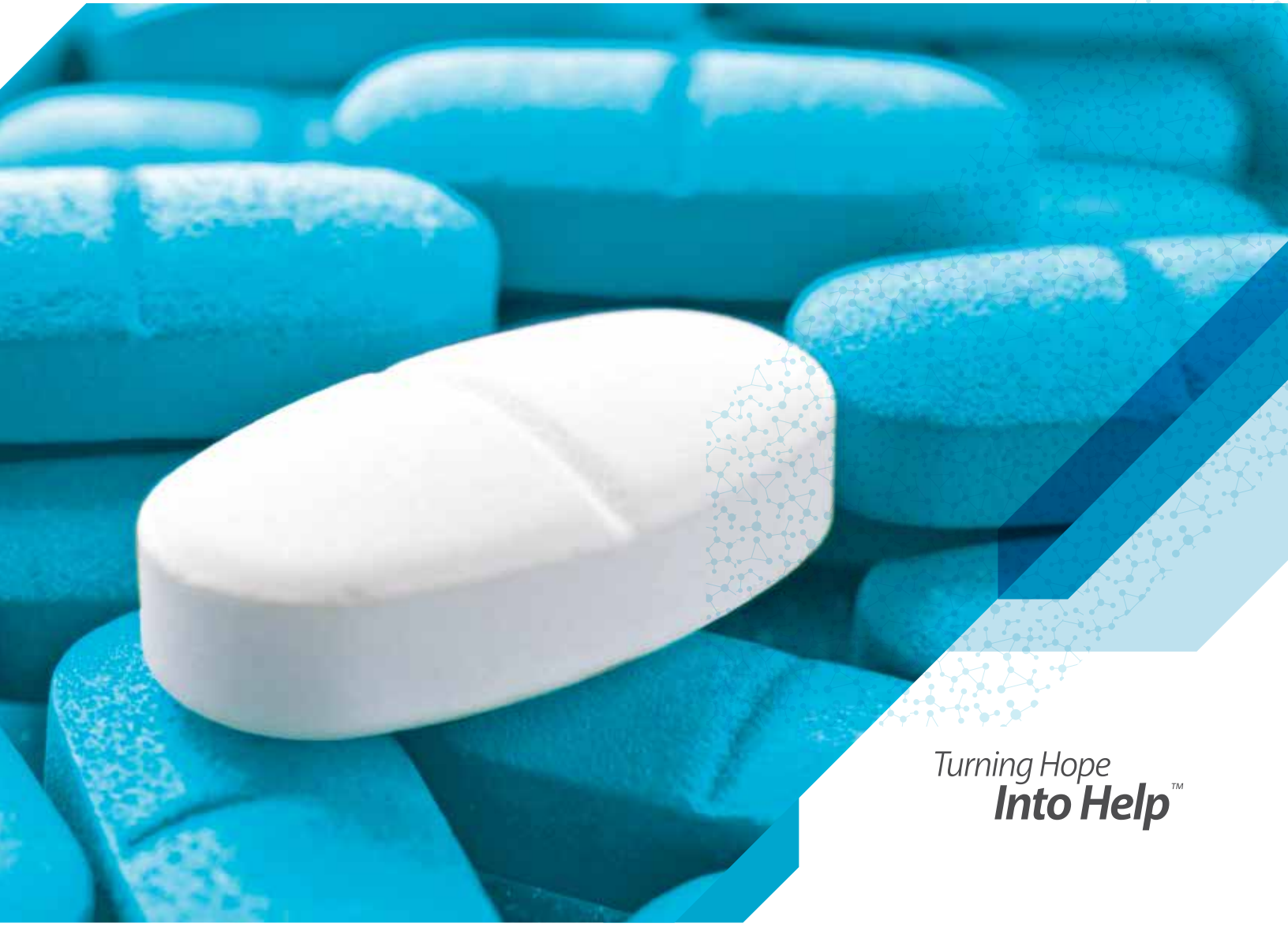
Q² Solutions®



Turning Hope
Into Help™

Companion Diagnostics Expertise

A companion diagnostic (CDx) is a medical device, often an in vitro device, that is a companion to a therapeutic drug, providing essential information for the safe and effective use of the corresponding drug or biological product.

Companion diagnostics enable personalized medicine, or precision medicine, by identifying likely responders based on efficacy or safety. Guidance released from the FDA in 2014 urges developers of therapeutic products to consider CDx earlier in the drug development, and to plan for co-development of the product with a companion diagnostic.[1] The objective of the guidance is to foster relationships that will result in faster access for patients to promising new treatments.

Q^2 Solutions has been able to successfully support drug developers in many of these clinical development programs globally from the early stages of biomarker identification through clinical trials testing to commercialization.

Managing complexities – delivering targeted therapeutics with CDx

Drug manufacturers are aware that companion diagnostic tests can greatly increase the clinical success of drugs by delivering their targeted therapeutics to a subpopulation of patients that has been carefully identified. As a diagnostic assay is part of a patient trial investigation, diagnostic device clinical trials are **two trials in one,** often co-development studies – a patient trial and a diagnostic device trial, or a trial on the instrumentation and/or reagents. This adds intricacies for the clinical trial laboratory advancing a study through analytical and clinical validation, regulatory approval, and market launch to enable optimal market uptake and commercial success of CDx/Rx combination. For instance:

- An investigator is needed for the diagnostic device part of the trial
- Patient samples from the drug trial are used as part of the CDx/IVD (in vitro diagnostic) portion of the trial
- CDx IVDs are usually classified by the FDA as Class III diagnostic devices, and have the highest regulatory hurdle
- Additional regulations might impact the trial, depending on the geographical location of the testing or where the recruited patients are located

We have the scientific and technical expertise and global reach to deliver successful CDx trial execution.

150 clinical studies
conducted with an intended CDx use

[1] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm262327.pdf

From early engagement to launch and commercialization

We are flexible in our offerings to suit clinical development in helping provide testing and data strategies to identify patients for the clinical trials, as well as providing laboratory testing data in the submitted Clinical Study Report (CSR) or provided back to the IVD to support a CDx assay submission. Our laboratories are CAP accredited and CLIA certified – or equivalent – at all our global locations.

Leveraging our parent organizations, we help in the early engagement around trial design and patient identification; and if the CDx obtains regulatory approval, a path for commercial testing globally is available.

Across the CDx life cycle we are able to tailor our offerings to meet the needs of the particular study, beginning with advisory services for development, trial enrollment and commercialization and reimbursement planning. Beyond the feasibility phase, we work with our partners around assay development, laboratory and clinical validation through scale-up, leveraging our global footprint of laboratories and complementary services, for IVD, single site pre-market approval (ssPMA), and inter-lab reproducibility (ILR) studies. We have collaborated over many years with IVD partners, structuring 3-4 way multiparty deals. For an ssPMA route, we can manage the assay design control elements and FDA submission responsibilities, allowing for successful premarket approval.
We have the right relationships to ensure proper access to GMP reagent manufacturers. Our advisory services provide consultation on global implementation of CDx commercial strategies. And, we partner with our parent company's leading commercial laboratory to offer a global commercial solution.

	Biomarker identification	Biomarker selection	Assay development & validation	Global clinical trials	Clinical validation	Submission	Pre-launch	Analytics
Q² Solutions®	✓	✓	✓	✓	✓	✓	✓	
Parent Organizations			✓			✓	✓	✓

Scientific expertise

- Our global central laboratories have laboratory directors and Principal Investigators that specialize in specific CDx disciplines: Anatomic Pathology, Immunohistochemistry, Genomics and Flow Cytometry.
- Our CDx services include in-house global Anatomic Pathologists who have been trained and proficient to report out often complex IHC results. Capabilities in FISH and ISH with specific immuno-oncology capabilities for tumor infiltrating lymphocytes (TIL) measurement are available globally.
- We have a comprehensive suite of genomics services and expertise to help design and deliver CDx using Next Generation Sequencing (NGS) for applications such as tumor mutational burden (TMB) and expression profiling. Most of our Genomic capabilities have been replicated at our Beijing, China facility. For more, see the "NGS CDx" case study in this brochure.

Options for in vitro diagnostic (IVD) or single site pre-market approval (ssPMA) paths

Our experts provide a flexible approach, working in collaboration with our pharmaceutical company partners to choose the right regulatory pathway for optimized CDx commercialization via an IVD or ssPMA path.

Option 1

IVD

Traditional path:

- Most FDA approved CDx, e.g. HER2, PD-L1, EGFR
- IVD leads Regulatory and Commercialization
- Central Labs used for testing – Clinical trials or reproducibility studies

Option 2

ssPMA

May be appropriate when:

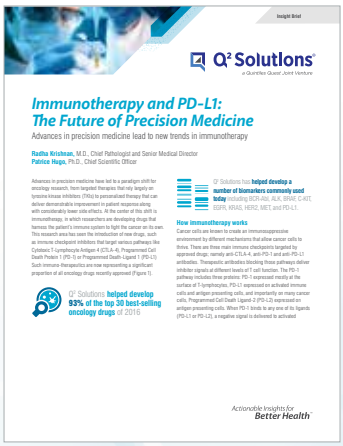
- Defined geography
- Limited size of market
- Short timelines (between clinical phases)
- Big investment in IVD is risky
- Complex testing technology

Option 3

Transfer ssPMA to IVD

Transfer occurs at some milestone, typically before design control:

- De-risks program for all stakeholders



We have helped develop many of the FDA-approved oncology precision medicine drugs, and have extensive experience in the PD-L1 IHC CDx assay. Read more in our insight brief on PD-L1 and the future of precision medicine.

Experience in CDx collaboration and partnering

We have many years of experience in collaborating with established and emerging IVD and life science partners in developing companion diagnostics for simplified multi-party engagements and seamless trial execution. As leaders in co-development, we develop strong partnerships and forge broad and deep relationships between pharmaceutical companies and the IVD CDx partners. Below is an example of a collaboration with NGS:

Case Study: NGS CDx

Situation

- Large pharma and RUO instrument provider (NGS) developing novel, second-generation CDx
- Complexity of data analysis, sophistication of assay platform, and challenges NGS-based CDx necessitated a lab with technical and analytical expertise

Solution

- Collaborative study planning and ongoing, direct communication with diagnostic partner for resource planning and assay-specific SOP development
- With pharma/Dx partners, Q^2 Solutions developed processes and procedures for NGS diagnostics, including development of validated databases in support of the CDx trial and FDA submission

Results

- On-time delivery of quality data for ssPMA submission for a novel CDx assay
- Establishment of approved SOPs and best practices for pharma and Dx sponsor for ready implementation commercially as well as future studies

Integrated solutions for our clinical trial partners

With our global network, dedicated team of experts, and extensive experience, we are uniquely positioned to provide successful companion diagnostics delivery.

Global delivery excellence

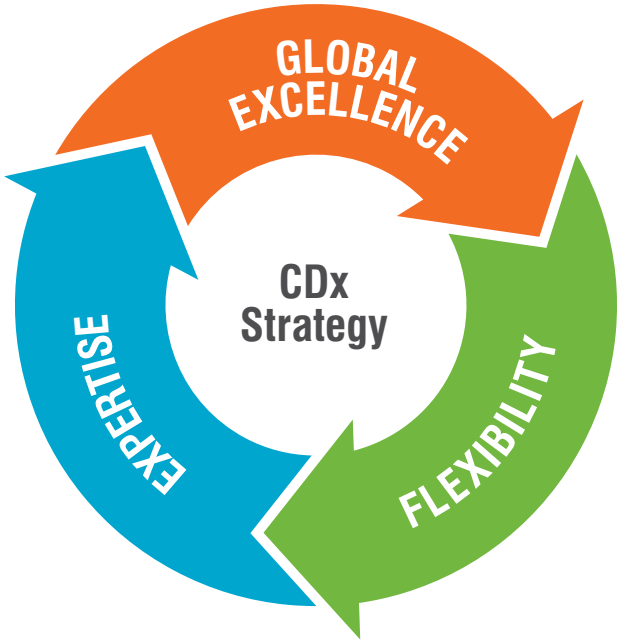
We leverage extensive scientific, clinical, regulatory and operational capabilities & expertise to manage the complexity of CDx trials on a global scale.

- Robust infrastructure with leading methods and processes around managing studies, site support, regulatory requirements, at each of our sites; China CDx experience
- Anatomic Pathology footprint in North America, Europe, Asia-Pacific and China
- Unique software solution for sample tracking through their lifecycle across the ecosystem of sites, labs, biorepositories, and other trial partners. BioFortis, a Q² Solutions company, associates virtually any kind of data, using a powerful query tool to allow rapid identification of stored samples – with specific profiles for demographics, disease state, clinical outcomes, therapy, biomarker results, and other parameters, in addition to consent eligibility. Learn more about the true end-to-end sample tracking technology and services solution, and seamless integration with eConsent.
- Global commercial/clinical diagnostic testing – clinical trial technical and testing capabilities, including China
- Established governance model with oversight management for global delivery excellence, with a logistics and courier network to route samples. Regulatory compliance experts knowledgeable in U.S. and ex-U.S. regulations. Compliance across all sites from setup to data submission, delivering a harmonized and standardized infrastructure. Local and global project management with project managers experienced in CDx studies.

Flexible approach

We work in collaboration with our customers and provide flexible solutions, providing multiple approaches for CDx commercialization.

- Our collaborative method allows flexibility in our delivery
- We can adopt an IVD or ssPMA path towards regulatory submission and commercialization



Proven companion diagnostics

Our strong scientific and technical expertise to allow us to execute on the technologies of today and tomorrow.

- **Commercial** – Extensive knowledge in CDx allows us to provide recommendations on multiple approaches for CDx commercialization
- **Scientific** – We use technologies such as NGS; our network includes global in-house AP services with onsite Anatomic Pathologists
- **Regulatory** – We have a thorough understanding of the regulatory landscape on a global scale, and can define the assay characteristics to take for regulatory approval

As a leading clinical trials laboratory services organization, we have years of experience in companion diagnostics services. There are many factors to consider with companion diagnostics, and our solutions deliver the science, clinical, regulatory, and commercial expertise to support development of your companion diagnostic. Contact us to learn how we can help you.

Contact us

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Q² Solutions®