MolecularMD: Linking Molecular Discoveries to Breakthroughs in Cancer Treatment

By Linda Barney, Barney and Associates

As defined by the President's Council of Advisors on Science and Technology, " **Personalized Medicine** " refers to the tailoring of medical treatment to the individual characteristics of each patient…to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment. Preventative or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not." Personalized medicine is used in cancer applications for screening, diagnosis, testing, treatment, and predicting disease recurrence.

A key concept of personalized medicine in cancer is that treatments can be tailored to certain unique characteristics of the patient's disease. As such, " targeted" therapies refer to drugs that target specific pathways, processes and physiology that are uniquely disrupted in cancer cells. Some of these disruptions have been discovered to be linked to genetic mutations in the cancer cells. Clinical tests that detect and identify these genetic mutations are called molecular diagnostics. Thus, the availability of the molecular diagnostic test can help detect genetic mutations that might be treated with a targeted therapy. Most importantly, targeted therapy may have fewer side effects than other types of cancer treatments, especially chemotherapy. The discovery of cancer-related genetic mutations, the design of targeted drugs, and the development of molecular diagnostics provide potential great benefits to the mission of personalized medicine.

MolecularMD Oncology Biomarker Diagnostics

MolecularMD, located in Portland, Oregon, provides innovative and reliable molecular diagnostics products and services to support clinical development, regulatory approval, and commercialization of targeted cancer therapies. "At MolecularMD, we are committed to accelerating the pace of targeted therapy development and personalizing medicine for cancer patients," states Dan Snyder, MolecularMD President and Chief Operating Officer.

MolecularMD history

MolecularMD launched their Portland operations in 2006 as a spin-off of Oregon Health & Science University (OHSU) with early seed funding and management support from **BioCatalyst International** . MolecularMD founders include Brian Druker (lead clinical investigator for Gleevec, the first molecularly-targeted anticancer agent) and Sheridan G. Snyder, MolecularMD Chief Executive Officer, (entrepreneur, founder of Genzyme, Upstate Biotechnology and a variety of other companies.) They came together with the concept of a company that could provide precise, standardized molecular testing for new oncology drugs. Dan Snyder, MolecularMD President and Chief Operating Officer, has 20 years of experience in the life science research and diagnostic fields supporting the market development of high value products and services to both pharmaceutical and academic clients. Chief Scientific Officer is Stephane Wong who has over 10 years' experience in cancer research and molecular testing and who started the MolecularMD laboratory in Portland.

Snyder indicates that while Gleevec was the poster child of targeted cancer therapy at that time, and most patients responded well to Gleevec, there was still the need to monitor the patient's disease and the most sensitive way of doing that is through **molecular diagnostics** . Many physicians were not doing molecular diagnostic testing and would miss the fact that a patient was becoming resistant to a drug and there was a potential for relapse and recurrence of the disease. There were also inconsistencies in the existing diagnostic testing. MolecularMD began by developing molecular diagnostic tests with improved performance, reproducibility and sensitivity. Snyder says, "Our mission is to provide innovative, reliable molecular diagnostics that improve and advance personalized medicine to cancer patients."

Evolution of molecular diagnostic testing

In 2001, large companies such as Novartis, Bristol-Myers Squibb (BMS) and ARIAD Pharmaceuticals were working on the next generation of Gleevec-like drugs and required more sensitive tests to measure the efficacy of their new compounds. "These pharmaceutical companies began working with MolecularMD to develop tests that would show why their drugs were an improvement over Gleevec," states Snyder. All three of the pharmaceutical companies adopted the MolecularMD tests for the clinical trials submitted to the FDA and these drugs were later approved as front-line treatments.

MolecularMD's molecular diagnostics menu was initially developed for chronic myeloid leukemia (CML) but has expanded into testing and diagnostics for lung cancer, melanoma, colon cancer, endometrial cancer and hematologic cancers. Molecular testing services are performed in the firm's centralized CLIA-certified and CAP-accredited laboratory. The company's clinical trial services include customized reporting, trial site support, investigator education, laboratory certification and data management. MolecularMD has expanded its services outside of clinical trial research and now offers **Reference Laboratory services** such as BCR-ABL1 quantification monitoring that can be ordered by any physician. They also offer BCR-ABL1, BRAF, cKIT, KRAS, and NRAS mutation testing, histology and immunohistochemistry, and PGx profiler mutation screening. These tests can identify genetic mutations and their dysfunctional proteins that may spur cancer growth. Snyder suggests using the **mycancergenome** website to learn more about tests and therapies that are available for cancer treatment relating to genetic mutations.

Companion diagnostics: Helping develop effective drugs

Increasingly, the FDA, regulators and insurers are pushing pharmaceutical companies to have supporting molecular diagnostic tests to identify which patients will benefit from a drug—this is known as companion diagnostics. MolecularMD develops tests that will later become companion diagnostics; first, the test is used to help pharmaceutical companies with patient selection and to find patients who will most likely respond to a particular therapy in clinical trials based on their cancer genome biomarker (often by identifying patients with a subset of specific gene mutations.) If the drug is approved by the FDA, the molecular diagnostic test used in trials can become the companion diagnostic test to identify the patients that will benefit from the drug.

Molecular diagnostic testing can help identify which patients might be candidates for a particular targeted therapy. Unfortunately, such tests and treatments are not yet available for all forms of cancer. The treatment for cancer often depends on the stage of the cancer. If the cancer is detected early and is localized, then treatment is often surgery or chemotherapy. Targeted cancer therapies are usually reserved for stage four metastatic cancers. However, the cost of treatment with targeted therapies can cost $50,000 to $100,000 a year. “It is critical to get the drug to a patient who will respond based on genetic testing, which is why molecular diagnostic testing is so important,” states Snyder. The response to targeted drugs is also based on the type of cancer. For example, Gleevec was designed to inactivate a specific enzyme and slow the cancer. Other types of cancers, such as lung or pancreatic cancer, can be more complex to target and may require more than a single targeted therapy. Therefore, the biggest challenge in solid cancers is to extend the response time to the drug.

Services across the entire pharmaceutical life cycle

MolecularMD provides services and testing to pharmaceutical companies across the entire pharmaceutical life cycle. “It is exciting work – we get involved in phase 1 clinical development by partnering to help determine which bio-markers and tests are needed to identify the correct patient group. We then validate the testing in a phase 2 clinical trial so the pharmaceutical company can go to the FDA for phase 3 testing. The FDA wants drug companies to have an FDA-approved diagnostic test for the particular drug,” states Snyder.

An example of this collaboration occurred in 2011, when MolecularMD began working with ARIAD Pharmaceuticals on diagnostic tests for a drug designed to treat some of the most resistant chronic myeloid leukemia (CML) cases. The ARIAD drug addresses a patient population having no other treatment alternative so it is being fast-tracked through the FDA approval process. MolecularMD needed to develop the molecular diagnostic test to the highest FDA regulatory standards and was able to develop and submit the tests to the FDA within 18 months; typical submissions to the FDA take 3 years to complete.

Collaboration in personalized medicine

MolecularMD works collaboratively with leading academic cancer institutions and research universities such as OHSU, Dana-Farber Cancer Institute and New York University Medical Center, supporting cancer research and the discovery of genetic biomarkers that are the cornerstones of personalized medicine. The partnership in turn allows MolecularMD to purchase the right to commercialize the diagnostic test to support targeted therapies. MolecularMD subsequently works with pharmaceutical companies developing the drugs whose clinical benefit is measured by the diagnostic test developed at MolecularMD. In this way, the partnership joins the cancer research institute and the drug developers leading clinical trial research with the commercial capability to make the test available to the public. MolecularMD also sub-licenses its diagnostic rights and tests to other labs to ensure the discoveries and technologies are available to patients and physicians. “We believe it is important for community health and for the rights of cancer patients to have access to appropriate testing,” states Snyder.

Future growth at MolecularMD

MolecularMD continues to grow and has big plans for the future. “We have expanded into a 20,000 square foot facility. We grew our staff from 39 at the start of 2011 and now have a staff of 58 and continue to grow. We are an example of a successful life science company within the growing Oregon Bio-Science community,” states Snyder.

Working together to strengthen bioscience in Oregon

MolecularMD is also involved with the Oregon Bioscience Association and has participated in their annual Conference and attends events. “We appreciate the networking events and chances to meet other companies in the bioscience arena. We use their website to help identify and recruit talent to MolecularMD. We have also attended various BioPro training sessions and found them invaluable—this was especially true of the BioPro FDA requirements course which helped our team prepare for FDA submissions. I hope they continue to offer this service to the bioscience community,” states Snyder.

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