Regulatory needs and business case for ensuring product sustainability

March 23, 2017

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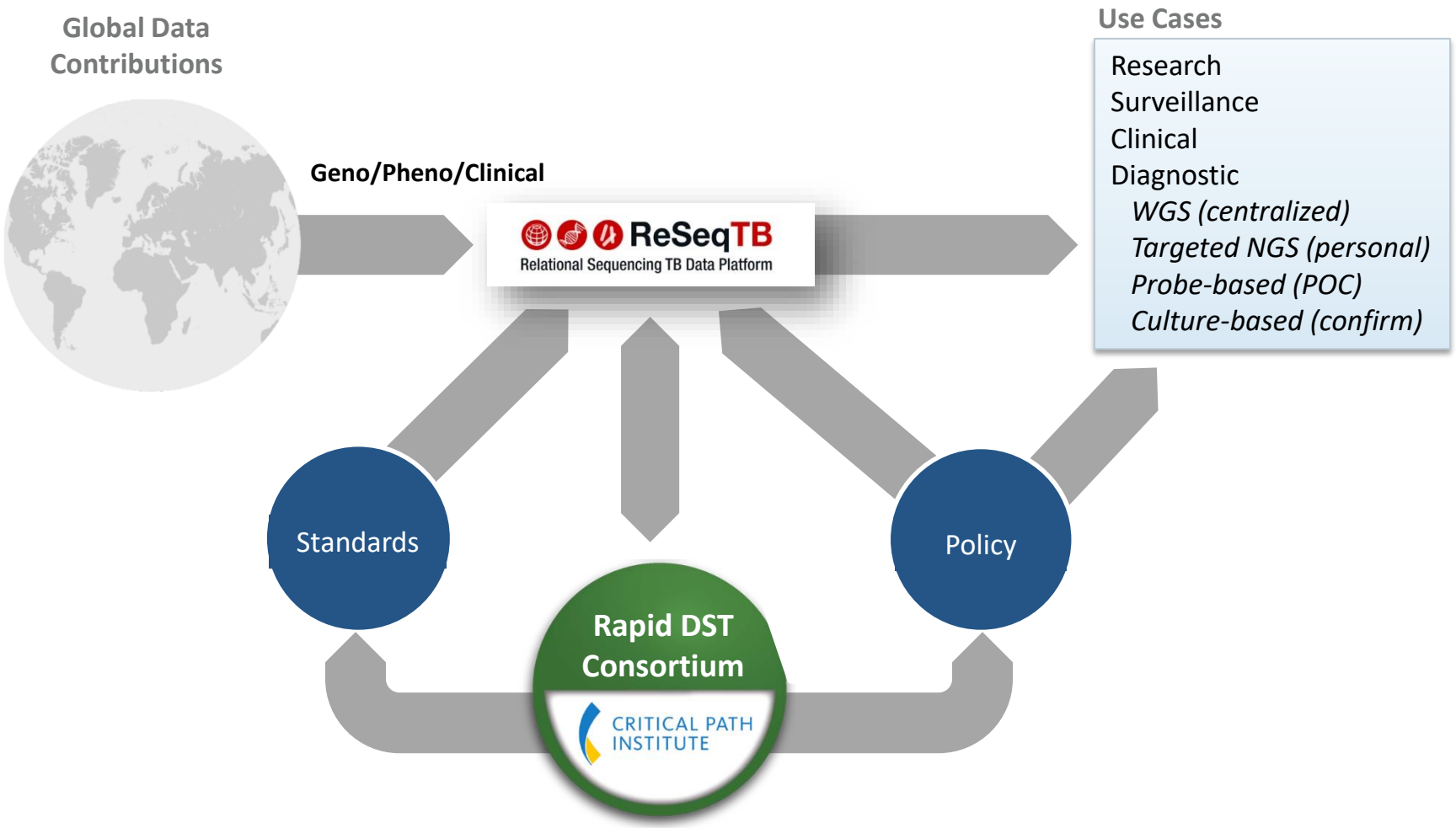
CRITICAL PATH INSTITUTE

VISION FOR RDST



DIAGNOSTICS: THE 'UGLY STEPCHILD' OF GLOBAL HEALTH

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POLICY

Neglected Diseases, Delinquent Diagnostics

DIAGNOSTIC TESTS CONSTITUTE 3 TO 5% OF HEALTH CARE SPENDING BUT INFLUence ~70% of health care decisions (*1*). Furthermore, less than 5% of annual spending on R&D is allocated to diagnostics for neglected diseases (*2*)—tropical infections common in underdeveloped countries, such as malaria, leishmaniasis, and tuberculosis (TB) (*3*).

Last month, the United States and 26 other countries commenced an effort—the Global Health Security Agenda—to prevent and address infectious disease outbreaks before they can spread around the world (*4*). The effort will focus on improving disease monitoring and developing tests for various pathogens. Although the initiative recognizes the need for new diagnostics, the expenditures for the entire effort are hardly sufficient for the extensive undertaking ($40 million this year from the U.S. Centers for Disease Control and the U.S. Department of Defense and $45 million being sought for next year).

Kessel M. Sci Trans Med 2014

GLOBAL CONCERN OVER AMR

No antibiotics without a test, says report on rising antimicrobial resistance

Report by economist Jim O'Neill says global cost of problem could be loss of 10 million lives a year by 2050 and $100tn a year

Many antibiotics no longer work. Photograph: Murdo Macleod for the Guardian

http://www.theguardian.com/society/2016/may/19/no-antibiotics-without-a-test-says-report-on-rising-antimicrobial-resistance?CMP=share_btn_tw

PRODUCT DEVELOPMENT IS STALLED FOR MANY GLOBAL HEALTH DIAGNOSTICS

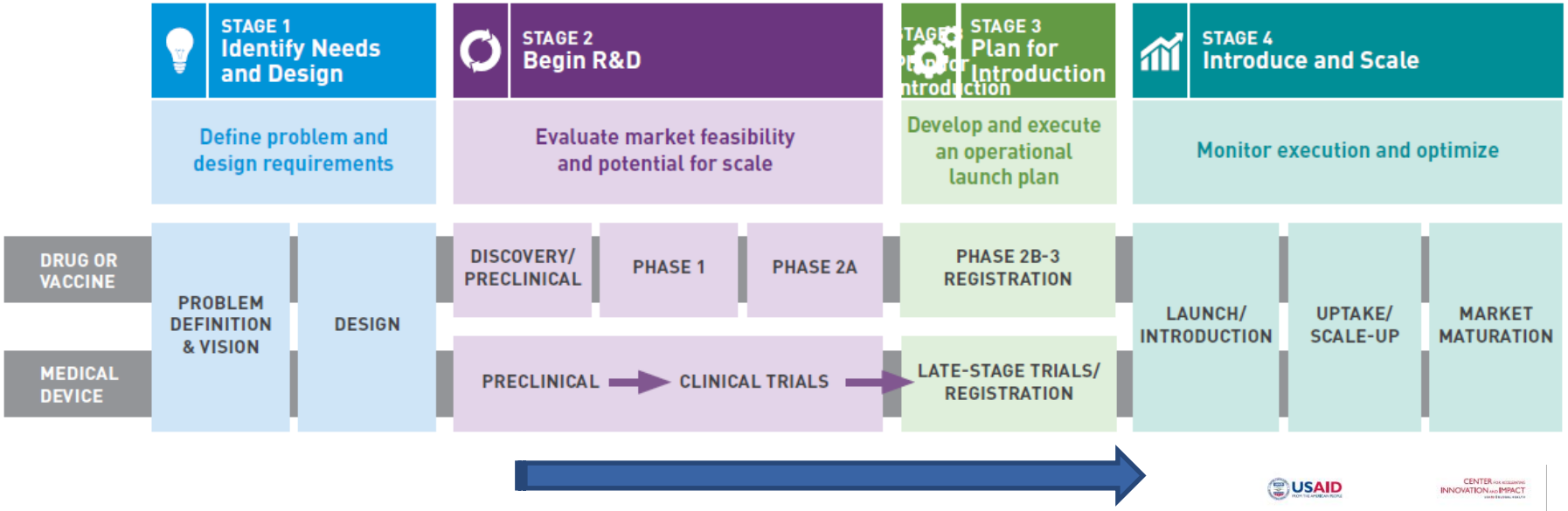
Diagnostic landscape reports for global diseases

- Insufficient investment (money, time)
- Academics and funders are risk-averse
- Inadequate public-private partnerships
- Market forces and decisions
- Regulatory hurdles

End result

1. Likelihood of getting a product across the finish line is low
2. Larger diagnostic companies buy out the small number of successful entrepreneurs

THE IDEAL: SINGLE, LINEAR VALUE CHAIN



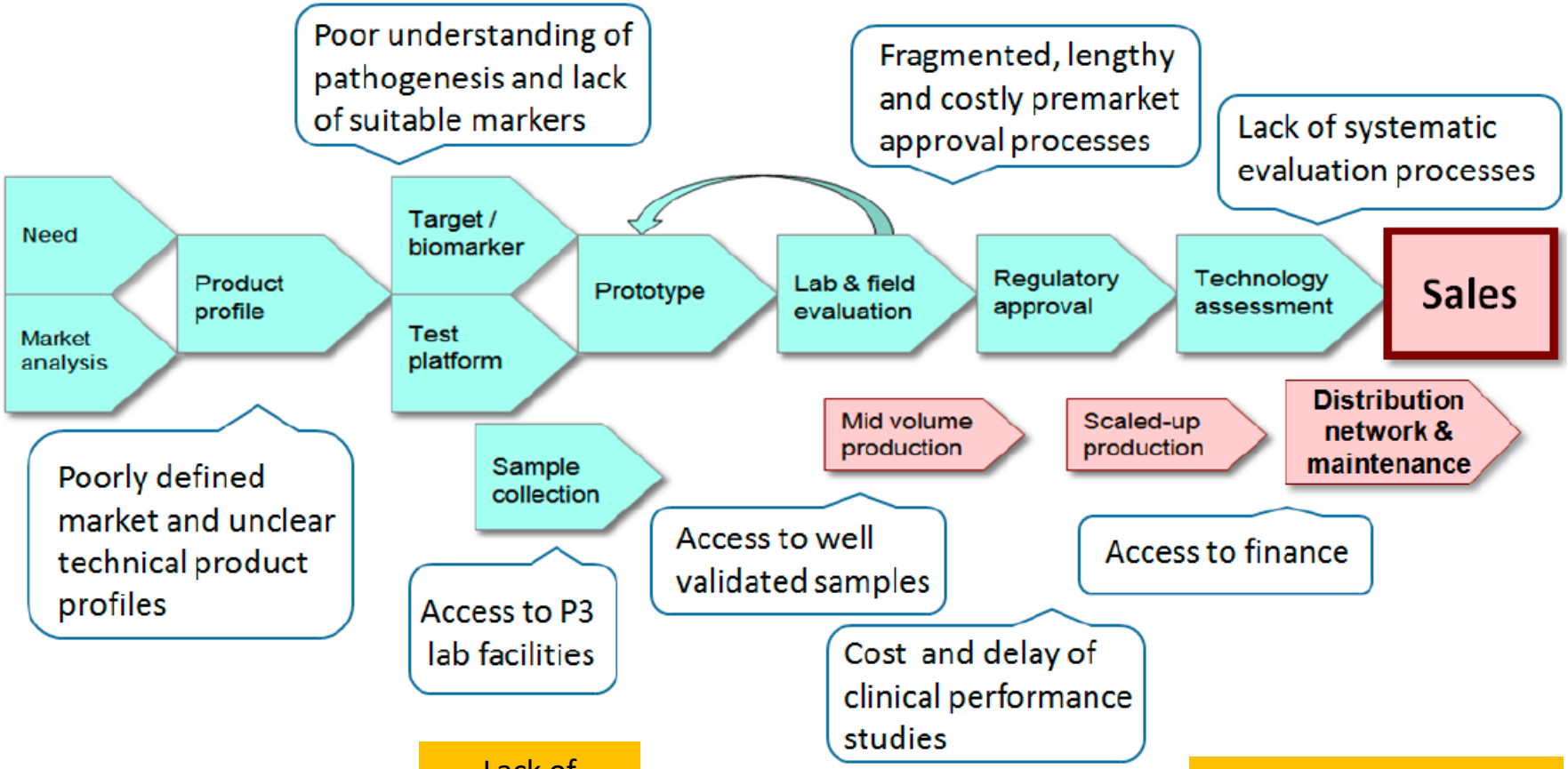
In reality, several intersecting* value chains…

- Product development value chain
- Product evaluation value chain (clinical trials and evidence)
- Policy value chain (global and country-specific)
- Implementation value chain (scale up)
- Impact assessment value chain

- All have different stakeholder groups with different agenda and goals

*often, these value chains do not intersect and that is a problem!

THE REAL: FRAGMENTED VALUE CHAIN



McNerney, Diagnostics 2015

BUT, IF WE WANT TO SOLVE A PROBLEM, WE CAN!

- 80 companies in development & 11 commercial Dx with authorization by FDA or WHO

	Product	Manu-facturer	Manufacturer Sensitivity[1]	Manufacturer Specificity[1]	Independent verification	Targets	Additional materials[4]	Time to results (hrs)
FDA and WHO EUA	ReEBOV	Corgenix	92%[2]	85%[2]	LoD verified; performance[3] field-tested	ZEBOV	3	<0.5
	Xpert Ebola	Cepheid	90-100%	100%	LoD verified	ZEBOV	6	1.5
WHO EUA only	Liferiver	Shanghai BioTech	Label unavailable	Label unavailable	LoD verified	ZEBOV + 3 other EV	10	4-6 or less
	RealStar Filovirus	Altona	100%[5]	100%[5]	Performance verified	ZEBOV + 4 other EV	12	4-6 or less
FDA EUA only	RealStar Ebolavirus	Altona	100%	100%	None	ZEBOV + 4 other EV	12	4-6 or less
	BioThreat-E	BioFire	96%	100%	None	ZEBOV	5	1.25
	NGDS BT-E	BioFire	87-92%	100%	None	ZEBOV	5	1.25
	LightMix	Roche	98%	100%	None	ZEBOV	18[6]	4-6
	EZ1	US DoD	100%	100%	None	ZEBOV	14	4-6
	CDC NP	CDC	98-100%	100%	None	ZEBOV	24	4-6
	CDC VP40	CDC	100%	94-100%	None	ZEBOV	24	4-6

Strength of product:

- High
- Medium
- Low

Technology:

- PCR
- Antigen detection

[1] Results from manufacturer-reported contrived clinical specimen studies; [2] Results from WHO clinical evaluation vs. RealStar; [3] Sensitivity and specificity; [4] Number of instruments, reagents, and other materials required but not provided; [5] Based on analytic studies; [6] Automatic nucleic acid extraction

SOURCE: WHO Selection Of IVD Guidance June 2015, FDA Emergency Use authorizations, Device labels

Slide courtesy: Jim Gallarda, BMGF

EVEN WHEN TESTS EXIST, EMPIRICAL RX IS WIDESPREAD

Engel et al. BMC Health Services Research (2015) 15:550
DOI 10.1186/s12913-015-1223-3

BMC Health Services Research

RESEARCH ARTICLE Open Access

Point-of-care testing in India: missed opportunities to realize the true potential of point-of-care testing programs

Nora Engel[1*], Gayatri Ganesh[2], Mamata Patil[2], Vijayashree Yellappa[2], Caroline Vadnais[3], Nitika Pant Pai[4] and Madhukar Pai[3]

Tropical Medicine and International Health doi:10.1111/tmi.12450
VOLUME 20 NO 4 PP 493–500 APRIL 2015

Use of standardised patients to assess quality of tuberculosis care: a pilot, cross-sectional study

Jishnu Das, Ada Kwan, Benjamin Daniels, Srinath Satyanarayana, Ramnath Subbaraman, Sofi Bergkvist, Ranendra K Das, Veena Das, Madhukar Pai

Summary
Background Existing studies of the quality of tuberculosis care have relied on recall-based patient surveys, questionnaire surveys of knowledge, and prescription or medical record analysis, and the results mostly show the health-care provider's knowledge rather than actual practice. No study has used standardised patients to assess clinical practice. Therefore we aimed to assess quality of care for tuberculosis using such patients.

Lancet Infect Dis 2015
Published Online August 10, 2015
http://dx.doi.org/10.1016/S1473-3099(15)00077-8

Compounding diagnostic delays: a qualitative study of point-of-care testing in South Africa

Nora Engel[1]*, Malika Davids[2]*, Nadine Blankvoort[1], Nitika Pant Pai[3], Keertan Dheda[2] and Madhukar Pai[4]

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2 Lung Infection and Division of Pulmonology and UCT Lung Institute, University of Cape Town, Cape Town, South Africa
3 Division of Clinical Epidemiology, McGill University and McGill University Health Centre, Montreal, QC, Canada
4 McGill International TB Centre, McGill University, Montreal, QC, Canada

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PLOS ONE

RESEARCH ARTICLE

Barriers to Point-of-Care Testing in India: Results from Qualitative Research across Different Settings, Users and Major Diseases

Nora Engel[1]*, Gayatri Ganesh[2], Mamata Patil[2], Vijayashree Yellappa[2], Nitika Pant Pai[3], Caroline Vadnais[4], Madhukar Pai[4]

Treatment as diagnosis and diagnosis as treatment: empirical management of presumptive tuberculosis in India

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Purohit et al. BMC Infectious Diseases (2015) 15:322
DOI 10.1186/s12879-015-1037-2

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

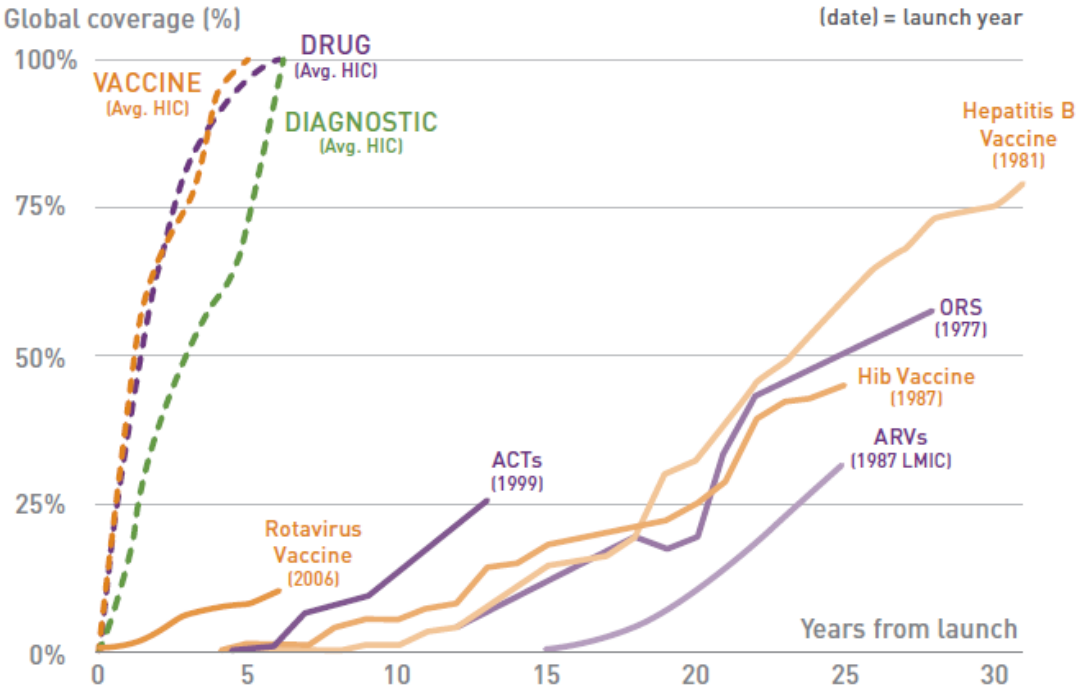
'Multiple-test' approach to the laboratory diagnosis of tuberculosis -perception of medical doctors from Ujjain, India

Manju Raj Purohit[1,2,3*], Megha Sharma[3,4], Senia Rosales-Klintz[3] and Cecilia Stålsby Lundborg[3]

Slide courtesy: Madhukar Pai (McGill)

SCALE UP HAS OFTEN DRAGGED ON FOR DISEASES IN LMIC

Figure 1. Years to scale-up



ACT: artemisinin-based combination therapy
Hib: *Haemophilus influenza* type b
LMIC: lower- and middle-income countries
ARV: antiretroviral
HIC: high-income countries
ORS: oral rehydration solution

While drugs, diagnostics, and vaccines typically scale within the first two years of launch in developed countries, they often take decades to scale in lower- and middle-income countries.

Source: Bill & Melinda Gates Foundation

ADDITIONAL DIAGNOSTIC IMPLEMENTATION CHALLENGES

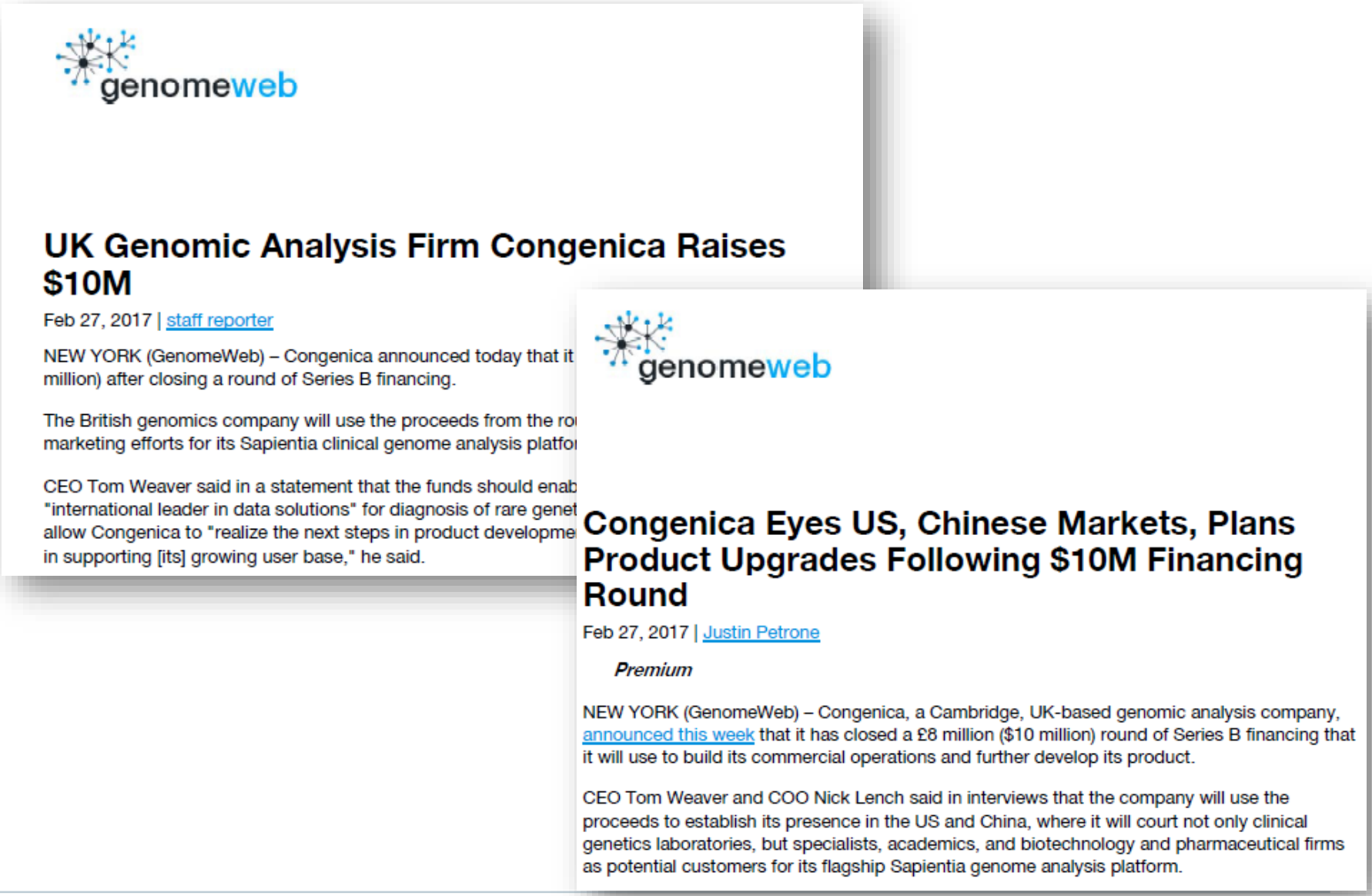
- Reducing diagnostic value chain fragmentation
- Defining diagnostic approval process
- Strengthening linkage to care and treatment
- Health care system strengthening (including connectivity)
- Supply chain management
- Adoption of country policy to address local challenges (algorithms)
- Maintenance and repair
- Training and retention

LOOK AHEAD AT TODAY'S SESSIONS

1. Regulatory and policy: shape country policy and drive markets
   - Current thinking from FDA, EUCAST and WHO around use of NGS for TB
   - Panel discussion including thoughts from industry leaders

2. What is the business case for developing IVD for addressing diseases of global health importance?
   - Models for addressing sustainability
   - Viewpoints from developers

3. Closing Remarks



genomeweb

UK Genomic Analysis Firm Congenica Raises $10M

Feb 27, 2017 | staff reporter

NEW YORK (GenomeWeb) – Congenica announced today that it
million) after closing a round of Series B financing.

The British genomics company will use the proceeds from the ro
marketing efforts for its Sapientia clinical genome analysis platfo

CEO Tom Weaver said in a statement that the funds should enab
"international leader in data solutions" for diagnosis of rare genet
allow Congenica to "realize the next steps in product developme
in supporting [its] growing user base," he said.

genomeweb

Congenica Eyes US, Chinese Markets, Plans Product Upgrades Following $10M Financing Round

Feb 27, 2017 | Justin Petrone

Premium

NEW YORK (GenomeWeb) – Congenica, a Cambridge, UK-based genomic analysis company, announced this week that it has closed a £8 million ($10 million) round of Series B financing that it will use to build its commercial operations and further develop its product.

CEO Tom Weaver and COO Nick Lench said in interviews that the company will use the proceeds to establish its presence in the US and China, where it will court not only clinical genetics laboratories, but specialists, academics, and biotechnology and pharmaceutical firms as potential customers for its flagship Sapientia genome analysis platform.