prism/RA™
Step Forward
MOLECULAR SIGNATURE TEST

New Strategy for Avoiding Waste and Improving Response for Highest Cost Therapies in Rheumatoid Arthritis

August 2020

Speakers

James Kenney

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One of the biggest problems in **healthcare**

We have expensive drugs that don't work well

Financial Strain

Drugs are costly

#1 targeted therapy sells for almost $20B a year[1]

Clinical Strain

Lack of patient response

66% of patients prescribed do not adequately respond[2]

1) IQVIA, https://www.documentcloud.org/documents/7033463-IQVIA-2019-Drug-Spending-Report.html
2) Strand V, et al. Economic burden of patients with inadequate response to targeted immunomodulators for rheumatoid arthritis 2018; J Manag Care Spec Pharm 2018; 24(4):344-52.

Especially bad in **rheumatoid arthritis**

Stats for leading TNFi therapy

Cost per QALY[1]

$232,644

per Quality Adjusted Life Year
(acceptable range is $50-150k)

Cost per Response[2]

$194,488

annually per patient
achieving an ACR50 response

1) Institute for Clinical and Economic Review (ICER). Targeted immune modulators for rheumatoid arthritis: effectiveness and value, April 7, 2017.
2) Best JH, et al. Rheumatology and Therapy 2020; 7:165-71.

Drugs are **failing**
most autoimmune disease patients

$33B

annual sales of TNFis, the world's largest selling drug class[1]

2 in 3

biologic-naïve RA patients on TNFis have an **inadequate response to treatment**[2]

188%

increase in TNFi spend from 2012 to 2019[3]

0%

change in drug **response rates**[2]

1) Humphreys A. Top 200 medicines annual report 2019: the king of medicines. https://www.pharmalive.com/top-200-medicines-annual-report-2019-the-king-of-medicines.
2) Package inserts from approved therapies.
3) Bowen K and Gleason PP. Prevalence and Cost of Autoimmune Specialty Drug Use by Indication in a 4.4 Million Member Commercially Insured Population. Prime Therapeutics LLC and internal Scipher analysis.

State of **rheumatoid arthritis**

Chronic progressive autoimmune disease

Causes **inflammation** throughout affected areas of the body

Results in **chronic pain, joint destruction,** and **disability**[1]

1.28 to 1.36 million patients within the commercially insured U.S. population[2]

Prevalence increased nearly **30%** from 2004 to 2014[2]

1) Kvien TK. Pharmacoeconomics 2004; 22(2 Suppl 1):1-12.
2) Hunter TM, et al. Rheumatology International 2017; 37:1551–7.

When TNFi therapy **doesn't work**

Health systems waste money and time

Patients with RA who do not respond to TNFi therapy experience:

Response rates decline by additional 27%[1]

83% more **surgeries**[2] and higher likelihood of irreversible **joint damage** and **chronic pain**[3,4]

Continued **opioid**[5-7] and **steroid**[8] use

Time and money **wasted** on ineffective treatments[9]

1) Package inserts from alternative approved therapies after first failing an TNFi compared to taken first-line; 2) Grabner M, et al. Arthritis Res Ther 2017 May 15;19(1):92;
3) Kavanaugh A, et al. Ann Rheum Dis 2018;77:289–292. 4) Scott IC, et al. BMC Rheumatol 2018; 2:32; 5) Day AL and Curtis JR. Curr Opin Rheumatol 2019; 31(3):264-70;
6) Curtis JR, et al. Arthritis Rheumatol 2017; 69(9):1733-40. 7) Zamora-Legoff JA, et al. Clin Rheumatol 2016; 35(5):1137-44. 8) https://www.mayoclinic.org/steroids/art-20045692 <accessed June 10, 2020>;
9) Johnson KJ, et al. Clin Rheumatol 2019; 38:2967–76.

Guidelines **support** biomarker testing

eular

fighting rheumatic & musculoskeletal diseases together

"The major weakness of our current treatment approaches is the **lack of biomarkers** for immediate **stratification** of an individual patient to the most appropriate drug."

— **EULAR**
2019 Guidelines

Founded by **world leaders** in medicine and physics
to solve the knowledge gap between diseases and treatments

Joseph Loscalzo MD, PhD

Chief of Medicine at Brigham & Women's Hospital

Hersey Professor of the Theory and Practice of Medicine at Harvard Medical School

Albert-Laszlo Barabasi, PhD

Director of Northeastern University's Center for Complex Network Research

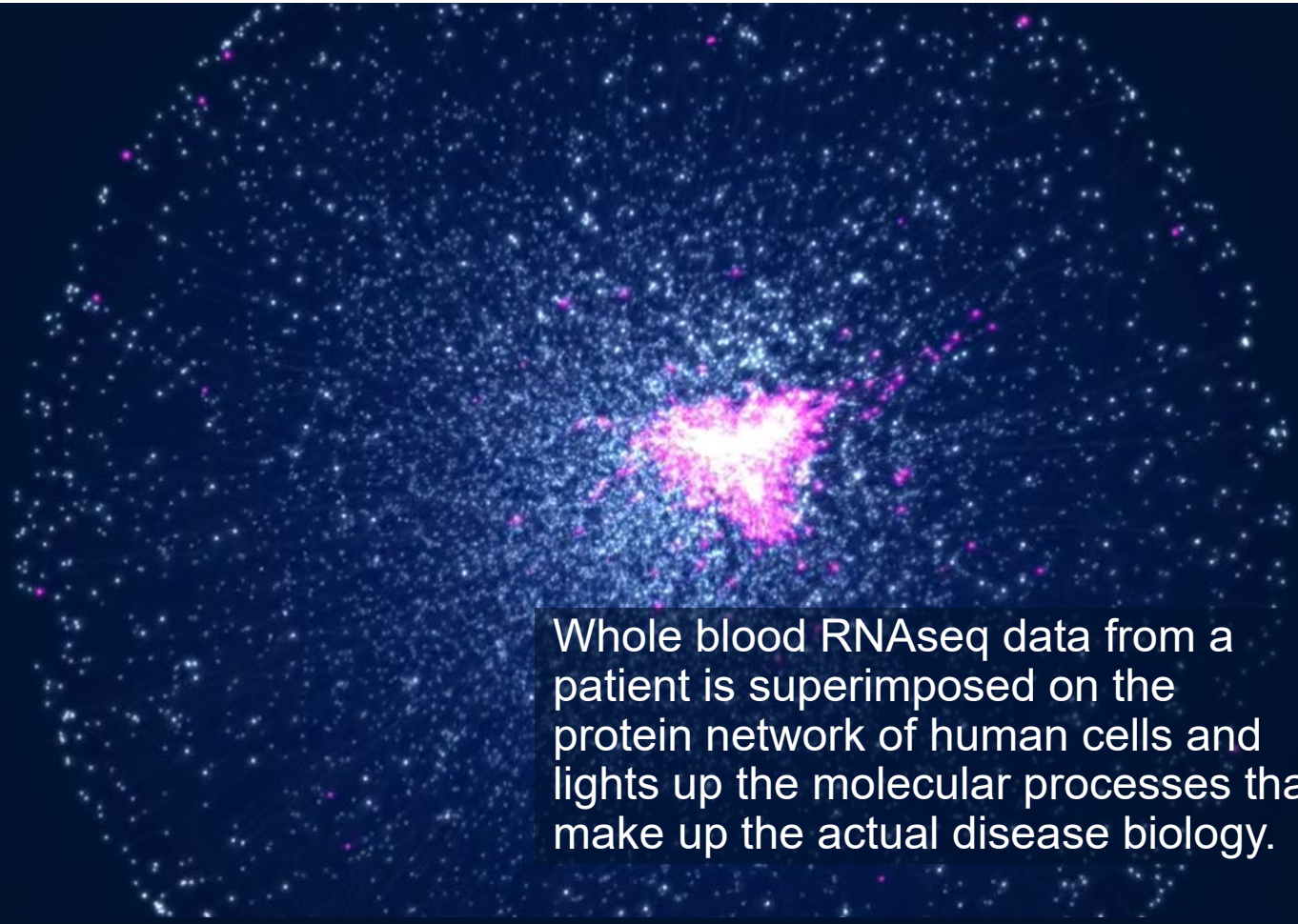
BWH BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL

netsi Northeastern University Network Science Institute

Decade of research with leading network science & AI experts
to identify a patient's individual disease signature

We have developed an AI driven data platform that identifies your disease's molecular signature and determines whether you will respond to a drug.



Whole blood RNAseq data from a patient is superimposed on the protein network of human cells and lights up the molecular processes that make up the actual disease biology.

OXFORD ACADEMIC · Cell · nature communications · PLOS · SCIENTIFIC REPORTS · nature

Purpose-built **technology**

Collaborated with payers to solve pain point caused by excessive cost of TNFi therapies

Partnered with rheumatology experts to optimize adoption

Medicare

PALMETTO GBA® MolDX®

Medicare

Private Payers

OPTUM®

PREMERA BLUE CROSS

aetna™

BlueCross BlueShield Minnesota

FLORIDA

BlueCross BlueShield of North Carolina

WEA trust

UNIVERSITY OF UTAH HEALTH SCIENCES

HealthNow

Humana.

UnitedHealthcare

Introducing **PrismRA®**

Molecular signature test that identifies patients who are unlikely to respond to TNFi therapies

First predictive laboratory test in RA

Intended for use prior to **initiating targeted RA therapies** in patients who had inadequate response or **intolerance to csDMARDs**

prism/RA™ Step Forward™ MOLECULAR SIGNATURE TEST

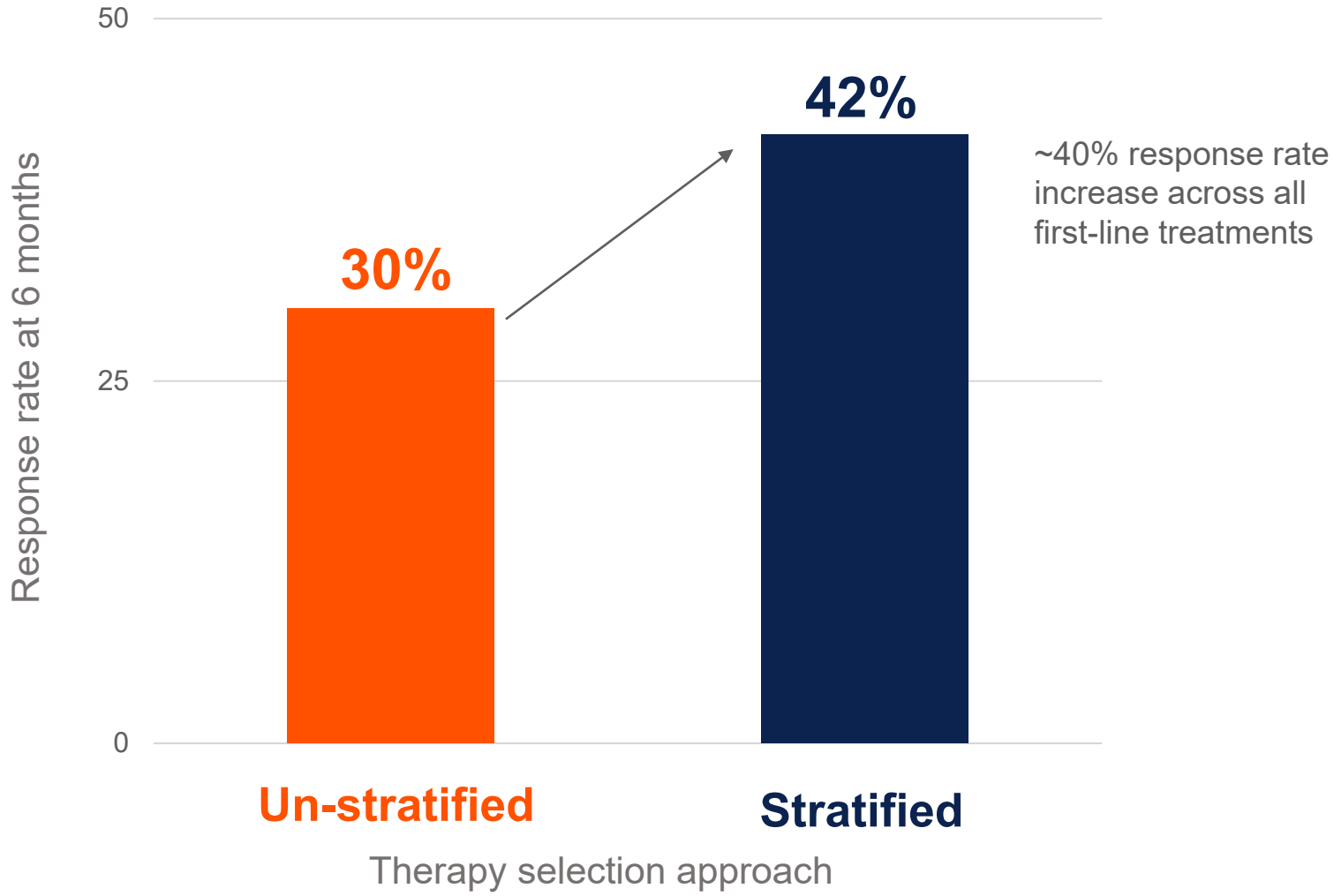
23-BIOMARKER PANEL

Test **performance** characteristics*

* For identification of inadequate responders, defined as achieving less than ACR50

Mellors TW, Withers JW, Ameli A, et al. Clinical validation of a blood-based predictive test for stratification of response to tumor necrosis factor inhibitor therapies in rheumatoid arthritis patients. Netw Syst Med. 2020;3(1):91-104.

Stratifying patients with PrismRA®
can improve response rates by up to 40%



Mellors TW, Withers JW, Ameli A, et al. Clinical validation of a blood-based predictive test for stratification of response to tumor necrosis factor inhibitor therapies in rheumatoid arthritis patients. Netw Syst Med. 2020;3(1):91-104.

Clinical **use** scenarios

All patients considering first-line targeted therapy

Patient failed csDMARDs, considering initial targeted therapy

Administer PrismRA

Molecular signal of non-response

- Detected → Alternate Therapy
- Not Detected → TNFi

Similar clinical symptoms
but vastly different molecular disease biology

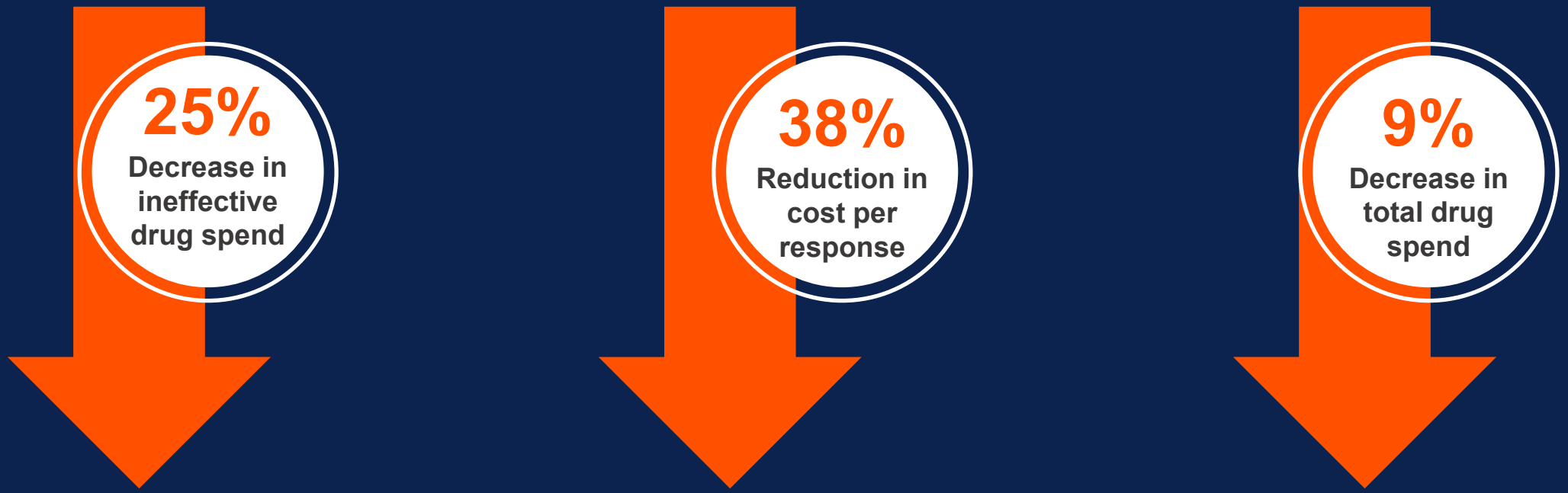
Two similar female patients have failed conventional csDMARD for 3 months and are initiating their first targeted therapy

Mary Wilson
Age: 57
Anti-CCP: Negative
C-reactive Protein: 0.78
Swollen Joint Count: 8

Sarah Carter
Age: 57
Anti-CCP: Negative
C-reactive Protein: 3.63
Swollen Joint Count: 8

PrismRA result	**12.2**	**No Signal**
Non-response signal	**High**	**N/A**
Likelihood of non-response	**>90%**	**N/S**
Results interpretation	**< 5% chance of responding adequately to TNFi**	**No evidence of inadequate response**
Appropriate initial targeted therapy	**Alternative Therapy**	**TNF inhibitor therapy**

Reduction in healthcare system costs



Based on internal budget impact model and actuarial analysis using 2019 drug cost data for 1-million-member plan using default values as published in the PrismRA® clinical dossier.

Transformation Summary

Improve patient response and speed up access to effective treatment with PrismRA®

More patients respond to therapy[1] which preempts disease progression

Avoid wasting time trying multiple drugs[2] leading to more effective drugs from day one

Increase likelihood of targeting correct disease pathway[3] avoiding unnecessary drug exposure and side effects

1) Mellors T, et al. Network and Systems Medicine 2020; 3(1):91-104.
2) Johnson KJ, et al. Clin Rheumatol 2019; 38:2967–76.
3) Drug insert response rates for JAK, IL-6, TNFi for RA patients using ACR50 at 6 months.



Step Forward

Before starting a patient on a targeted therapy,
let PrismRA® help inform your choice.

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prismra.com