Dynamic Levels of Evidence Tiering to Support Evolving Guidelines in Variant Assessment

Duren R[1], Tackes N[1], Smith R[1], Neeley S[1], Shiller M[2], Li XS[1]
[1]MolecularMatch, Inc, [2]Baylor Scott & White Health

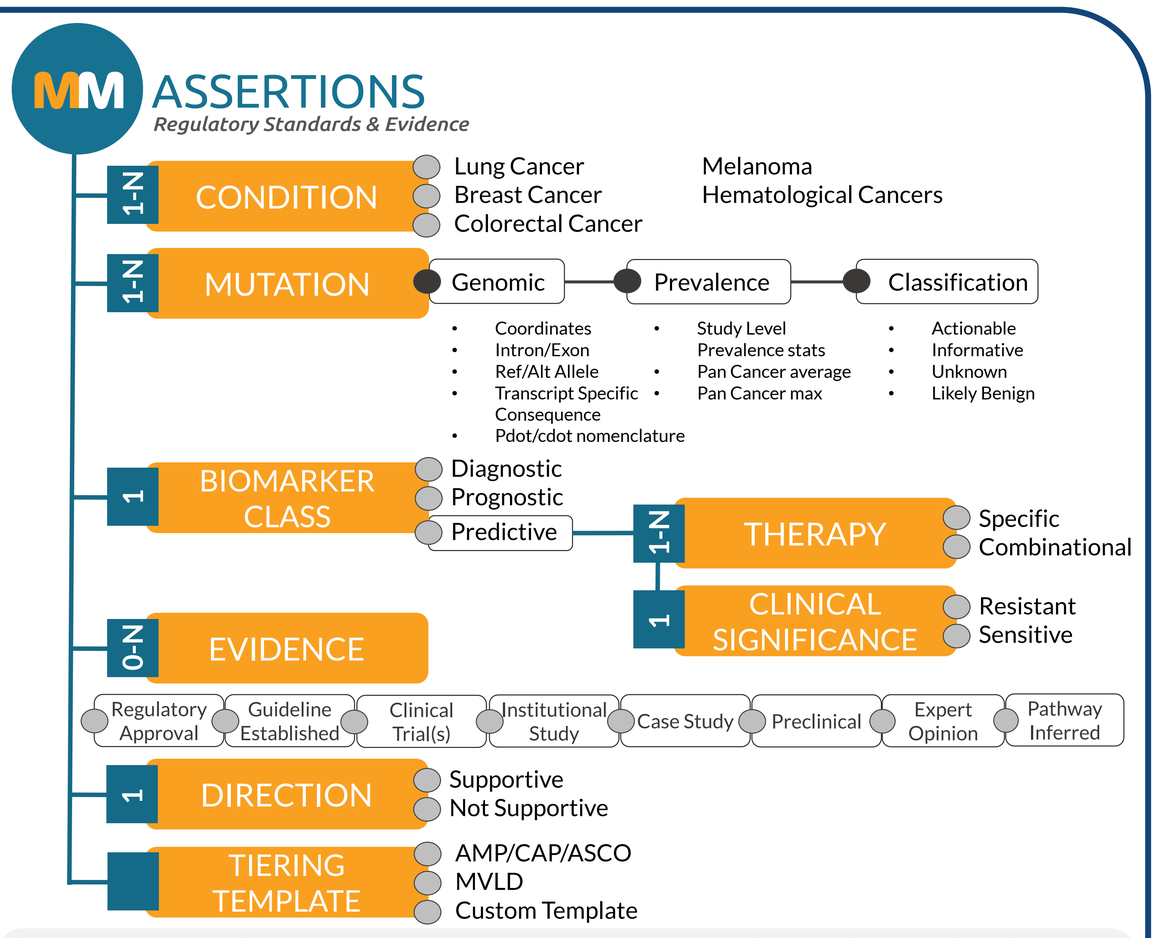

Figure 1. Assertions Data Model: Leverages attributes defined by ClinGen/MVLD and AMP/CAP/ASCO guidelines to establish concrete linkage between a given condition, molecular alteration, clinical significance, (prognostic, diagnostic, predictive), therapeutic, and citation or source. Additional mutation attributes, including genomic coordinates, cancer prevalence, and clinical classification are also incorporated into Molecular Assertions output.

Molecular Assertions Release Cycle

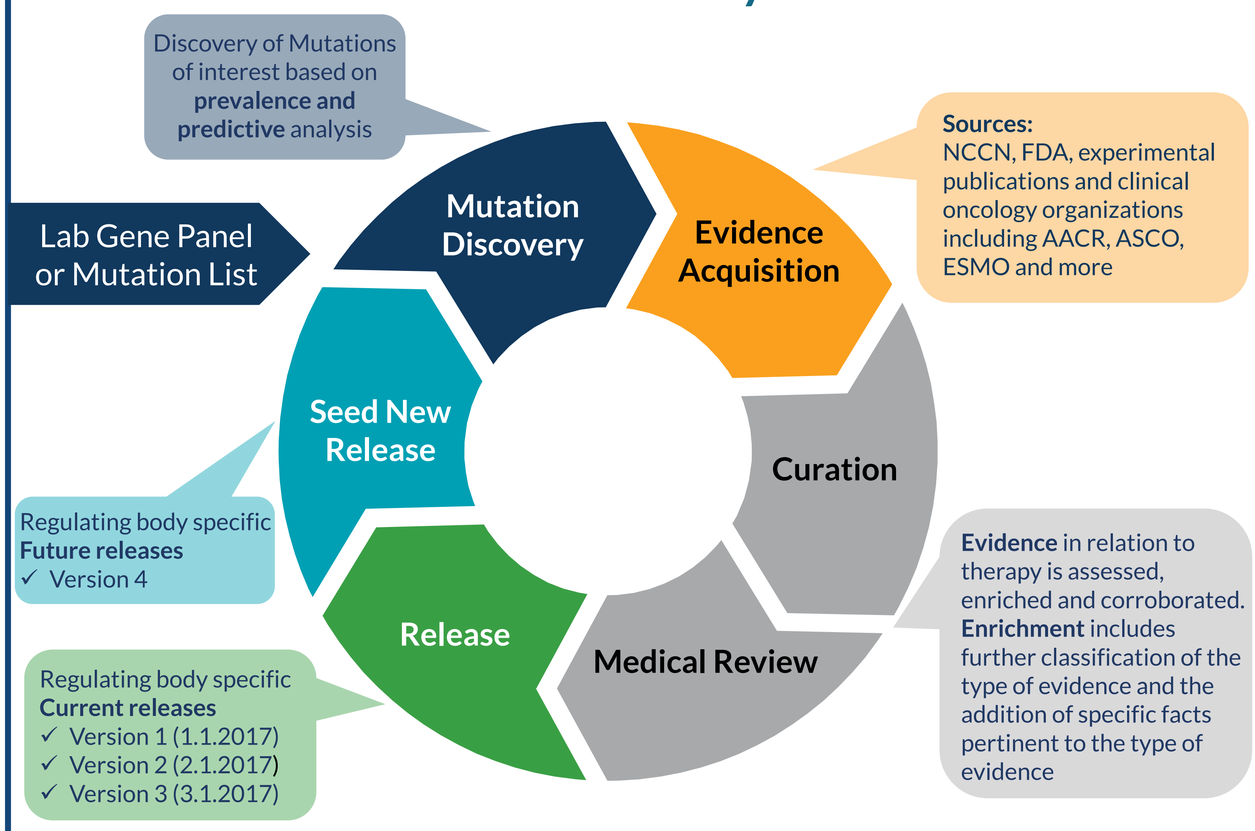

Figure 2. Release Cycle: Assertions are autogenerated by condition and mutation list specifications in Mutation Discovery. Evidence Acquisition is through MMPower Publications search with Google Scholar comparisons. Mutations with evidence proceed to Curation and Medical Review (manual steps). Upon Release validation checks, tier calculations, and conflict flags are run and released versions create monitored scenarios for auto updates.

Regulatory Standards and Evidence Tiering Model

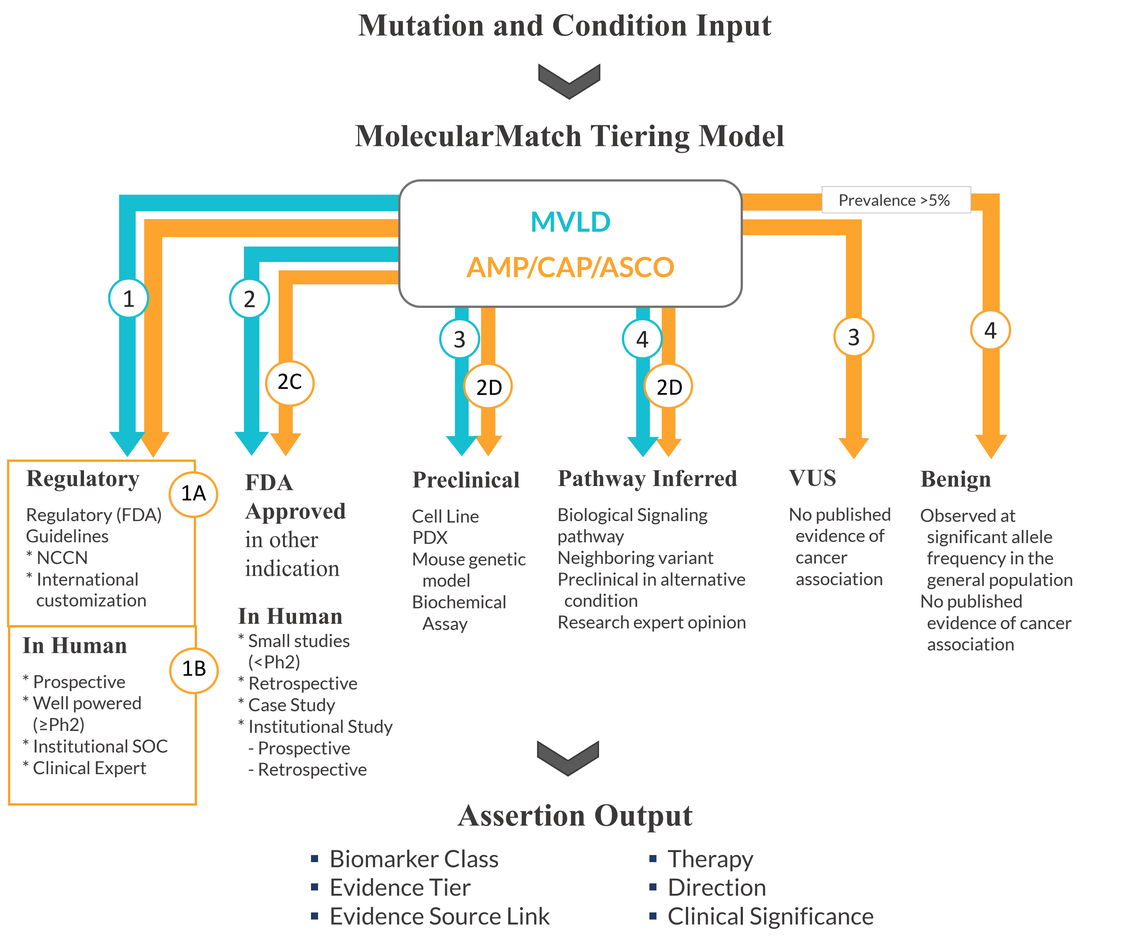

Figure 3. Decoupled Tiering Model: The underlying data model attributes are decoupled from guideline tiering models, allowing automatic recalculation of guideline tier upon introduction of new evidence, flexible conversion between tier models, and adherence to refined tier models without re-curation of assertions evidence.

Real World Application of Molecular Assertions

1. 65 year old woman diagnosed with metastatic colorectal cancer
2. Biopsy sequencing identified BRAF V600E mutation
3. Pathologist reports test results to oncologist
4. Oncologist uses MolecularMatch Portal to access Molecular Assertions to find evidence based treatments

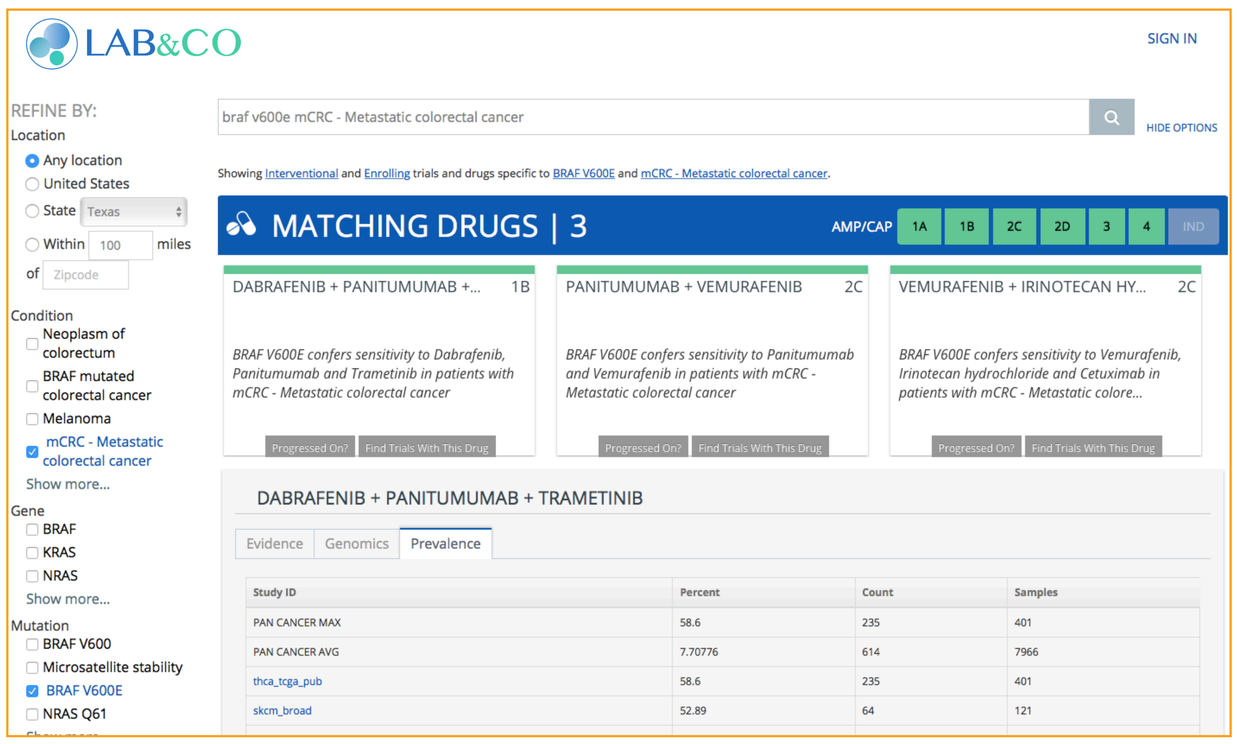

Figure 4. Molecular Assertions Application: MolecularMatch Portal surfaces condition and variant specific drug recommendations assigned to evidence based tiers. Each drug card presents published evidence supporting the molecular assertion, genomic information and variant cancer prevalence for the condition.

Multifaceted MMSolutions Utilized Throughout Your Clinical Workflow

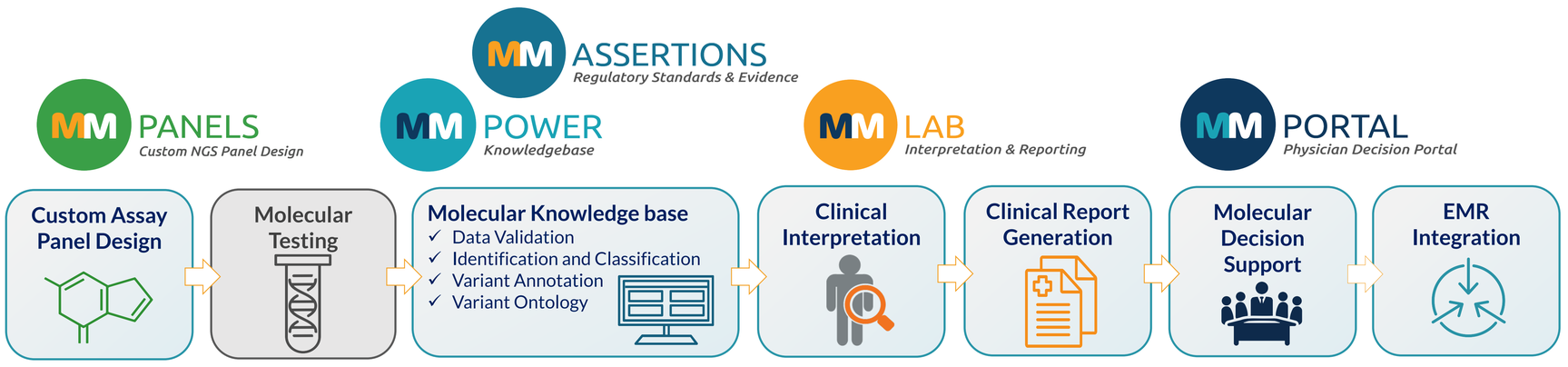

Figure 5. MolecularMatch Easily Integrates into a Clinical Workflow: MolecularMatch has developed technology that increases efficiencies and obtains molecular knowledge to address needs throughout the diagnostic workflow. All are founded on the MMPower knowledgebase and are incorporated into existing systems and/or ingestion of legacy data.

MolecularMatch
CLINICAL INTELLIGENCE ON-DEMAND

MolecularMatch Sustains over 5,000 Molecular Assertions

Available Curated Assertions

Lung Cancer	4,636
Breast Cancer	595
Colorectal Cancer	365
Hematological Cancer	551

2018 Advances:
Incorporate 350 more Genes, more than 10 additional Cancer Types and a total of 20,000 variants