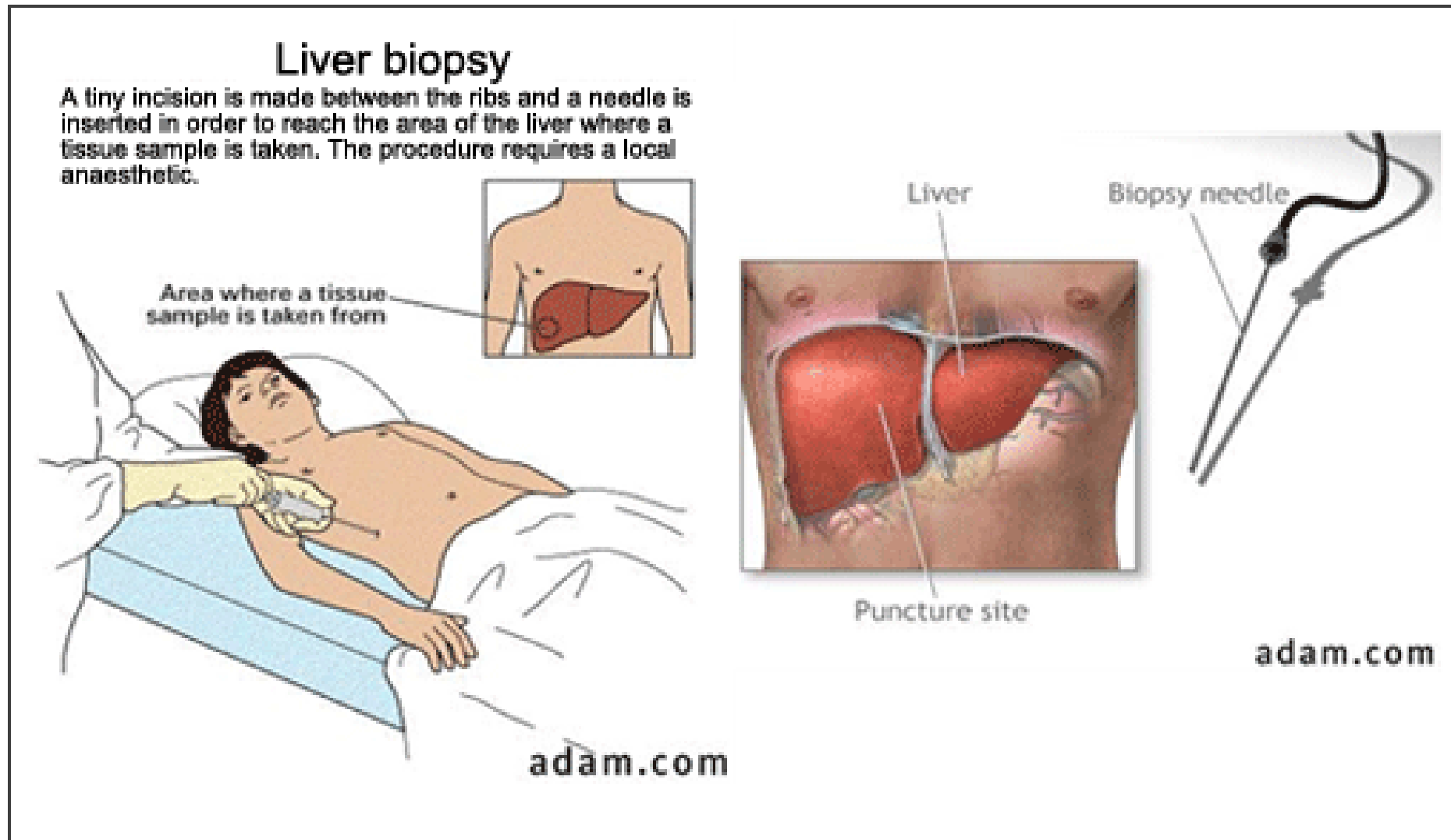
STAGES OF LIVER DAMAGE



Source: <https://www.endocrineweb.com/conditions/type-2-diabetes/liver-disease-what-you-need-know-about-common-problem-diabetes>

Diagnostic Challenge With NASH

Gold Standard Is Percutaneous Liver Biopsy



NIS-4 – Newest Game in Town to Detect NASH With Simple Blood Test

ROC not >0.90 – and not big separation from other modalities

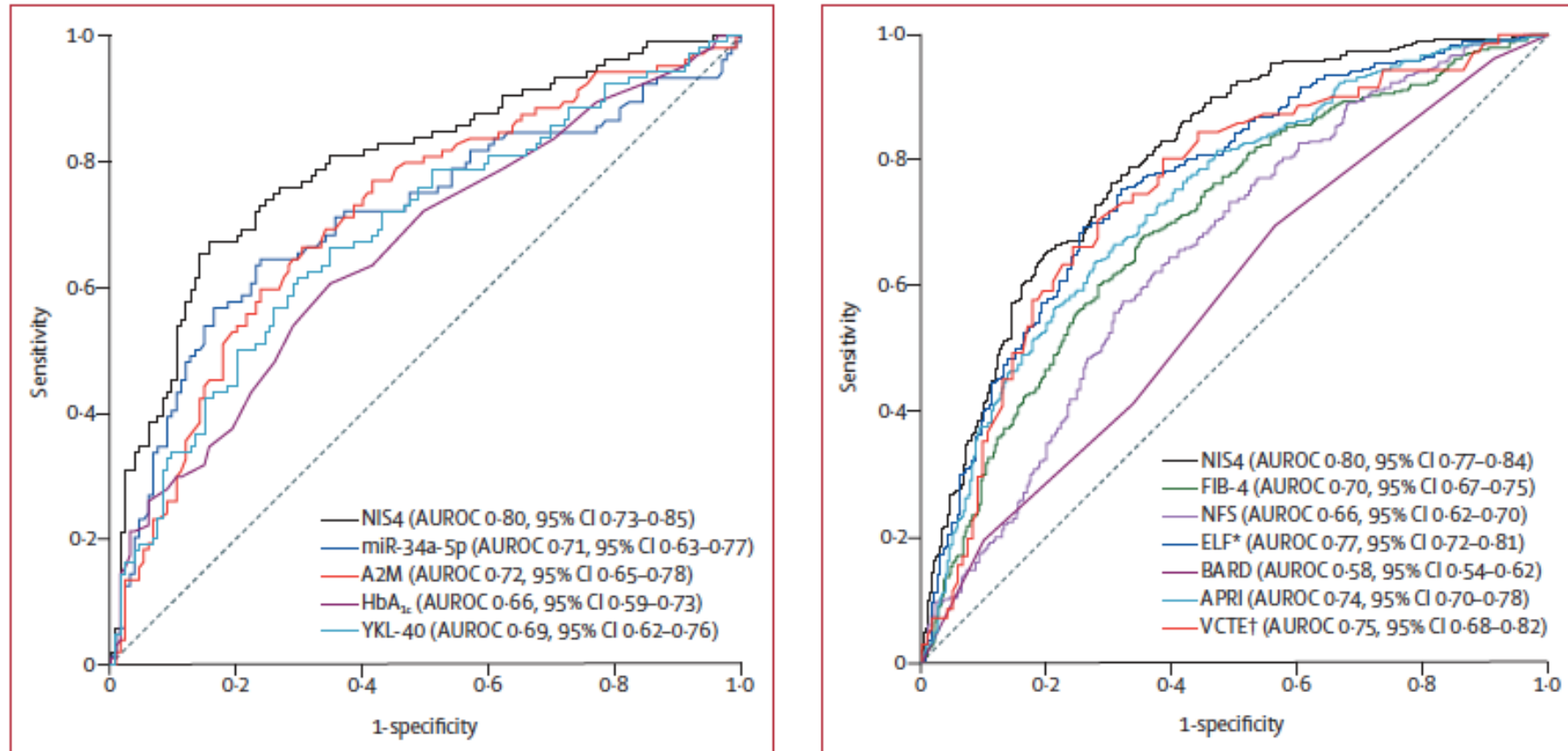
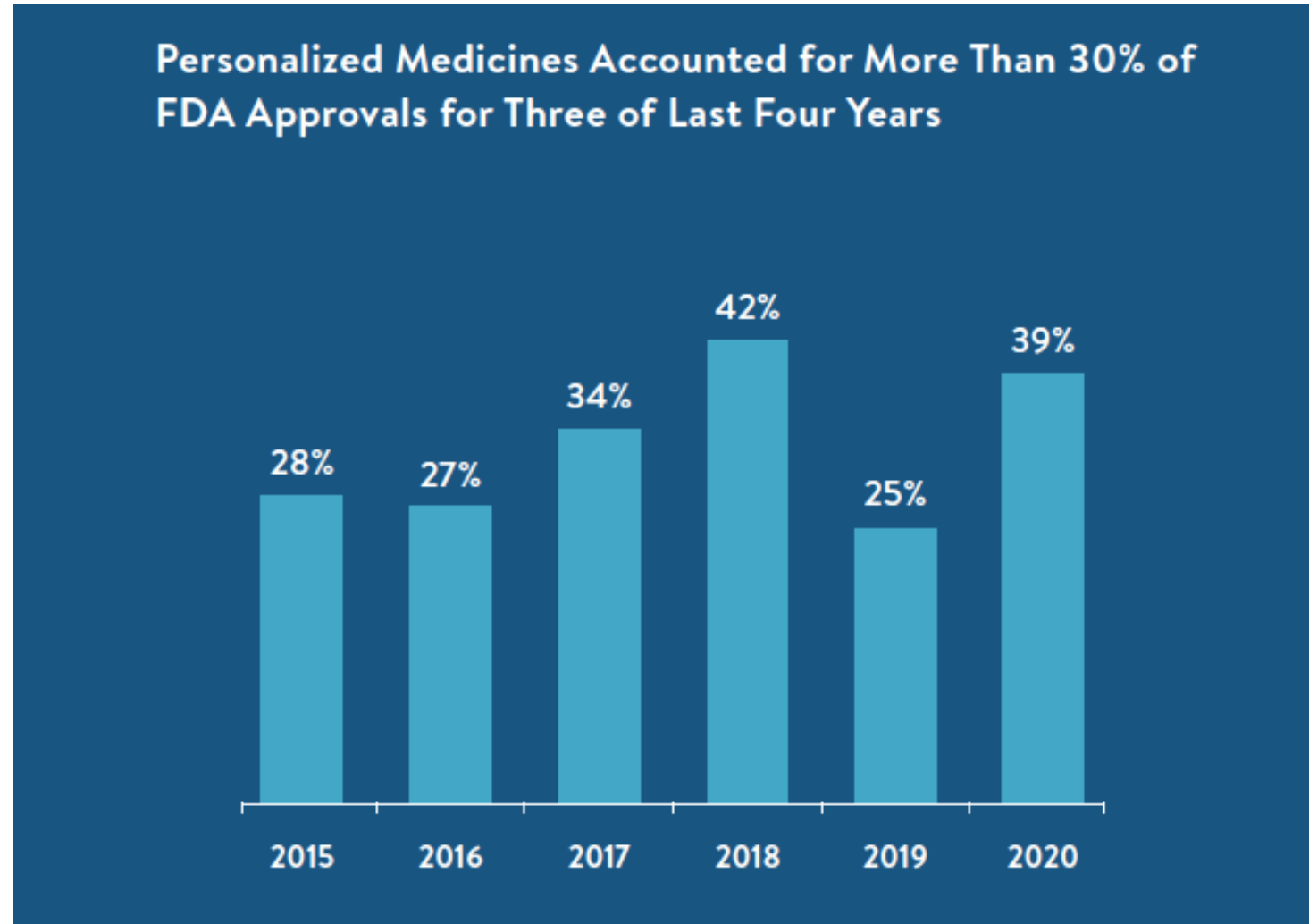


Figure 3: Comparison of ROCs and AUROCs obtained in the pooled validation cohort (n=702)

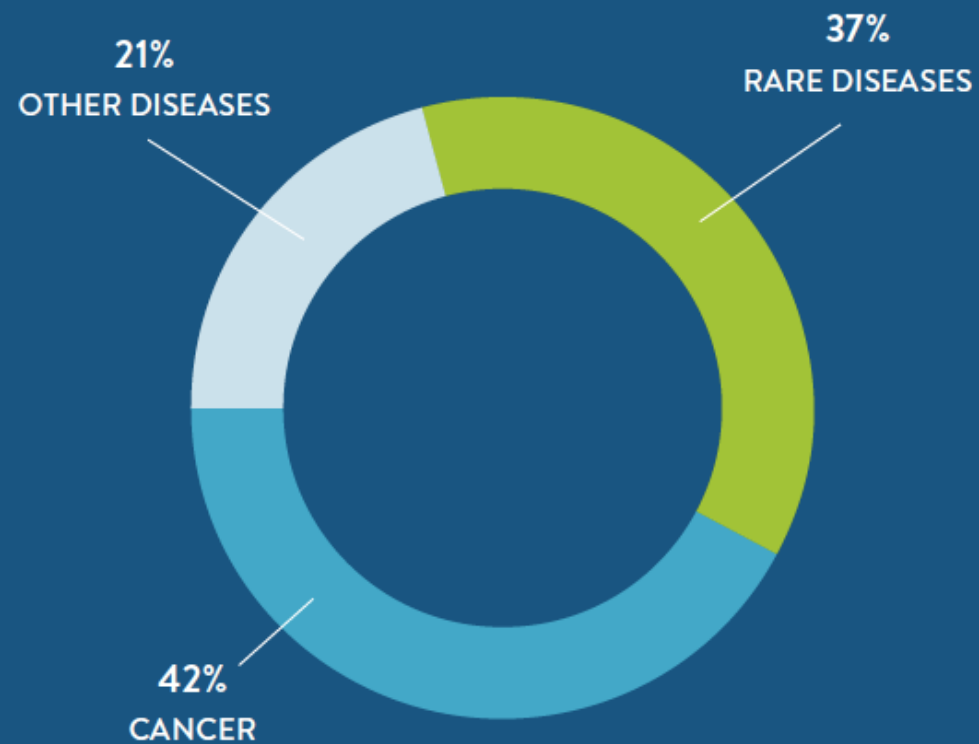
2. Drug Pipeline: Full and Impacting New Diagnostics Especially Personalized Medicines



Source: https://mma.prnewswire.com/media/1436855/PM_at_FDA_The_Scope_Significance_of_Progress_in_2020.pdf?p=pdf

Fewer Than Half Are for Cancer

New Molecular Entities Are Indicated for Treatment of
Cancer, Rare Diseases, and Common/Infectious Diseases



2020 P.M. Approvals and New Tests Involved

Drug	Disease	Test
Avapritinib	Metastatic GIST	PDGFRA exon 18
Bempecoic acid	FH	LOLR, APOB, PCSK9
Tucatinib	Metastatic breast cancer	HER2
Pemigatinib	Cholangiocarcinoma	FGFR2 fusion, rearrangements
Sacatuzumab	Metastatic triple negative breast cancer	ER, PR, HER2
Caprnatinib	NSCLC	MET exon 14
Selpercatinib	Lung, thyroid cancer	RET fusion
Inebilizumab-cdon	Neuromyelitis optica spectrum disorder	AQP4
Fostemsavir	Severe HIV – with multi-drug resistance	HIV expression levels
Risdiplam	Spinal stenosis	SMN2
Oliceridine	Acute pain	2d6
Viltolarsen	Duchenne's MD	DMD exon 53
Satralizumab-mwge	Neuromyelitis Optica Spectrum disorder	AQP4
Pralsetinib	NSCLC	RET fusion
Lonafarnib	Progeroid laminopathies	LMN4 and/or ZMPSTE24
Lumisiran	Hyperoxaluria Type I	HAO1
Setmelanotide	Obesity due to POMC deficiency	POMC, PCSK1, LEPR
Berotrastat	Hereditary angioedema I and II	CI-INH
Margetuximab-cmkb	Breast cancer	HER2

Global Market for Companion Diagnostics Increasing 12.9% Annually

Attractive Opportunities in the Companion diagnostics market

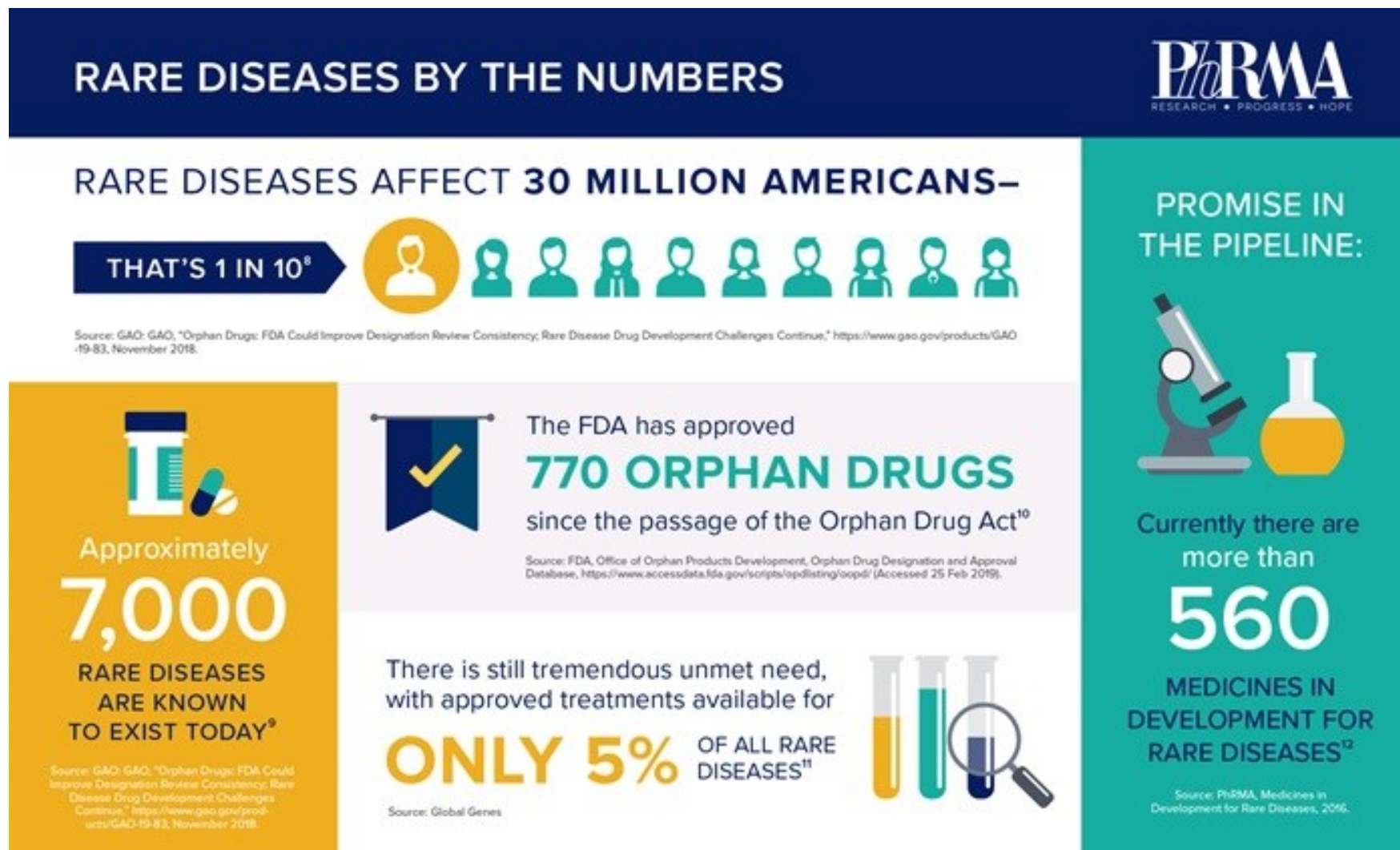


Source: <https://www.marketsandmarkets.com/Market-Reports/companion-diagnostics-market-155571681.html>

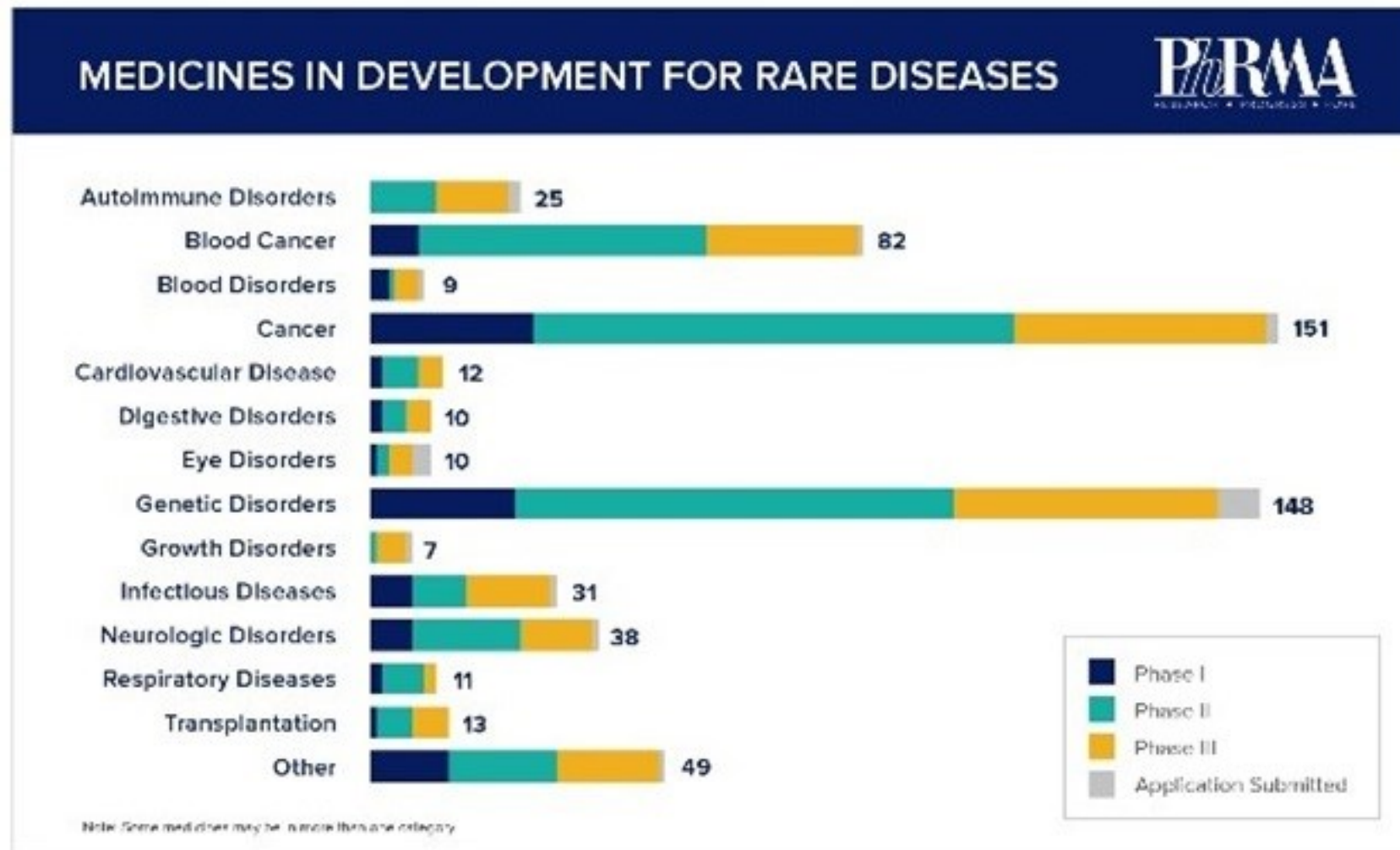
3. Rare Disease Treatments

- ▶ Rare diseases
 - Defined as <200,000 people in USA with the disease by FDA
- ▶ Orphan Drug Act of 1983 spurred development of treatments
 - Since then, >700 drugs approved for rare indications/diseases
- ▶ Most of these require specific diagnostic tests to ensure the right patient gets the right therapy

Only 5% of Rare Diseases Have a Treatment, but 550+ Drugs Under Development – Most With Diagnostics



550 Pipeline Drugs for Variety of Rare Diseases



Technologies Used in Rare Disease Diagnostics

- ▶ Mass spectrometry,
- ▶ Microarrays,
- ▶ Next-generation sequencing (NGS),
- ▶ PCR,
- ▶ Sanger sequencing and
- ▶ other (e.g., karyotyping, fluorescent in situ hybridization).

Project Baby Bear – Others in Development

Background

- ▶ Funded by California state legislature (Medi-Cal)
- ▶ 5 hospitals from 11/18 thru 5/20
- ▶ Child <1 y.o. with critical care admission with no clear non-genetic cause

Results

- ▶ 74/184 babies had genetic disorder diagnosed (40%)
- ▶ 58 babies had change in care (surgery, meds, diet) – 32%
- ▶ Costs saved between \$3K-6K per baby screened
 - 89-93% related to LOS reduced
 - Avoided major procedures (tracheostomies, g-tube insertions)
 - 7-11% avoided other testing

Future Considerations

- ▶ **Technology assessment critical** as these tests can be expensive
 - Clinical validity
 - Analytic validity – in the intended population?
 - Clinical utility – does anything change knowing the result?
- ▶ **Devil is in the details**
 - Even if test idea makes sense – technology to produce the test can differ
- ▶ **Policy** decision-making has to **balance benefits and costs**
- ▶ **Communication/interpretation** with healthcare providers more challenging than ever – role of CDSS, CME, KOLs

Summary

- ▶ Full pipeline of diagnostic tests on the horizon
- ▶ Near-term diagnostics follow the evolving sciences
- ▶ Opportunities of these new tests is to gain efficiencies, remove error and tailor care better—which is the upside
- ▶ Challenges
 - Evidence generated may be lacking
 - Clinician understanding may not be present
 - Nuanced differences between tests
 - Integration of testing into total care

Final Thought...

The best way to predict the future—is to create it

PETER DRUCKER

EPSTEIN HEALTH

ANALYZE · PREDICT · TRANSFORM · LEAD



IMPROVING CARE AND REDUCING COSTS BY MANAGING LAB SERVICES

Fireside Chat With Mark Werner & Sherry Mullies of Blue Cross and Blue Shield of North Carolina

Moderated by Martha Owens Perry
Retired VP of Health Care Services
BlueCross BlueShield South Carolina



30 Sep 2021 | Press Release

Blue Cross NC, Avalon Healthcare Solutions Collaboration Yields \$112 Million in Cost Savings, Quality Improvements for Lab Services

DURHAM, N.C. – Blue Cross and Blue Shield of North Carolina (Blue Cross NC) has found success in delivering cost savings in another area of health care—laboratory services. The company, working with Avalon Healthcare Solutions, a leading lab benefits manager...





CLOSING REMARKS

Bill Kerr, M.D., Chief Executive Officer, Avalon

SAVE THE DATE

NOVEMBER 16 | 2:00-3:00 PM EST

Hot Topics Impacting Health Plans and Member Health

- Impact of COVID-19 on Preventive Lab Screenings
- Deeper Dive Into No Surprises Act From Julie Barnes
- How the Democratic Spending Bill Will Impact Healthcare Policy

Thank you

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