What’s next
Innovating and elevating our product pipeline
Dale Muzzey, Ph.D., Chief Scientific Officer
Outline

GeneSight
Additional clinical support for efficacy

Precise Tumor and Liquid
Robust tumor profiling & therapy selection

Precise MRD
Superior minimal residual disease monitoring

FirstGene
4-in-1 prenatal screening
PRIME Care Randomized Clinical Trial (RCT)
Why GeneSight matters

8.4% of U.S. adults suffer from major depressive disorder

63% of US adults with major depressive disorder do not achieve remission with first-line drug

~4 weeks to switch from a drug that is not working to another drug

1 2020 National Survey on Drug Use and Health (NSDUH, NIH)
2 Rush et al., STAR*D report, 2006, American Journal of Psychiatry
3 Ogle et al., 2012, Journal of Pharmacy Practice
# History of evidence supporting GeneSight efficacy

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N</th>
<th>References</th>
</tr>
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<tbody>
<tr>
<td>Hamm</td>
<td>Prospective, open-label, controlled</td>
<td>44</td>
<td>Hall-Flavin et al. 2012</td>
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<td>La Crosse</td>
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<td>Pine Rest</td>
<td>Prospective, blinded, RCT</td>
<td>49</td>
<td>Winner et al. 2013</td>
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<tr>
<td>GUIDED</td>
<td>Prospective, blinded, RCT</td>
<td>1,167</td>
<td>Greden et al. 2019</td>
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<td>GDI GUIDED post hoc analysis</td>
<td>Post-Hoc, green-bin meds included</td>
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<td>HAM-D6 GUIDED post hoc analysis</td>
<td>Post-Hoc, HAM-D6 outcomes</td>
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<td>Dunlop et al. 2019</td>
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<td>65+ GUIDED post hoc analysis</td>
<td>Post-Hoc, Age 65+ cohort</td>
<td>184</td>
<td>Forester et al. 2020</td>
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<td>Med Blood Levels GUIDED post hoc analysis</td>
<td>Post-Hoc, validation algorithm</td>
<td>191</td>
<td>Shelton et al. 2020</td>
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<td></td>
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<td>124</td>
<td>Parikh et al. 2022</td>
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<tr>
<td>CPGx vs Single Gene GUIDED post hoc analysis</td>
<td>Post-Hoc, Blood level (B) &amp; outcomes (O)</td>
<td>O: 1.022</td>
<td>Rothschild et al. 2021</td>
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<tr>
<td></td>
<td></td>
<td>B: 1.034</td>
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<td>Meta-Analysis</td>
<td>Hamm, La Crosse, Pine Reset, GUIDED</td>
<td>1,556</td>
<td>Brown et al. 2020</td>
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<td>IMPACT</td>
<td>Prospective, open-label, controlled</td>
<td>1,871</td>
<td>Hebert et al. 2018</td>
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<td>Tanner et al. 2018</td>
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</table>
PRIME Care randomized clinical trial investigated efficacy of GeneSight

- 1,944 U.S. Veterans, age 18-80 inclusive
- Suffering from major depressive disorder
- At least one prior treatment episode or intent to switch treatment

Study design:

**GeneSight Arm**

**Usual Care Arm**

**Follow-up Visits**

**End of Intervention Phase**

**Remission:** PHQ-9 score ≤ 5* (e.g., 20 to 4)

**Response:** > 50% reduction in PHQ-9 score* (e.g., 20 to 10)

**Symptom Improvement:** Change in PHQ-9 score (based on the group average)
PRIME Care RCT: Both co-primary outcomes were met

Co-primary outcome #1:
Does access to GeneSight testing lower the proportion of antidepressant prescriptions with predicted gene-drug interactions compared to TAU?

YES

GeneSight® Psychotropic COMBINATORIAL PHARMACOGENOMIC TEST

Antidepressants

<table>
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<tr>
<th>Use as Directed</th>
<th>Moderate Gene-Drug Interaction</th>
<th>Significant Gene-Drug Interaction</th>
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<tr>
<td>desvenlafaxine (Pristiq®)</td>
<td>1</td>
<td>bupropion (Wellbutrin®)</td>
</tr>
<tr>
<td>levomilnacipran (Fetzima®)</td>
<td>1</td>
<td>mirtazapine (Remeron®)</td>
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<tr>
<td>vilazodone (Viibryd®)</td>
<td>2</td>
<td>amitriptyline (Elavil®)</td>
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<tr>
<td>trazodone (Desyrel®)</td>
<td>1.4</td>
<td>clomipramine (Anafranil®)</td>
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<tr>
<td>venlafaxine (Effexor®)</td>
<td>3.4</td>
<td>desipramine (Norpramin®)</td>
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<tr>
<td>selegiline (Emsam®)</td>
<td>3.4</td>
<td>doxepin (Sinequan®)</td>
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<tr>
<td>fluoxetine (Prozac®)</td>
<td>3.4</td>
<td>duloxetine (Cymbalta®)</td>
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<tr>
<td>citalopram (Celexa®)</td>
<td>3.4</td>
<td>imipramine (Tofran®)</td>
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<tr>
<td>escitalopram (Lexapro®)</td>
<td>3.4</td>
<td>nortriptyline (Pamelor®)</td>
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<tr>
<td>sarizotline (Zydoft®)</td>
<td>3.4</td>
<td>vortioxetine (Trintellix®)</td>
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<tr>
<td></td>
<td></td>
<td>fluvoxamine (Luvox®)</td>
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<tr>
<td></td>
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<td>paroxetine (Paxil®)</td>
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TAU = treatment as usual

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PRIME Care RCT: Both co-primary outcomes were met

Co-primary outcome #2:
Over a 24-week timeframe, does access to GeneSight testing significantly improve the likelihood of achieving depression remission compared to TAU? **YES**

The GeneSight arm had a **28%** greater likelihood of achieving remission (p=0.02)

<table>
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<tr>
<th>Week</th>
<th>GeneSight</th>
<th>TAU</th>
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<tbody>
<tr>
<td>4</td>
<td>OR-1.21</td>
<td>P=0.27</td>
</tr>
<tr>
<td>8</td>
<td>OR-1.38</td>
<td>P=0.02</td>
</tr>
<tr>
<td>12</td>
<td>OR-1.59</td>
<td>P=0.001</td>
</tr>
<tr>
<td>18</td>
<td>OR-1.21</td>
<td>P=0.14</td>
</tr>
<tr>
<td>24</td>
<td>OR-1.11</td>
<td>P=0.45</td>
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</table>

TAU = treatment as usual
The road ahead for GeneSight R&D

- Continued clinical validity and clinical utility assessment in patients with major depressive disorder
- Verifying efficacy for treatment of postpartum depression:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Adequate Treatment</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>40,000</td>
<td>6,400</td>
<td>3,200</td>
<td>1,600</td>
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</tbody>
</table>

- 90% of PPD cases unrecognized
- 84% of diagnosed cases untreated
- 50% of treated cases treated adequately
- 50% of adequately treated cases fail to remit

Only 0.4% of PPD cases are successfully treated – a huge opportunity for Myriad to improve care.
Precise Tumor and Liquid Biopsy
Challenging to pick the right therapy for a given cancer
Genomic profiling of the tumor can pinpoint which therapy is best
Patients need targeted therapy-selection guidance via either tissue or liquid biopsy

- Offered in collaboration with Illumina and Intermountain Healthcare
- Both solid and liquid assays test >500 genes, including DNA and RNA analysis
- Precise Liquid can serve as stand-alone product for certain indications and reflex for cases where solid tumor sample is insufficient or low-quality

Launch planned for 2023
Building a complete suite of oncology services

MyRisk™ Hereditary Cancer Test
High Risk Screening

MyRisk® RiskScore®
Surgical Decisions

MyChoice® CDx
Myriad HRD Companion Diagnostic Test

Precise™ Tumor
Molecular Profile Test

BRACAnalysis CDx®
Germline Companion Diagnostic Test

EndoPredict®
Breast Cancer Prognostic Test

Treatment Selection & Clinical Trials

Precise Liquid in 2023
Building a complete suite of oncology services

MyRisk™ Hereditary Cancer Test
RiskScore®

High Risk Screening

Surgical Decisions

Treatment Selection & Clinical Trials

EndoPredict®
Breast Cancer Prognostic Test

MyChoice® CDx
Myriad HRD Companion Diagnostic Test
Precise™ Tumor
Molecular Profile Test

BRACAnalysis CDx®
Germline Companion Diagnostic Test

← Precise Liquid in 2023

Measurable Residual Disease
Precise Minimal Residual Disease (MRD)
MRD monitoring helps address two fundamental questions

If not:
Shift to a new approach

If so:
Option to resume treatment early

Is my cancer treatment working?
Has my cancer recurred?
MRD detects DNA ejected from dying tumor cells: More DNA = More tumor

First step in MRD: Profile tumor cells

Later steps in MRD:
Use tumor profile to assess presence of tumor cells

Detectable & quantifiable by MRD

Detectable by imaging

Pre-treatment
Post-treatment
Early recurrence
Late recurrence

Normal cell
Tumor cell
Dying cell
In-house MRD built upon Myriad’s existing core competencies

Pre-operative tumor assessment
- Tumor + normal sample prep and sequencing
- Bioinformatic identification of somatic variants

Post-operative residual-disease monitoring
- cfDNA isolation and targeted sequencing
- Detect presence or absence of tumor cfDNA

Comparable Myriad test:
- MyChoice® CDx
  Myriad HRD Companion Diagnostic Test
- Prequel®
  Prenatal Screen
- FirstGene™
  4-in-1 Prenatal Screen
Myriad MRD expected to more deeply interrogate the tumor than other MRD offerings

- **Somatic variant identification**
  - Competitor
  - Exome
  - Whole genome

- **Number of sites interrogated in plasma sample**
  - Competitor: 16 sites
  - Exome: ≥500 sites

**Comparison**:
- More sites
- Higher sensitivity
- Earlier detection of recurrence
Assessing analytical performance on Stage II breast cancer sample

Somatic variant identification:
- Tumor WGS
- Normal WGS

17,694 Putative somatic variants

777 Selected for Bespoke assay

Analytical validation via dilution series:

Normal DNA

Run capture assay on each mixture

1% Tumor DNA (approx. stage IV breast cancer)

0.1% Tumor DNA (approx. stage II breast cancer)

0.01% Tumor DNA

0.005% Tumor DNA

0.001% Tumor DNA
Excellent analytical performance on Stage II breast cancer sample

% of sites where tumor DNA detected

Tumor fraction (%)

Detection limit of competitor’s assay

MRD can be detected when the solid line is above the dashed line

- p=2.2e-292
- p=5.9e-11
- p=3.3e-06
- p=1.8e-85
- p=0.047
- p=0.75

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Looking at more somatic sites enables superior detection at low tumor fraction
Pursuing a range of MRD initiatives

• Amassing samples to power analytical validation study

• Leveraging pharma partnerships from MyChoice CDx

• Collaborating with Intermountain Healthcare on a prospective study for MRD

• Planning a large, multi-site, prospective clinical utility study that will launch in 2023

• Preparing laboratory automation for research use only (RUO) launch in early 2023
An OBGYN may see more than 30 women in a day
Each patient needs multifaceted care

10-week visit checklist
- Breast exam
- Pelvic exam
- Pap smear
- Vaccination check for MMR
- Rh type testing
- Emotional status check
- Noninvasive prenatal screening
- Carrier screening
OBGYNs tell us that they sometimes don’t have time to offer genetic testing
Carrier screening requires two tests and education about the complexity of underlying genetics

Is my child going to be affected with a severe genetic condition?

Screen mother for recessive carrier status

If mother is a carrier of certain condition(s), screen the father to determine carrier status for those conditions

If both are carriers, then the fetus has a 25% chance of being affected
Each patient needs multifaceted care

“If you make me talk about genetics for 30 more seconds per patient, I hate you.”

—OBGYN at MWH ad board
50% of women don’t currently get carrier screening

<table>
<thead>
<tr>
<th>Not offered carrier screening</th>
<th>Screened positive; Reproductive partner unscreened</th>
<th>Screened positive; partner also screened</th>
<th>Screened negative</th>
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<tbody>
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Graphic is for illustrative purposes only. Actual patient populations will vary.
>50% of women also don’t currently undergo NIPS

Graphic is for illustrative purposes only. Actual patient populations will vary.
The integrated solution for basic prenatal screening

FirstGene
The integrated solution for basic prenatal screening

FirstGeneticTest
The integrated solution for basic prenatal screening

FirstGeneticTest

FirstGene™
4-in-1 Prenatal Screen
Single blood draw on one person

No need to screen!

NIPS for common aneuploidies

Carrier screening for common conditions

Fetal recessive status (affected, carrier, normal)

Feto-maternal blood compatibility
FirstGene is not simply a combination of Foresight and Prequel

- NIPS for common aneuploidies
- Carrier screening for common conditions
- Fetal recessive status (affected, carrier, normal)
- Feto-maternal blood compatibility

**Gamechanger**
- Eliminates need for sequential testing workflow
- Fewer pregnancies need diagnostic follow-up
- Those undergoing diagnostic testing much more likely to be positive
What is tested on FirstGene?

- NIPS for common aneuploidies
- Carrier screening for common conditions
- Fetal recessive status (affected, carrier, normal)
- Feto-maternal blood compatibility

**Additional Tests:**

- **Trisomies 13/18/21** *(guideline-recommended)*
  - (Opt-in) Sex-chromosome analysis
  - (Opt-in) 22q11.2 microdeletion syndrome

- **Cystic Fibrosis** *(guideline-recommended)*
- **Spinal Muscular Atrophy** *(guideline-recommended)*
  - (Opt-in) Beta-chain hemoglobinopathies (e.g., Sickle Cell Disease)
  - (Opt-in) Alpha thalassemia
  - (Opt-in) 10 additional common genes selected to maximize equity in care
  - (Opt-in) Fragile X (maternal carrier status only)

- (Opt-in) Maternal and fetal RHD copy-number analysis
Multiple levels of fetal-fraction amplification in FirstGene

Take the AMPLIFY technology from Prequel...

... and port to FirstGene for superior fetal fraction

FirstGene estimated to have 3X fewer samples with inconclusive fetal recessive results due to low fetal fraction*

*Based on comparison between FirstGene internal data and Westin et al., 2022, American Journal of Hematology
FirstGene clinical study underway

- Will power FirstGene analytical and clinical validity publications
- Enrolling 500 patients for development and validation – enrollment underway
- For each pregnancy, we will collect:
  - Screening sample (plasma)
  - Diagnostic sample (CVS or amniocentesis)
Advantages relative to alternative approaches

**FirstGene™**
4-in-1 Prenatal Screen

- **3X** the number of genes\(^1\)
- **2X** faster turnaround time for fetal affected status\(^2\)
- **3X** fewer samples with inconclusive fetal recessive results due to low fetal fraction\(^3\)
- **3X** lower COGS\(^4\)

---

1. Expected panel size of FirstGene compared to UnityScreen panel
2. FirstGene will perform fetal recessive testing in a single assay, rather than two sequential assays
3. Based on comparison between FirstGene internal data and Westin et al., 2022, American Journal of Hematology
4. Based on internal analysis of running FirstGene versus separately running carrier screening, aneuploidy NIPS, and single-gene NIPS
FirstGene is a truly integrated offering

**Competitor's offering**

- NIPS
- Fetal recessive status
- Maternal carrier screening
- Blood compatibility

- All four assays run separately but offered in an integrated report
- Longer TAT
- Higher COGS

**FirstGene™**

4-in-1 Prenatal Screen

- NIPS
- Fetal recessive status
- Maternal carrier screening
- Blood compatibility

- All four assays run in single, integrated assay
- Shorter TAT
- Lower COGS
Myriad prenatal portfolio can serve all needs

FirstGene expected to be available 2023
## Roadmap

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<tr>
<th>2022</th>
<th>2023</th>
<th>2024</th>
<th>2025</th>
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<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
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<tr>
<td>NovaSeq Transitions</td>
<td>Prenatal products shift to advanced sequencing</td>
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<tr>
<td>FirstGene</td>
<td>New Prenatal combined test offering</td>
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<tr>
<td>New Facility Construction</td>
<td>South San Francisco innovation campus construction</td>
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<tr>
<td>Shift Operations to New Facilities</td>
<td>Transition Innovation operations to new South San Francisco facility</td>
<td>Transition Prenatal production to Salt Lake City</td>
<td>Transition Salt Lake City Research Park products to new campus</td>
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<tr>
<td>Advanced Automation</td>
<td>Design and build first phases of automation</td>
<td>Early phase Prenatal lab automation</td>
<td>Fully automate Prenatal labs</td>
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<tr>
<td>MRD</td>
<td>New Measurable Residual Disease detection offering</td>
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<td>Phased approach</td>
<td>RUO</td>
<td>LDT</td>
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* >85% of investment is estimated to be Capitalizable expense

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