The Promise of Genomics

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Rick Schatzberg
President & CEO, Generation Health

Julie Yoo
Vice President of Clinical Product Strategy, Generation Health

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Agenda

- Generation Health: Addressing the Opportunities and Challenges in Personalized Medicine
- Genetics for Individualized Health Care
- Our Genetic Benefit Management Strategy
- The Right Starting Point: Expanded Pharmacogenomics

Generation Health: Addressing the Opportunities and Challenges in Personalized Medicine

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Genetic Testing Trends to Consider

Increasing Genetic Testing Utilization & Cost

- Molecular diagnostic testing is expected to grow 14% annually to $5 billion by 2012[1]
- 1 in 5 genetic tests paid by health plans are ordered inappropriately[2]
- Roughly 100 genetic tests are introduced every year[3]

Growing Opportunity To Optimize Drug Use & Safety Through Testing

- The FDA has identified 30+ valid biomarkers, where a genetic test may help inform an Rx decision[4]
- The market for "targeted therapies" where efficacy can be informed by a test is expected to reach $21 billion by 2015[1]
- Each year, an estimated 2 million hospitalizations occur because of adverse drug response, resulting in 100,000 deaths[5]

1. PricewaterhouseCoopers, The New Science of Personalized Medicine – Translating the Promise into Practice, October 2009. 2. Evidence cited by large insurers and AHIP. 3. GeneTest.org.
4. http://www.fda.gov/downloads/drugs/scienceresearch/researchareas/pharmacogenetics/ucm085505.pdf, accessed January 20, 2010. 5. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A met-analysis of prospective studies. JAMA April 15, 1998; 279:1200-1205.

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Payors' Challenges with Genetics

- What are my genetic testing costs?
- What tests should I cover?
- Who should get tested?
- Who should perform the test?
- What are the benefits of testing?

Personalized Medicine: Genetics for Individualized Health Care

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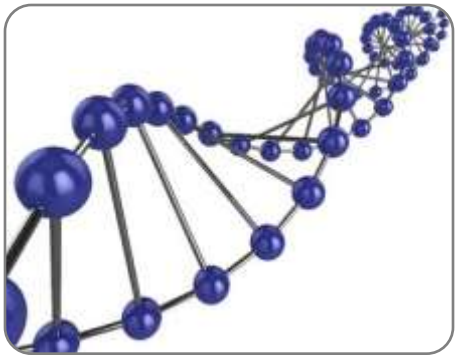
Personalized Medicine: Driven by Innovations in Genetics

- Scientific, clinical and technological advancements have led to the increased accessibility of genetic information for informing personalized health care

23andMe

Knome®

Navigenics



Human Genome Project
First map of human genome completed in 2003 at a cost of $2.7B[1]

DTC Genetics
In 2007, consumers can purchase genetic tests over the Internet for as little as $399

Complete Genomics
Began offering commercial whole genome sequencing service for $5,000 in 2009[2]

1. U.S. Department of Energy Human Genome Program http://www.ornl.gov/hgmis/home.shtm
2. Singer, Emily. "Five Thousand Bucks for Your Genome." Technology Review, February 6, 2009.

Personalized Medicine: Genetics for Individualized Health Care

Personalized medicine has been implemented through the use of genetic tests for numerous applications, including:

Disease susceptibility	Predict future onset of inherited disease
Disease diagnosis	Determine specific disease subtype to inform individualized course of treatment
Disease prognosis	Stratify patients by disease severity to allow for adjustment of treatment regimen
Therapy selection	Determine appropriate drug and treatment regimen based on an individual's genetic code

Source: National Human Genome Research Institute.

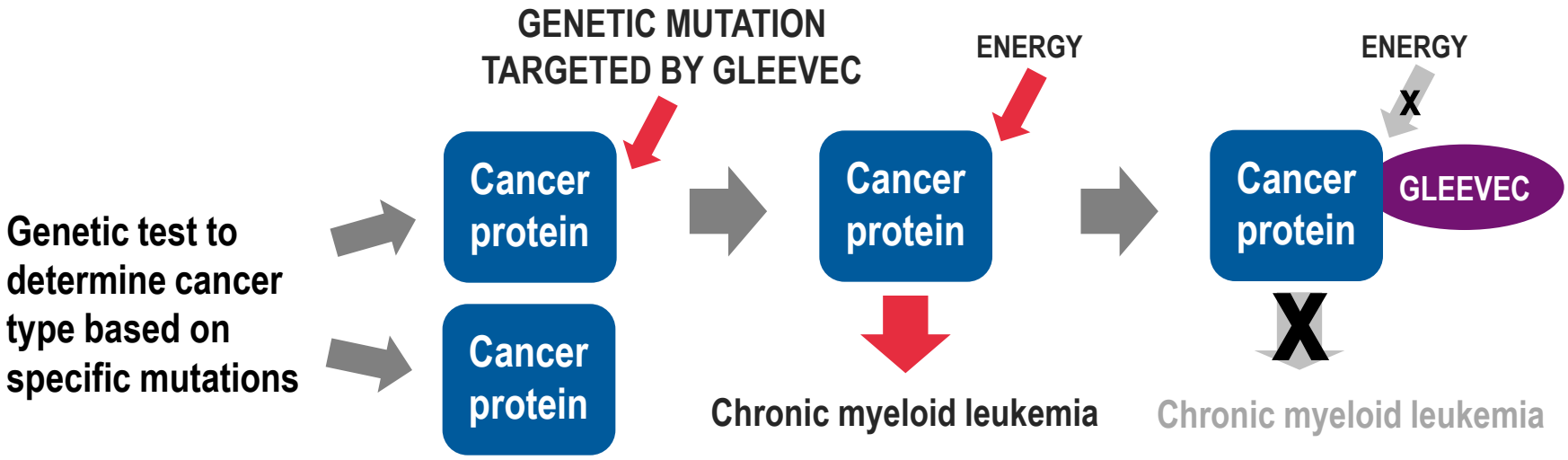
Pharmacogenomics: The Right Drug, For The Right Person, At The Right Dose

Information from a genetic test can inform response and likelihood of adverse reactions to a growing number of drugs.

Source: National Human Genome Research Institute.

Example of Pharmacogenomics: Targeted Cancer Therapy

- Leukemia patients harboring a specific genetic mutation in their tumor cells are administered **Gleevec® (imatinib)**

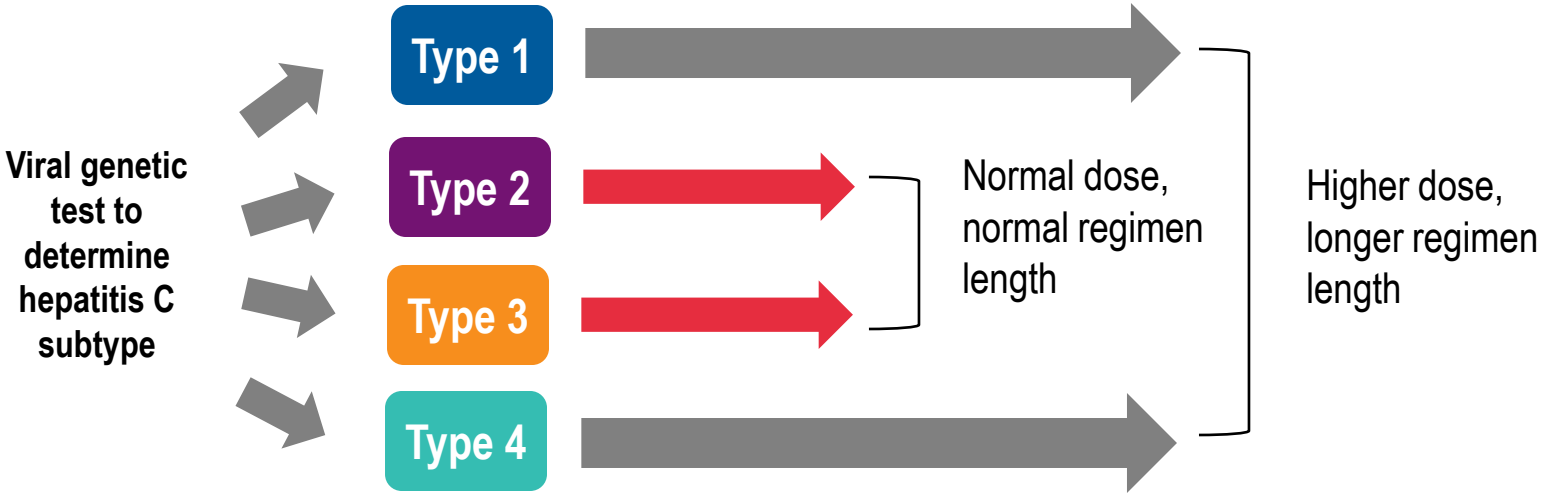


Gleevec results in 5-year survival rates of 90% for CML patients, compared to 30% prior to the drug's approval[1].

1. N Engl J Med. 2006 Dec 7;355(23):2408-17.

Example of Pharmacogenomics: Individualized Hepatitis C Therapy

- Several subtypes of **Hepatitis C virus** exist based on viral genetics
  - Some viral subtypes are associated with poorer prognosis
  - Patients infected with those subtypes benefit from more aggressive therapy regimen



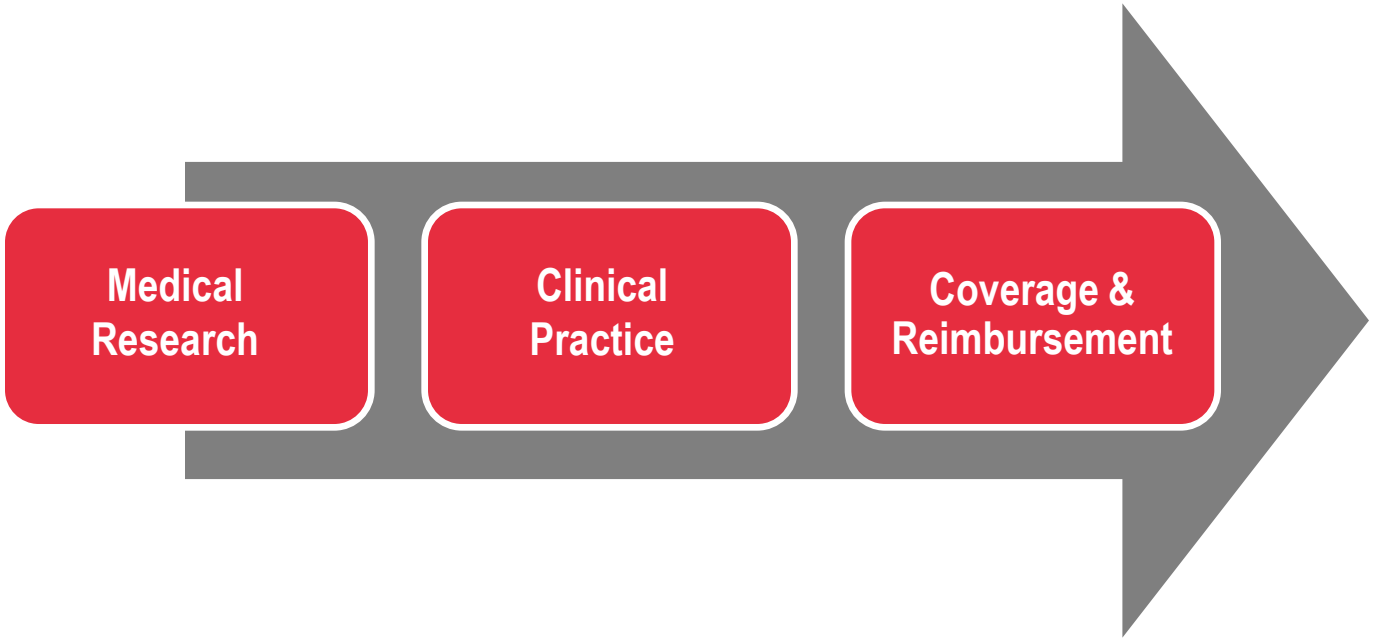
Individualized therapy based on viral subtype helps prevent progression to serious liver disease, including cirrhosis and liver cancer.[1,2]

1. Ann Intern Med. 1997 Nov 15;127(10):855-65.
2. JAMA. 2003 Jul 9;290(2):228-37.

Our Benefit Management Strategies

Premise of Generation Health

Genetic Benefit Management



Optimizing the use of genetic testing will become a critical challenge for payors.

Generation Health Founding Expertise

Pharmacy Benefit Management

Generation Health senior leadership helped build the PBM industry in the 1980s and 1990s

Genetic Testing Lab and Analysis

Significant intellectual capital in genetics and laboratory industry practices

Data Mining and Informatics

Medical claims data mining platform can identify gaps in care

Generation Health Value to CVS Caremark

Genetic Medicine Expertise

- Expert clinical consultative services and panel advice
- Predictive clinical outcome models and savings algorithms
- Identification of new tests for coverage
- Identification of tests that should not be covered

Genetic Benefit Programs

- Clinical outreach and education
- Test facilitation and coordination of lab services for physicians and members
- Utilization management
- Access to team of genetic experts

Best Test™ Genetics Network

- A preferred provider organization of genetic testing labs
- Negotiation of commercial terms
- Lab and test credentialing and monitoring

Expands genetic testing guidelines and provides access to high-quality diagnostics at preferred prices.

A Strategic Partnership

- Integrates the CVS Caremark experience in **pharmacy benefit management** with Generation Health's expertise in **genetic benefit management**
- Expands the CVS Caremark Specialty Guideline Management **pharmacogenomic intervention portfolio** to incorporate non-specialty therapies, the **latest genetic guidelines** and provide access to high-quality diagnostics at preferred prices
- **Enables** more precise prescribing, helping to **improve** patient **outcomes** and reduce overall health care **costs**

Our Comprehensive Genetic Benefit Management Strategy

ASSESSMENT

What are the benefits of testing?

- Clinical Outcomes Studies
- Economic Outcomes Studies
- Test Utilization Rx Analysis
- Medical Savings Analysis

What are my genetic testing costs?

- Targeted Rx Opportunity Analysis
- Self-Assessment Tools
- Retrospective Claims Audit
- Claims Enrichment / Analysis

EVALUATION

CLINICAL CONSULTATION

What tests should I cover?

- Medical Policy Guidance
- Best Test™ Guidance
- Educational Content

LAB NETWORK

Who should perform the test?

- Qualified Best Test™ Labs
- Price Discounts
- Test Selection Support
- Ongoing Lab Credentialing

OPTIMIZATION SERVICES

Who should get tested?

- Target Rx Identification
- Physician Outreach / Intervention
- Patient Education / Test Facilitation
- Medical Appropriateness Services
- Genetic Counseling Services

The Right Starting Point: Expanded Pharmacogenomics

Types of Genetic Testing

Pharmacogenomics (PGx)

- **Goal:** Evaluate the genetics of individuals, tumors and infections to help select the best therapy
- **Uses:** Determine right drug and dosage; minimize adverse events
- **Example:** Herceptin efficacy for cancer patients with HER2 gene over-expression
- **Testing Costs:** $100s

Medical Diagnostics (MDx)

- **Goal:** Evaluate risk or confirm diagnosis of genetic or hereditary disease
- **Uses:** Inform medical management or family planning decisions
- **Example:** Risk of hereditary breast cancer confirmed through BRCA1/2 genetic test
- **Testing Costs:** $1,000s

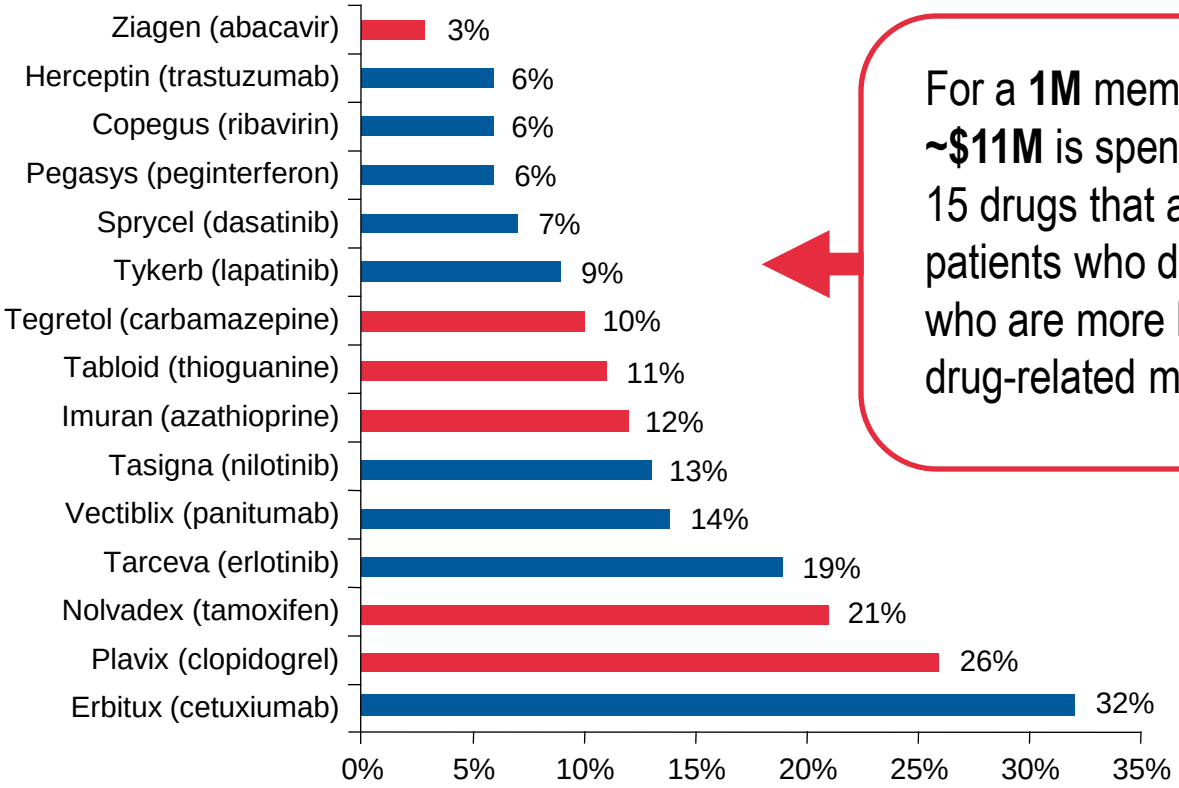
PGx Program Goals

Reduce Waste and Risk	Associated with trial-and-error prescribing
Improve Health Outcomes	Through greater accuracy and precision in drug therapy
Reduce Overall Health Care Costs	Related to inappropriate drug utilization and associated medical costs
Facilitate High-Quality Genetic Tests	By providing access to credentialed labs at preferred prices

More precise prescribing information leads to improved therapy outcomes and plan savings.

PGx Removes Waste

Percent of Drug Spend Associated with Suboptimal Clinical Benefit



For a **1M** member population, **~$11M** is spent each year on 15 drugs that are administered to patients who do not respond and who are more likely to experience drug-related medical complications

Source: Data derived using Generation Health's economic modeling platform, which leverages representative cost and epidemiological metrics from peer-reviewed literature, government information resources and administrative health care claims databases. Current as of March 17, 2010.

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PGx Improves Outcomes and Avoids Cost

Select PGx Examples

Target Therapy	Patient Health Concern	FDA Label Reference to PGx	Prev. of High-Risk Genotype	Relevant Clinical Consequence and Severity	Impact of Genetic Variant	Complication Cost per Episode (Est.)
Plavix (CYP2C19)	Efficacy	Boxed warning	1 in 4	Major cardiac event (heart attack, stroke)	SEVERE	$20,000[1]
Imuran (TPMT)	Safety	Recommendation for consideration of gene/gene product	1 in 9	Leukopenia	MODERATE	$5,000[2]
Ziagen (HLA-B*5701)	Safety	Recommendation for screening	1 in 18	Abacavir hypersensitivity	MODERATE	$2,000[3]
Tegretol (HLA-B*1502)	Safety	Recommendation for testing	1 in 490	Stevens Johnson Syndrome/Toxic Epidermal Necrolysis	SEVERE	$20,000/ $60,000 [4]

Complication costs are derived from studies listed. 1. Cohen D, et al. TRITON-TIMI 38 ECONOMIC SUBSTUDY: Cost-Effectiveness of Prasugrel vs. Clopidogrel from a Prospective Randomized Trial of Patients with ACS Undergoing PCI. 2. Caggiano V, et al. Incidence, cost, and mortality of neutropenia hospitalization associated with chemotherapy. Cancer. 2005 May 1;103(9):1916-24 3. Schackman BR, et al. The cost-effectiveness of HLA-B*5701 genetic screening to guide initial antiretroviral therapy for HIV. AIDS. 2008 Oct 1;22(15):2025-33 4. Kagan RJ, et al. DRG 272: does it provide adequate burn center reimbursement for the care of patients with Stevens-Johnson syndrome and toxic epidermal necrolysis? J Burn Care Res. 2007 Sep-Oct;28(5):669-74. Information valid as of March 12, 2010.

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Best Test™ Genetics Network

Solutions to address the limitations of traditional PPO purchasing

Technology	Technology assessment process and specimen collection standardization
Quality	Lab credentialing, proficiency testing, report guidance
Service	Preferred and managed network turn-around times
Price	The highest quality genetic testing with competitive negotiated pricing

Provides quality genetic testing that is accurate, timely and economical.

Physician and Patient Experience

Example: **Plavix Program**

STAGE	Script Identification	Outreach & Education	Criteria Eligibility	Test Management	Report Guidance
QUESTION	Is Plavix safe for the patient?	Will a PGx test help the patient?	Does the patient meet the criteria for testing?	What is the testing process?	What do the test results mean?
STEPS	• A prescription for Plavix is identified by CVS Caremark • The prescribing physician is identified • CVS Caremark sends fax to prescribing physician, indentifying opportunity and value of CYP2C19 genetic testing	• File sent to Generation Health (GH) for follow-up • GH coordinates testing with physician and member	• GH applies clinical criteria to determine member eligibility for CYP2C19 genetic test • GH communicates with physician and member	• GH recommends laboratory within Best Test™ Genetics Network • GH facilitates testing process for member • Sample collected through in-home collection kit (buccal)	• Lab sends results to physician and GH • GH sends results summary report to physician • Based on report and evidence provided by GH, physician determines whether to continue with Plavix or alter therapy

A Superior Pharmacogenomics Offering

- **Actionable** genetic information can help improve therapy outcomes and increase health care savings
  - Independent and impartial clinical recommendations help establish appropriate utilization rules
  - Broad array of drug therapies target and address increased value of Genetic Benefit Management
  - Preferred lab network helps to ensure quality, timeliness and negotiated pricing for genetic testing
  - Targeted therapies, centered around evidence-based medicine, focus testing on interventions proven to increase safety and efficacy

Independent laboratories lead to more objective and cost effective utilization.

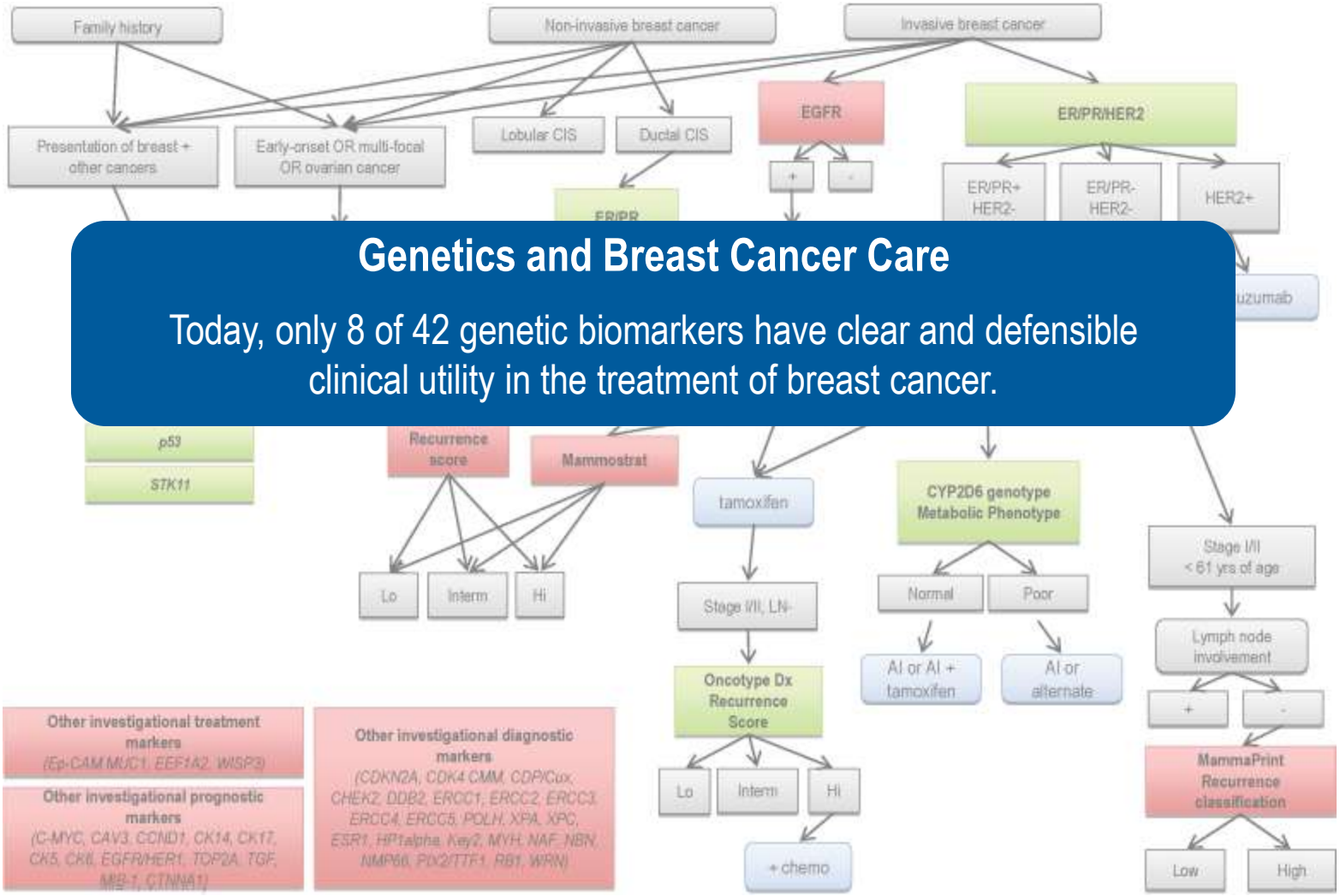
Appendix

Assessment Tools Can Clarify Costs

- Plan edits and utilization reporting is complicated by reimbursement system that identifies laboratory processes but not test-level details

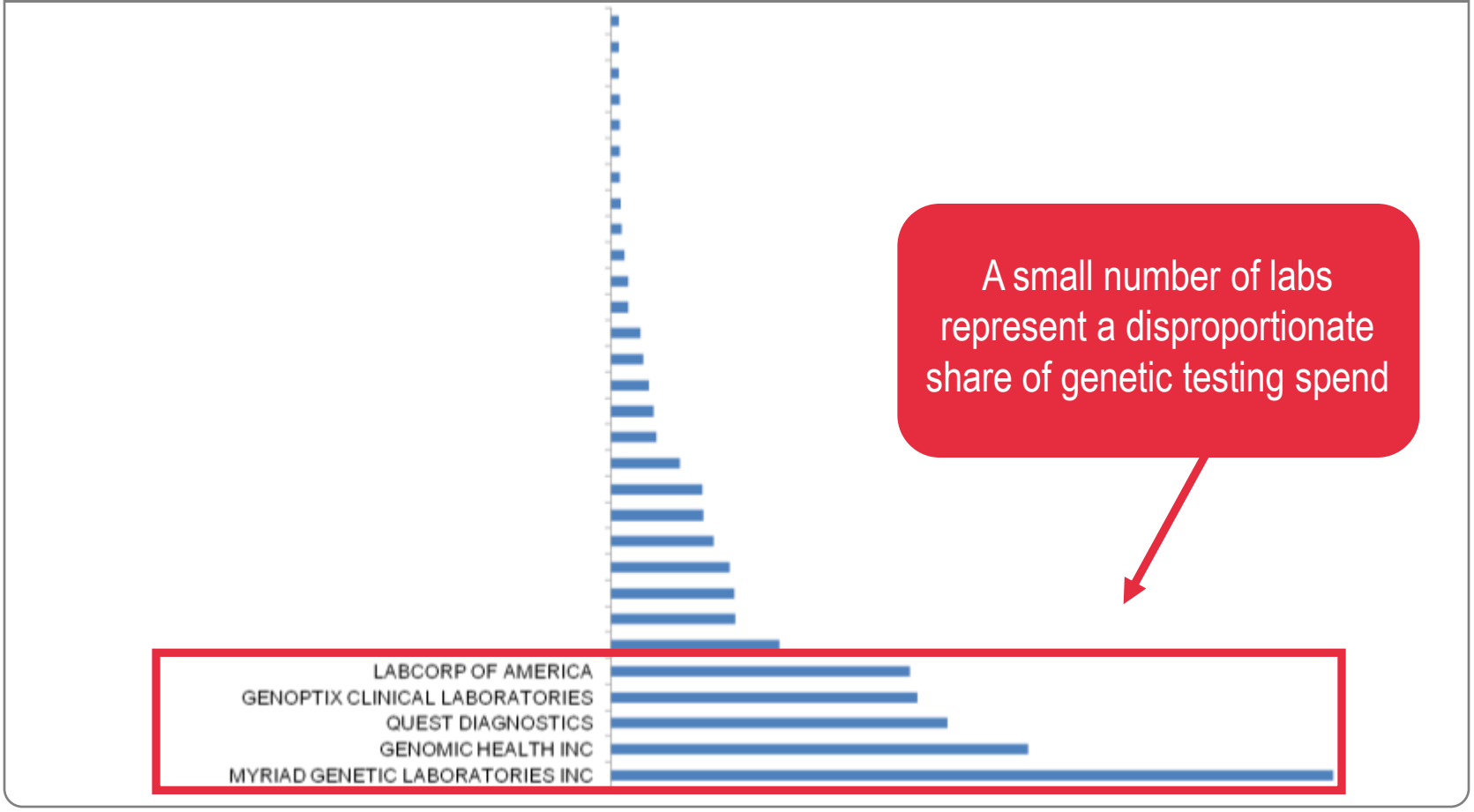
CPT CODE ASSIGNMENT		
Test Code: None	**Test Name**: AMD (Age Related Macular Degeneration) DNA Sequencing Test	
Test Composition: ARMS2, C3, CFB, CFH DNA Sequencing		
CPT CODE	**CODE DESCRIPTION**	**# OF UNITS**
83891	Molecular diagnostics; **isolation** or **extraction** of highly purified nucleic acid, each nucleic acid type (e.g.DNA or RNA)	1
83892	Molecular diagnostics; **enzymatic digestion**, each enzyme treatment	1
83898	Molecular diagnostics; **amplification**, target, each nucleic acid sequence	**78**
83904	Molecular diagnostics; mutation identification by **sequencing**, single segment, each segment	**156**
83909	Molecular diagnostics; separation and identification by high resolution technique (e.g., capillary electrophoresis), **each nucleic acid preparation**	**156**
83912	Molecular diagnostics; **interpretation** and **report**	1

Coverage Framework for Genetic Testing



Targeted Medical Appropriateness Services

Top Genetic Test Lab Providers By Paid Amount



Source: GH internal research of top genetic test lab providers 2009.

Best Test™ Genetics Network Addresses Cost and Quality

To order a genetic test for **Hereditary Nonpolypopis SP-Colorectal Cancer (HNPCC),** a physician must make the following decisions:

Which lab?	Which genes?	Which laboratory method?
There are **9 laboratories** that perform the tests, including the Mayo Clinic and Myriad Genetics	There are **5 different genes** associated with risk of HNPCC	There are **6 different methods** available to perform the test

Need for Best Test Guidance

- The result: 79 brands of HNPCC tests with variations in cost, accuracy and timeliness of genetic information

Lab	Price	Turn-Around Time
Emory	$4,000.00	14 to 70 days
Emory	$3,400.00	
Harvard	$2,700.00	
Emory	$2,200.00	
City of Hope	$1,771.20	
Emory	$1,500.00	
City of Hope	$1,437.48	
Mayo Clinic	$1,100.00	
Baylor	$910.00	
Emory	$790.00	
City of Hope	$695.88	
City of Hope	$547.56	
Emory	$415.00	
Mayo Clinic	$366.80	
Mayo Clinic	$175.00	
Emory	$125.00	

Source: GH internal research 2009.

Complete CVS Caremark Portfolio of Pharmacogenomics Programs

Drug Type	Targeted Drug	Therapy
Traditional PBM/ Retrospective Intervention	**Ziagen** (abacavir)	HIV
	Imuran (azathioprine)	Rheumatoid Arthritis
	Tegretol (carbamazepine)	Seizures, Bipolar
	Plavix (clopidogrel)	Reduction of Atherothrombotic Events
	Nolvadex (tamoxifen)	Oncology
	Tabloid (thioguanine)	Oncology
Specialty*/Prospective Intervention	**Sprycel** (dasatinib)	Oncology
	Erbitux (cetuximab)	Oncology
	Herceptin (trastuzumab)	Oncology
	Revlimid (lenalidomide)	Oncology
	Rituxan (rituximab)	Oncology
	Vectibix (panitumumab)	Oncology
	Tasigna (nilotinib)	Oncology
	Tarceva (erlotinib)	Oncology
	Gleevec (imatinib)	Oncology
	Tykerb (lapatinib)	Oncology
	Pegasys/Copegus; Peg-Intron/Rebetol (peg-interferon/ribavirn)	Hepatitis C

*All Specialty products are currently available under the Specialty Guideline Management pharmacogenomics program; an additional five specialty drugs are being considered for inclusion in our 1/1/2011 portfolio.

This page contains references to brand-name prescription drugs that are trademarks or registered trademarks of pharmaceutical manufacturers not affiliated with CVS Caremark.

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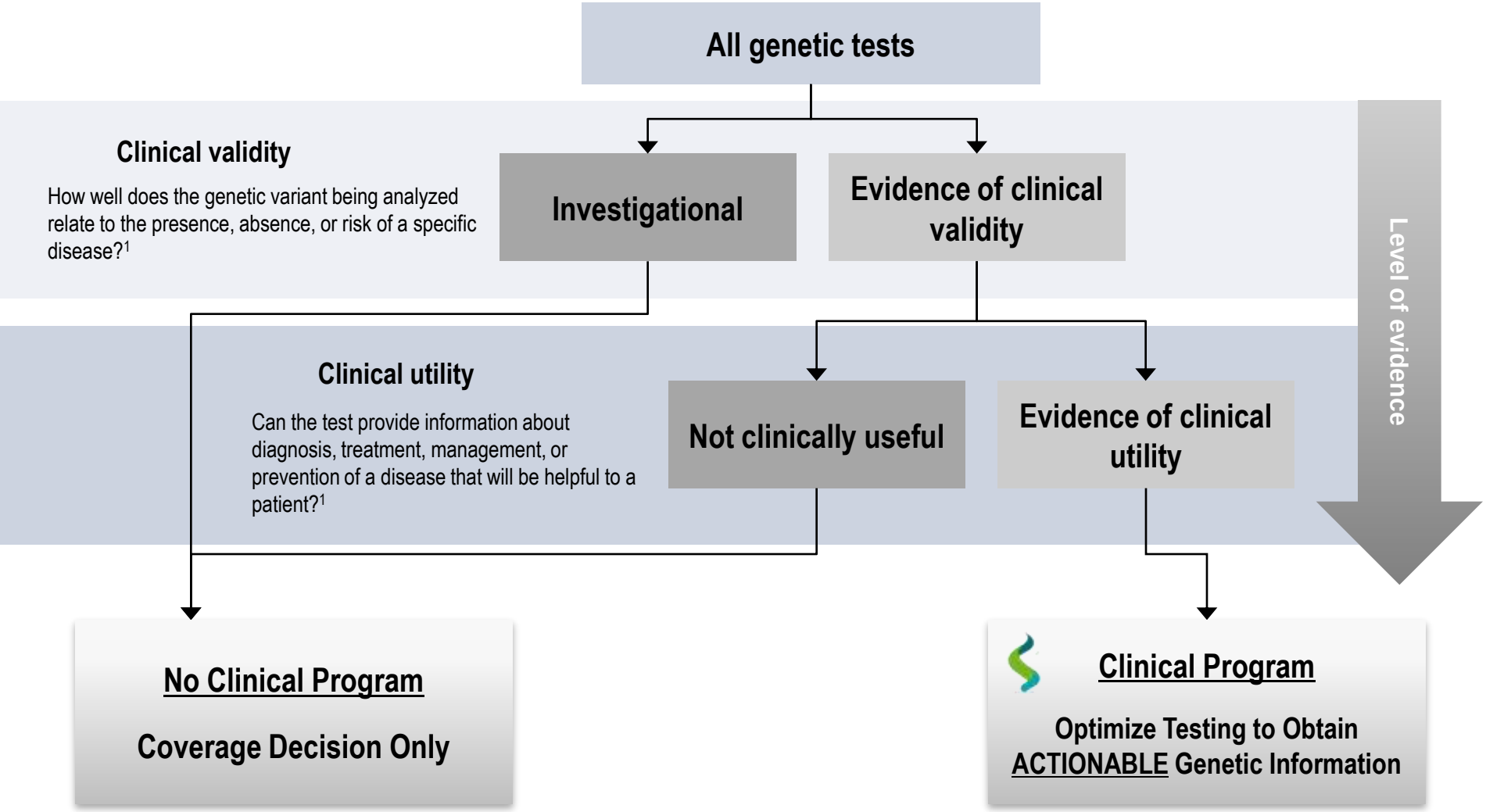
Establishing Clinical Utility



1: U.S. National Library of Medicine, http://ghr.nlm.nih.gov/handbook/testing/validtest

Program Selection Rationale

- Clinical Considerations
  - Weight of clinical evidence
  - Clinical utility; actions taken based on prospective data
  - Clinical utility; actions taken based on retrospective data
  - Value of the genomic information for the patient
- Operational Considerations
  - Feasibility of intervening at the optimal point in therapy
  - Turn-around time to obtain genetic test results
- Impact
  - Prevalence of high-risk genotype and recommended therapy changes
  - Complications and deaths avoided
  - Potential health care savings associated with optimal drug use

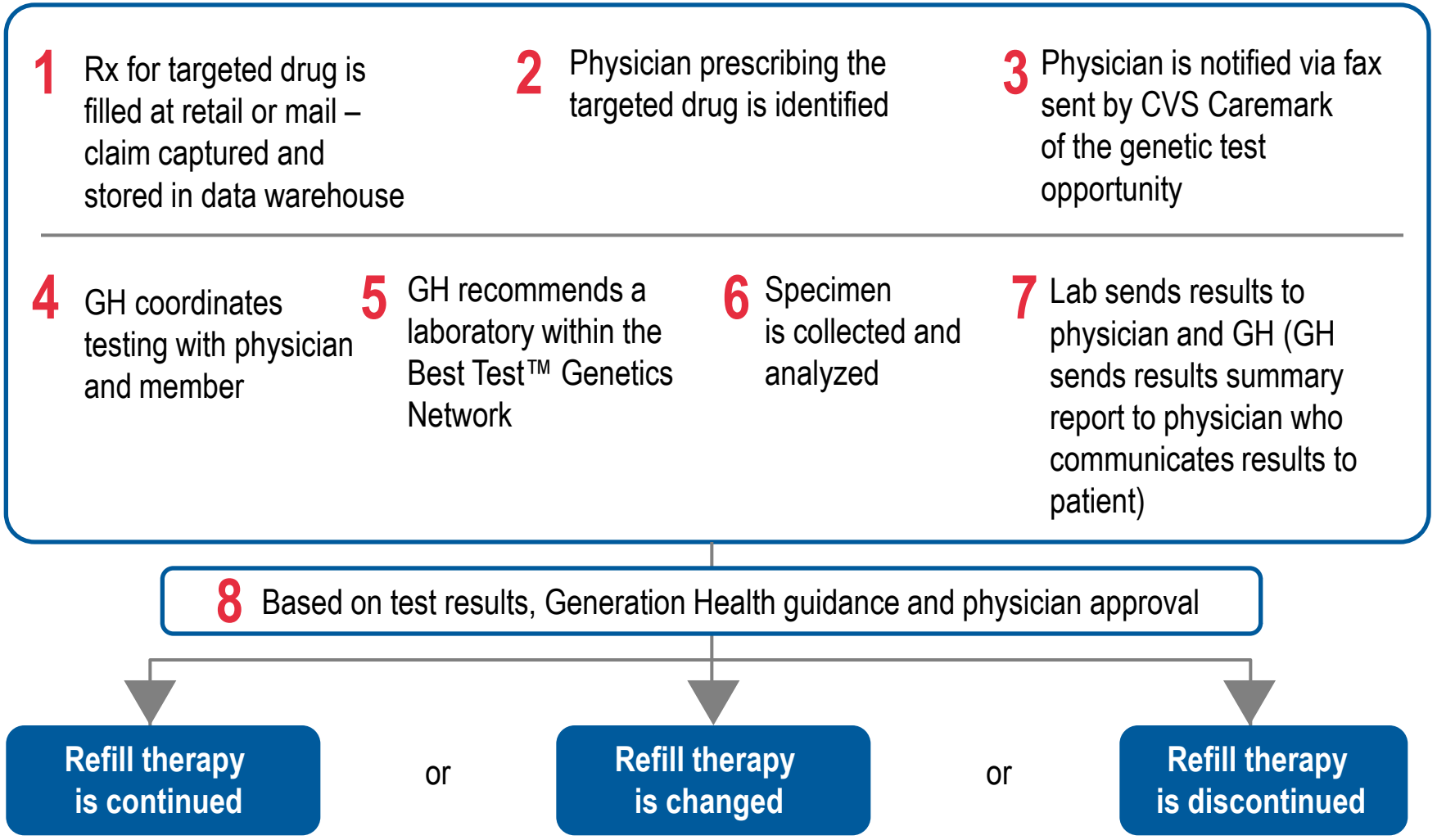
☑	• Plavix (clopidogrel) • Ziagen (abacavir) • Tegretol (carbamazepine)
☒	• Vfend (voriconazole) • Strattera (atomoxetine)

Scientific clarity and practical considerations will evolve and so will program choices and program design.

Clinical Advisory Board (CAB)

PROFESSIONAL CREDENTIALS (13 core plus 4 ad-hoc members)	• MD • PhD	• Masters in Public Health • PharmD	
SPECIALTIES	• Medical genetics • Breast oncology • Clinical pharmacology • Immunology • Infectious disease	• Evidence-based evaluation • Hematological oncology • Pediatric neurology • Thoracic oncology • Molecular diagnostics	• Molecular pathology • Cardiovascular genetics • Rheumatology • Microbiology
ACADEMIC & RESEARCH HOSPITAL AFFILIATION	• Harvard • Stanford • Howard • NYU • Columbia	• Yale • Memorial-Sloan Kettering • Wayne State • Pittsburgh Medical Center • Beth Israel Deaconess Medical Center	• Brigham and Women's Hospital • College of American Pathologists • Langone Medical Center • Barbara Ann Karmanos Cancer Institute
COMPENSATION	• Consulting fee per meeting or project • Standard travel expenses	• NO equity • NO bonuses tied to business results	

PBM Retrospective Intervention



Specialty Prospective Intervention

1. Targeted drug claim received; SGM case intervention triggered
2. Physician responds to clinical criteria with CVS Caremark SGM Team
3. PGx test completed?
   No = Move to step 4
   Yes = Move to step 9
4. SGM recommends a genetic test within Best Test™ Genetics Network

5*. Physician contacts GH to Authorize Genetic Testing with network lab
6. Specimen is collected and analyzed by lab
7. Lab sends results to physician and GH; physician communicates results to patient
8. GH sends results to CVS Caremark to make case determination

9

Case is approved and Rx filled

or

Case is denied and claim is rejected

*Steps 5-8 illustrate new genetic lab test facilitation services managed by Generation Health.

Compliant With ALL HIPAA and GINA Rules and Regulatory Requirements

- HIPAA: Health Insurance Portability and Accountability Act
  - All programs and specific patient information fully compliant to protect the privacy of individual health information
  - Includes the Patient Safety Rule
- GINA: Genetic Information Nondiscrimination Act
  - Prohibits discrimination in health coverage and employment on the basis of genetic information
  - Prohibits health insurers or health plan administrators from using genetic information in coverage determination decisions
- Expanded offering not impacted by GINA
  - CVS Caremark will not use genetic information to determine premiums or eligibility

Program is also compliant with established state laws.