11th Annual WORLD CB & CDx

AN INTERVIEW WITH

Dr Jude O'Donnell
Head, Regulatory Strategy

ALMAC

Ahead of the digital **11th World Clinical Biomarkers & CDx Summit** (Sept 29– 30), we caught up with Dr Jude O'Donnell from Almac Diagnostic Services to speak on her experience of planning ahead when it comes to clinical trial assay and CDx development and tying this to Dx performance, regulatory compliance and downstream success of a drug development program.

ABOUT DR JUDE O'DONNELL

Following completion of her PhD in Trinity College Dublin and post-doctoral studies in Queen's University College Belfast, Jude joined Almac Diagnostic Services in 2006. Since then, Jude has acted as Team Leader and Program Manager for the development and validation of a series of in vitro diagnostic clinical trial and companion diagnostic assays on behalf of Almac and Almac's global pharmaceutical and biotechnology partners. Based upon the experience gained in these roles, inclusive of leading interactions with regulatory bodies such as the FDA, and her understanding of the entire diagnostic product life cycle, Jude was appointed Head of Regulatory Strategy within Almac Diagnostic Services in 2019 and is now responsible for regulatory compliance within the company.

Q1. This year's summit will be hosting a number of sessions to discuss how precision medicine developers can start to take earlier steps to plan for designing a CDx to advance their pipeline. With this, at what timepoint do you think developers should look to start planning for a CDx, & what criteria could be used to know when a predictive biomarker is needed for a drug?

DEVELOPMENT PLANNING

As the diagnostic strategy can impact the therapeutic development plan, and indeed vice versa, we recommend integrating a diagnostic as early as possible within the overall plan. Early integration will provide evidence supporting the feasibility, scientific validity and likely benefit of a diagnostic to the therapeutic programme. Essentially, the diagnostic should facilitate the therapeutic's ability to improve the standard of care and/or address an unmet clinical need for the therapeutic's intended use population by robust identification of the patient subset that will exhibit the best response.

Early diagnostic planning will also allow for identification of design iterations required to improve and maximise performance, either of the diagnostic or indeed the therapeutic.

It also allows for buy-in by key stakeholders such as operational teams, key opinion leaders, principle investigators, and regulators in the co-development plan which can be critical to the downstream success of the drug development programme.

Within Almac, we do recognise that the 'ideal' up front planning phase is often not realized early enough or practical to implement. In these cases, in support of our Biopharma partners, we have successfully supported key therapeutic milestones within extremely tight timeframes, by employing flexible solutions, whilst always ensuring safe performance of the device and safety of the patient and regulatory compliance.

Q2. We've seen the CDx industry to be highly sensitive to the regulatory & reimbursement fluctuations, how would you say the current landscape can be taken into account for early assay development & validation?

REGULATORY

A good diagnostic partner should be familiar, and keep up to date with the latest developments in regulation around assay development and validation and understand the requirements to provide evidence of safety and performance of the device as per its intended use (purpose). This should be in line with the 'state of the art' to support both regulatory and reimbursement submissions throughout the assay's lifecycle. A knowledge of these requirements is essential to define what is necessary to generate the required safety and performance evidence to maintain compliance at each stage of the assay's development, ranging from the investigational pre-market to the post-market phases.

REIMBURSEMENT

In terms of reimbursement activities, early planning and engagement with payers to address clinical utility evidence requirement for reimbursement submissions is also important. These requirements should be modelled out in a clear and transparent phased manner by your diagnostic provider so that the Biopharma partner is clear on the requirements, both in terms of risk, time and importantly budget.

> **Like Almac, good diagnostic partners should be able to offer global laboratory facilities in multiple regions, with a range of platforms and chemistry options for clients to choose from that can be adapted to multiple disease areas (oncology and non-oncology).**

Q3. In addition to the regulatory component to successful CDx development, what other important considerations are there for Biopharma to take into account for an efficient development & commercialisation strategy?

INTENDED USE

It is vitally important to clearly define the assay's intended use (purpose) as this influences all subsequent development and validation of the product. To do so, it is important to have a clear perspective on the commercial and competitive landscape for both the therapeutic and the diagnostic within the intended markets.

This will also help address key features of the diagnostic, such as platform selection (NGS, qPCR), distribution model (distributed kit V central laboratory delivery), sample collection method (blood, FFPE tissue, fresh frozen tissue) etc. Such planning may identify a suitable diagnostic already available on the market, for which an expansion of clinical claims may meet the therapeutic plan's requirements.

COMMERCIAL REQUIREMENTS DEFINED UP FRONT

Additionally, factoring in the commercial requirements such as the final delivery platform and installed instrument footprint, expectation for reimbursement of the assay by payers and the market landscape including local testing solutions and infrastructure early in the diagnostic plan may reduce the requirement for design changes later in the assay's lifecycle.

Phased planning throughout the assay and therapeutic lifecycle may indicate a requirement for change at particular stages e.g. transition from a central-delivery model to a distributed model due to a planned increase in market roll-out. Such awareness, by working alongside a diagnostic partner that can offer consultative advice and flexible options, can introduce efficiencies in assay development and validation up front whilst maintaining a pragmatic commercialisation plan.

PLAN FOR CHANGE

Finally, planning for change is another crucial aspect we recommend to all our Biopharma partners developing a therapeutic, particularly with respect to banking of tissue and derivative material from clinical trials. The availability of specimens from the intended use population can determine the success or failure of a device programme.

Therefore, we always advise our clients to employ a considered tissue banking strategy from the outset, where possible. This makes available tissue specimens from patients with rare biomarkers, such as NTRK fusions, for the purposes of assay development and validation. Additionally, banking tissue during a pivotal trial allows for future-proofing in the event that change occurs that may require a bridging study further down the line.

Q4. CDx tests have the potential to significantly improve health outcomes, however it can be a challenge for drug developers to identify a partner early on to progress their unique pipelines. Do you have any comments on how Biopharma can approach conversations as they look to secure their next partner?

FLEXIBILITY OF YOUR DIAGNOSTIC PARTNER

In Almac's experience, aside from the obvious indicators of being able to meet timelines and budget, flexibility of your CDx partner is key.

In early phase development, often the Biopharma partner doesn't yet know how the therapeutic is going to perform in early phase trials, and platform selection and other commercialisation options may change as the drug and diagnostic programme evidence is generated. As a result, Biopharma companies need a CDx partner that has the skills and flexibility to be able adapt quickly and pivot with changes in programmes as they arise.

Like Almac, good diagnostic partners should be able to offer global laboratory facilities in multiple regions, with a range of platforms and chemistry options for clients to choose from that can be adapted to multiple disease areas

(oncology and non-oncology). The diagnostic partner should be flexible enough to provide both central laboratory and distributed IVD kit delivery and commercialisation models or a hybrid of both. Additionally, if required the diagnostic partner should be able to facilitate a transition to a platform provider either pre- or post-commercialisation in future, should the need arise.

ADDITONAL FACTORS TO LOOK OUT FOR
In addition, when approaching CDx partners some other elements you should also expect from your diagnostic partner are as follows:

- Competency and experience to ensure development of a product that meets the device's intended use.
- A shared vision for the end goal of the CDx and therapeutic and alignment on the benefits to a defined patient population for the new therapeutic competency and experience to ensure development of a product that meets the device's intended use.
- Innovative capabilities as there are always issues that occur for which the answer is not obvious and may require some 'out of the box' thinking.
- Trustworthiness and open communication channels to ensure a transparent and honest relationship is maintained.
- Commitment – you need to believe that your diagnostic partner is committed to your therapeutic plan and goals and that they have the correct team in place to deliver.

Q5. Lastly, as we see companion diagnostics taking on increasing importance with the growth of precision medicine, what would be your best tips or advice to those considering investment in a CDx strategy for the first time?

Because the diagnostic landscape, both regulatory & commercial, differs significantly from that of the therapeutic landscape, it can be daunting for those within Biopharma to consider integrating a diagnostic into their therapeutic plan.

There is a natural concern over the complexity this will bring as well as the additional cost and timeline implications. Therefore, my best advice would be to select a flexible CDx partner that not only can prove to you that they have the experience required to negotiate the device lifecycle and associated regulatory requirements, but also one that you trust and with whom you have an honest and open dialogue throughout the programme.

This should allow for your diagnostic partner to clearly outline to you what is required, when it is required and what the impact of this will be for you, relieving you of the burden of determining the implications of a diagnostic strategy for the CDx, which is clearly a big commitment.

Thank you so much for sharing your thoughts with us today – We look forward to your session at the World Clinical Biomarkers & CDx Summit in September!

You can hear more from Jude at the 11th World Clinical Biomarkers & CDx Summit this September for her presentation on: 'Clinical Trial Assay & CDx Development in the Era of Precision Medicine – Planning for Success'

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