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BIOANALYTICAL SERVICES EDITION

POWERING THE EVOLVING DRUG DISCOVERY LANDSCAPE

CHRISTOPHER CREAN, FOUNDER & OWNER

XYZAGEN, INC.

COVER STORY

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The pharmaceutical drug discovery industry is evolving. Innovations in the sector are more-and-more powered by seed, NIH and VC-funded companies that are either spun out of academic institutions or are being incubated by venture capital firms based on licensed technology or public-private partnerships. In parallel, a wave of mergers and acquisitions is happening on the scientific operations and process side of pharmaceutical research due to the stability and growth of pharmaceutical outsourcing. CROs have been aggregating, and thus expanding their service areas to be more of a single source provider within either testing, regulatory or manufacturing. This narrowing field of nonclinical, clinical, bioanalytical, and manufacturing CROs that provide full support to large pharma are also looking to support the smaller innovators with their breadth of capabilities. These organizations are not just located within the US, and thus this reordering of "who does what" has also led to the expanded importance of individual consultants with scientific discipline expertise within the industry and the growing roll of consultancy organizations that support early innovators navigating the changing regulatory and CRO landscape while also quickly advancing their client's research programs.

Newer biotech companies don't have time to hire and develop specific in-house expertise to ensure that they are conducting the right scientific studies at the right time to move their programs forward toward their next value inflection points. This is the challenge of the evolving

> **We're not just a bioanalytical lab. We're a hybrid, client focused, drug development consulting and contract research organization**

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innovation environment within drug discovery. These early-stage companies are 'sprinkled' with consultants from regulatory, clinical, toxicology, as well as nonclinical ADME and clinical pharmacology/bioanalytical domains and getting the right team together can sometimes be the biggest challenge. During his early stint as a consultant, Christopher Crean, pharma entrepreneur and founder of Xyzagen, found it extremely challenging to conduct what he calls that First-in-Rodent® PK study for clients where a client may only have 100 mg of a molecule, no wet lab space, and a need to understand the PK/PD of this molecule to determine how or whether to continue to develop it or optimize the molecule chemically due to its poor ADME properties. These are the most challenging of studies to design since they are not guided by GLP or regulatory guidance documents. They are true science stripped down to the barest of objectives and endpoints within the most complex of systems but are still fraught with logistical and scientific challenges. "To run such a First-in-Mouse® or First-in-Rat® PK study, you need a company to develop an acceptable nonclinical formulation, an in vivo lab for dosing, sample collection and possibly pharmacodynamic/ biomarker data collection, a bioanalytical lab for drug concentration analysis and a pharmacokineticist to generate and interpret the pharmacokinetic parameters and evaluate the overall outcome of the study and potentially a consultant to have designed the study for you," says Chris. If this work has to be done at one of the larger nonclinical CROs with multiple capabilities, the client may need to wait for up to four months for a slot, which is a time frame that can cost them valuable time within their program development cycle, and if they go with a smaller CRO for the in-life then they may need to cobble together other CROs to complete the other aspects of their study and still end up delayed within their program development cycle. Chris developed these capabilities in two organizations he worked for in the late 90s and early 2000s and established Xyzagen to help address these challenges and better support the early nonclinical bioanalytical, ADME/PK research requirements that occur with early-stage innovator biotech companies.

After all, the underlying truth in drug development is the formation of teams and strength of relationships to successfully move a potential medicine towards approval. Innovation, logistics, experience and CRO contacts are core components of the successful teams in this sport called drug development—the stronger the team, the better the contacts, the quicker a company can reach its goal.

Since 2018, Xyzagen, has been quantifying its clients' molecules by LC/MS/MS in a variety of tissues and fluids, conducting PK analyses of their non GLP and GLP nonclinical studies, and clinical studies and providing senior-level regulatory consulting, IND/NDA writing, modeling and simulation, and scientific writing. "Our goal is to help clients develop their drugs through focused consultancy or by providing them with rapid data rich rodent PK and PK/PD studies, as well as nonclinical and clinical PK modeling and simulation that will allow clients to advance their programs to the next milestone as quickly and efficiently as possible," says Chris.

Xyzagen supports innovator biotechs as well as small CROs looking to add on either PK or bioanalytical capabilities to their own service offerings to their clients.

> **"Our consultants provide nonclinical & clinical PK/ pharmacology drug development expertise to clients and are the Study Directors for our contract research programs"**

Covering all Grounds

Xyzagen offers tiered accuracy and precision bioanalytical solutions tailored to a client's early discovery needs without the burden of additional costs of project management or QA that comes along in other labs. Xyzagen's senior management has been involved in small molecule bioanalysis since the late 1990s at big and small pharma developing fit for purpose discovery bioanalytical methods for the analysis of drug concentrations in plasma as well as tissue, urine, and feces. Coupled with its First-in-Rodent® approach to data rich PK study design, Xyzagen can support medicinal chemistry screening programs with rapid turnaround on analysis with as little as 48 hours from dosing if the PK studies are run in house at Xyzagen within its vivarium. "We know the importance of early discovery data and that timeliness of results is equally important as accuracy and precision of the method. Rarely is a validated method needed when entering a First-in-Mouse® or First-in-Rat® PK study," says Chris.

Xyzagen is unique within the market place in coupling senior level PK, Bioanalytical, ADME, and Clinical Pharmacology consulting with early-stage discovery bioanalytical and rodent PK/PD services. "We're not just a bioanalytical lab. We're a hybrid, client focused, drug development consulting and contract research organization. We grow with a client from early discovery through IND, and clinical development, and NDA submission," states Chris.

Delivering "fit-for-purpose" Solutions

As a consulting firm, Xyzagen is focused on not just offering a service but rather being a team member who is invested in the client's success. Besides, as consultants and drug developers, Xyzagen can tailor its bioanalytical services to be "fit-for-purpose" through its tiered pricing structure. The company offers three tiers of non GLP method qualification with increasing accuracy and precision. Tier 1 methods are usually for early compound screening, where Xyzagen only tunes the compound on the mass spectrometer and develops the necessary chromatography. These methods are very useful in conducting in vivo PK screens. Tier 2 methods typically include assessment of linearity, sensitivity, and precision in an extracted matrix standard curve. Finally, Tier 3 methods can include multiple batch runs of accuracy and precision as well as stability assessments and recovery. The level of acceptable accuracy and precision increases through the tiered structure, which is typically suited for the compound's stage of development.


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Further, Xyzagen focuses on select mouse and rat neurology, pain, and safety pharmacology models designed to help companies move their early discovery assets forward through focused screening paradigms. This can be used to generate useful data for IND candidate selection either as stand-alone studies or in combination with its pharmacokinetic services for PK/PD modeling or exposure-response comparison. Xyzagen can also collect blood and tissues for assessment of clinical chemistry/ hematology endpoints and histology or immunohistochemistry. Its pharmacology models can be integrated into the First-in-Rodent® PK studies. In addition, they also collaborate with other CROs and Academic Labs in Ophthalmology, Pain, and Neurology and thus can manage the design and oversight of the client's pharmacology program. "Our consultants provide nonclinical CRO vendor qualification, study monitoring and oversight for your nonclinical program," mentions Chris.

Team Holds the Key

What helps Xyzagen in these endeavors is the expertise fuelled by Chris and the team he's building in understanding early start-up companies' needs. Apart from his 25+ years in the industry and being the founder/owner of Xyzagen, the biotech entrepreneur founded and is the majority owner of 1st Order Pharmaceuticals, which developed 1OP-2198, a best in class Kv7.2/7.3 channel opener, that he divested to Xenon Pharmaceuticals in 2017 and is now in Phase 2 clinical development as XEN1101 for partial onset epilepsy. "Xyzagen is building the foundational components of bioanalysis and PK to help clients better understand what the body does to their drug as cost effectively as possible through unique study designs and PK modeling and simulation," says Chris.

In one instance, Xyzagen was able to run a tissue distribution study with non-radio labeled material and build a PK model where they could simulate exposure in the target tissue after repeat dosing, which was sufficient to obtain their next SBIR grant. In another instance, Xyzagen provided a suite of bioanalytical and PK services for a second client's SBIR grant at a cost-competitive price and allowed them to expand their efficacy work with their collaborator and not impact the overall development plan.

Growing with the Industry

Going forward, Xyzagen is focused on bringing new software and analytical innovation to in vivo nonclinical pharmacology and PK studies. Xyzagen is also expanding its services into the in vitro ADME field to support early microsome stability screens, protein binding assessments, and inhibition/ substrate studies. This will help reduce and refine the number of animal studies needed to run while generating more data from the conducted studies. "In the next 1-2years, we see providing expanded in vivo PK/PD services and in vitro drug metabolism study support that will supplement our suite of PK and bioanalytical capabilities," states Chris.

Within 2-3 years Xyzagen also plans to grow its clinical pharmacology and PK capabilities so that the company can operationalize a client's virtual clinical pharmacology and PK group for these up and coming innovator companies. "The first step in this 3 year plan is we're currently engaged in increasing our footprint by 50 percent within our current space so we can consolidate office space and increase lab space," concludes Chris. Ph