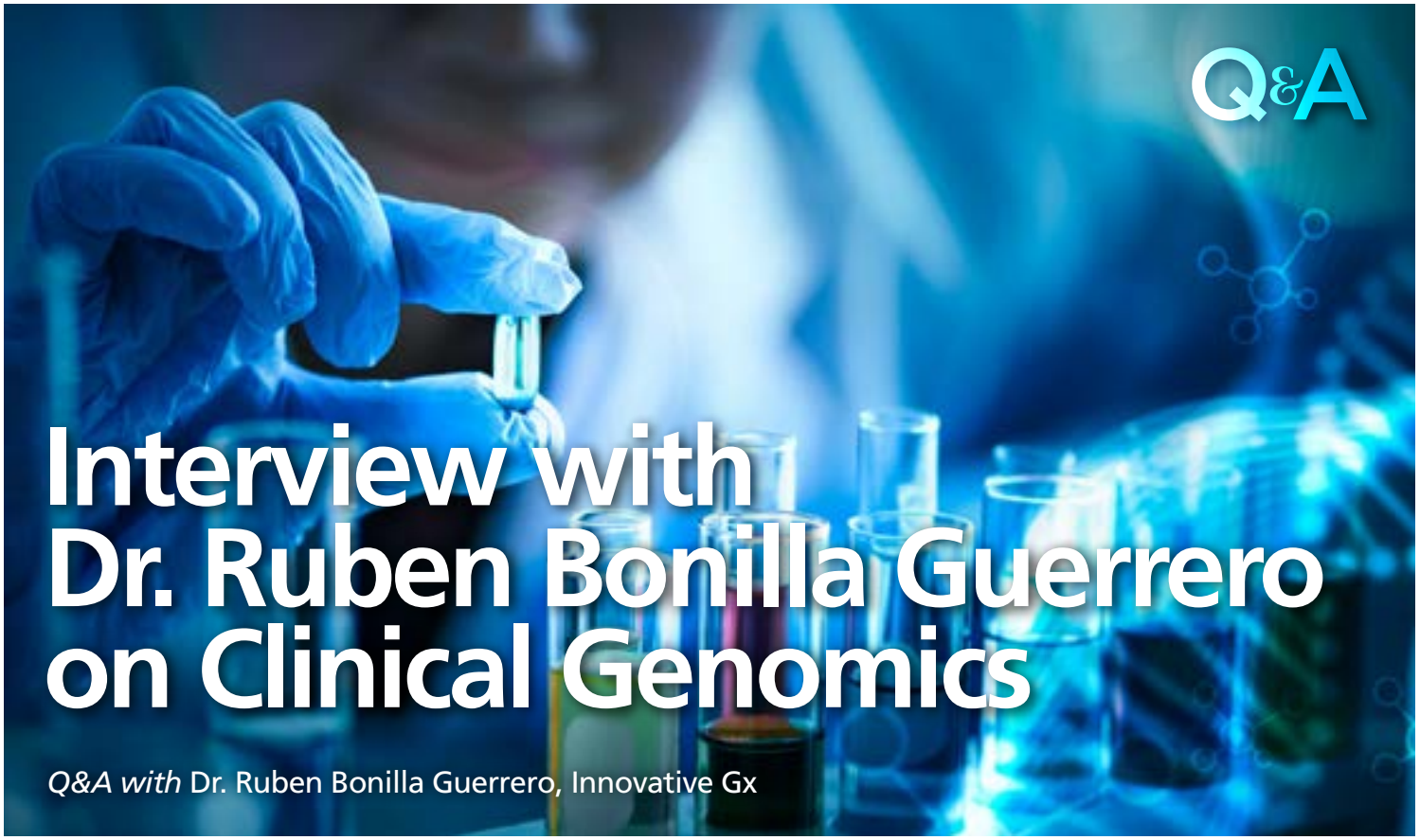

Interview with Dr. Ruben Bonilla Guerrero on Clinical Genomics

Q&A with Dr. Ruben Bonilla Guerrero, Innovative Gx

Innovative Gx (IGx) Laboratories, founded in 2019, announced its Molecular Diagnostic Laboratory opening in October 2020 (CLIA and COLA accredited in 2021). Rubén Bonilla Guerrero, the company's Chief Medical Officer, is responsible for clinical genomic-based testing at IGx and leads the Medical Affairs team.

Dr. Ruben Bonilla Guerrero is an internationally known practicing and laboratory physician with training general medicine, clinical biochemical genetics, molecular biology, and clinical pharmacology. This provides him not only with the proper knowledge to implement personalize medicine but also with the correct background to design and create full precision medicine tests, and in particular pharmacogenomics which requires a deep genetic and pharmacology understanding.

In a call prior to the Q&A session, Rubén mentioned that his experience taught him that even more important than "knowing what to do in molecular diagnostics testing" is "knowing what *not* to do in molecular diagnostics testing." He also learned that there is no such thing as "not in my scope – when it comes to healthcare diagnostics, everything is in scope." Rubén came to understand the need to start with the basics and to build a business on solid foundations.

He espouses the value of precision diagnostics and disavows "diagnostic fishing expeditions" that add cost, yield no information, and may enable off-label use of drugs (when the mechanism of action does not positively impact the pathophysiology of the patient's condition). In fact, he now sees precision diagnostics' potential to link test outcomes with therapies that are the most likely to be safe and effective for the patient.

Journal of Precision Medicine approached Rubén about addressing a few questions; he agreed, and his responses are below.

Q. How have you used your previous experience to create products and services at IGx? How does IGx differentiate its offerings from its competitors?

A. The previous experience that anybody has would allow you to identify the right components as well as the wrong components for everything that you're doing, any shortcomings, any deficiencies, any potential things that were missed, things that were not incorporated, whether it could be selecting technology, whether it could be selecting a mode of analysis, a report layout, all the way to something a little bit deeper such as the way to interrogate the genomic sequences of pharmacogenes or whatever panel we're talking about in general. In the case of pharmacogenomics, those genes that are associated with drug response to make sure that you have the right gene selection (the right gene content), the correct gene-drug pairs with a level of evidence that is not only clinically useful, but also safe.

In that mode, you are able to get the best you can from what you learned from your experience from what you or others did, both right and wrong. That's basically what one gains from experience on anything. It's just applicable here because we're able to identify the specific items that we want to make sure that we do and all the other things that we just don't want to do, because they were not the best or had the expected outcome before.

Now, all this is linked together because it plays into the fact that IGx is a new company, which allows us to do new things or to start things from the beginning rather than correcting things. It is true that it's a little bit more difficult to change something that is already there, even if you have the perfect way in. Perfect biology never happens, but even if you have the "perfect" or the most appropriate method and an already-established process – whatever that is – it becomes entrenched and is difficult to modify.

In this case, we're able to start from the beginning and do it to the best of our knowledge and ability from the start. We look at all the factors – everything that we could have, or should have, considered when building an offering. Those factors go all the way from the technology, the medical, the clinical, the payers' role, streamlining the

process, turnaround time, all the forms required to order the test, the local coverage determination, to whether it is by a government organization and or commercial. All those aspects are considered from the beginning. Since you start from scratch with an offering, you get to incorporate all those factors, to integrate them correctly, to build it as robust as possible, even taking into consideration all those things that may already have been in place if there were an existing assay. Otherwise, it would be more difficult to develop or insert new items.

Starting from scratch really enables innovation, and it's not just me. I am just one of the people who look at innovation this way. The entire organization and the subgroups or sub-teams inside the bigger team, we really encouraged a collaborative form of working. We have a project, a task that we separate into different subtasks. We divide it and assign it to which group would be best to tackle that task. Then we gather again and review all the components and we create it together. It would be the result of a collaboration of multiple people, multiple departments to produce the best for the patient in anything that we do. It could be a simple marketing collateral that's meant for the patient. It could be something as complicated as full-gene sequencing or genotyping. Everything is produced as teamwork.

Q. IGx has an extensive set of diagnostic offerings, does that same strategy go into selecting the types and diversity of the testing panels?

A. It all goes to the needs of the patient. We know that there are certain clinical areas that are prevalent, and they will always be there, for example, need for on time, accurate, precise diagnosing, and treatment. That's why IGx focused on infectious diseases first. Then we asked, how do we complement that? Well, you need to have the right medications. You need to make sure that for ID, and any other condition, the patient is treated correctly

That's where pharmacogenomics comes in. Once we have established those conditions, we may ask later, which of them requires genetic testing, either a proper prognosis or risk assessment, or a diagnosis and treatment, or personalized treatment, or accurate treatment, and timed treatment? We do not just include the most marketed treatment. It's not a popularity contest! Providers do send requests, but we consider the patient and the needs of the patient first. To that end, we always integrate data, and that's something that our CEO reinforces. So that's how we decide. That's the general aspect of the strategies.

We also consider the role of the payers, because the last thing we want to do, and what we will never do, is send an unexpected bill to a patient. We want to make sure that what we build not only meets the clinical and medical criteria to be useful, but also meets the technical and medical requirements of the payers to make sure that it has the right technology, the right analysis, the right level of evidence for anything that we produce. So that is, in a general sense, the strategy that we follow.

Q. Do you also ensure that if the test is positive or whatever indication, that there's a medication for that assay?

A. If there is a particular FDA approved medication for that diagnosis, yes. We make the link, and we bring to the provider's attention any other tests that may help to treat the condition directly or the added supportive care for the condition, even if we do not offer such test. A particular condition could be the treatment for that instance, but also other symptoms that the condition, or other aggregated comorbidities and the condition itself, may produce. So yes, we do that.

"One of the most critical parts is presenting that information in a clinically useful way – clear to understand in a safe statement for the provider to be able to implement for the patient. That is the part where you not only have to have a very good understanding of what you are analyzing, but also the clinical implications. The analysis and implication must be put in words that make sense for the provider, not as a recipe, not as an instruction, but to give them insights about what is going on with the patient so they can properly act on the patient."

Q. What are the means or the process of adding more tests to the portfolio?

A. We build or expand the portfolio to address patients' needs. There's nothing more personal than your DNA, so everything will be specifically for you. Of course, different areas will grow differently, whether it is hereditary cancer genetics, oncology genetics, neurology, hereditary cardiovascular genetics, you can speak of them as being part of the personalized medicine portfolio. But there would not be sudden growth in one area without due diligence.

Q. You spoke about the value of information in the context of the patient as well as the need. Can you talk about how IGx has created value and the information generated by its test compared to other offerings? For example, what types of data are generated from quality protocols? What differentiates the actual quality from IGx of the data?

A. Data is a very interesting item because data could be good data in a bad process and badly presented or bad data with a very good process and very well presented. So, it starts with the quality of the data. Of course, what comes out of the instrument must be of the highest quality – composed by the quality of the instrument; the quality of the design of the assay; the components of the actual assay; and what type of information we get out of the assay. It is important that all those components are considered when you put together an assay to ensure that the resulting data is reliable, reproducible, and truly reflects what the assay is meant to indicate clinically.

Then you follow up with processes to analyze the data further, the so-called bioinformatics. More recently, some want to go all the way to artificial intelligence, but it often boils down to the same thing.

If bad data goes into those processes, you are going to get bad, beautiful results. One of the most critical parts is presenting that information in a clinically useful way – clear to understand in a safe statement for the provider to be able to implement for the patient. That is the part where you not only have to have a very good understanding of what you are analyzing, but also the clinical implications. The analysis and implication must be put in words that make sense for the provider, not as a recipe, not as an instruction, but to give them insights about what is going on with the patient so they can properly act on the patient.

Q. Does the data include clinical panels for the patient? By that, I mean, do you run several different assays and turn that into a panel to come up with a more precise diagnosis and a more precise treatment?

A. It depends on what you need from an assay. Not all assays have to be a panel, but there are cases that require multifactorial analysis to produce a result. In that case, several assays may need to be analyzed, whether, as in our case, molecular genetics or it could be several different type of assays that need to be performed together and in parallel – meaning at the same time to produce a comprehensive approach and clinical assessment of the patient. Those cases will require panels. For those cases for which only one component is necessary to make the correct diagnosis or to establish the correct treatment, then they will be

treated as such. It is important to make sure that one only analyzes and uses the information that is required to produce the best outcome. That is not dictated by whether we want to have a single analyte test or a panel test, but by what is required by the principles and the clinical outcome that you need from that test. Above all, it is determined by the clinical necessity of what a potential given diagnosis requires to establish a correct result.

Q. Do you include patient history or family history as part of that analysis?

A. Everything that we do is related to the patient, so all assays require information to make sense of the analysis. Of course, you get the patient information, the patient's demographic, clinical history, pharmacological history, family history, and any other potential information that is useful. Some assays in the future may require a radiological assessment by another provider that could indicate that A plus B plus C equals D. Do you actually need that information? Let's say infectious diseases, which truly identifies only one pathogen in most cases, in which case you may not need a comprehensive clinical work-up. Other assays, however, require complex algorithms to come up with a risk assessment or potentially identify differential diagnosis between similar conditions. Some may even be associated with the same gene or potentially different variants at different locations – in those cases, yes, you will be using clinical information to help with that assessment.

Q. Along those lines of doing a risk assessment on more complex data types, what type of analytical or computational tools does IGx use to extract and validate data for its patients?

A. To start, we use the tools necessary to ensure the depth of analysis for the condition we are testing. For instance, analytical tools for infectious diseases will be very simple to ensure we are accurately detecting what we're supposed to detect and not detecting what we're not supposed to detect. On the other hand, for a genotype assay that targets specific sequences, we need to make sure that we detect those sequences and that we align them correctly to produce the correct genotypes, and then pair them with the correct databases for clinical information.

We would execute a deeper type of analysis if we were to do whole-gene sequencing in which we not only have to consider the clinical information but identify the clinical meaning of any variant that may have not been classified. Those that are classified that can be directly annotated, but those that are not, need further analysis.

We use several tools to make sure that the quality of the results is the highest possible. Our bioinformaticians, who have a genetics background, design and create tools and also suggest commercially available tools that we potentially could use if they meet our quality criteria and clinical criteria. Again, it's not just because there is popular software or one that everybody uses. We use the correct tool for the task in hand.

Q. How do you see your role in providing education to payers about circumstances for which a molecular diagnostic test would most benefit a patient? What is the process to engage in such dialogue?

A. We weight two components for this process, and it is something that is very near to my heart because I believe that everybody should get the benefit of modern medicine. I'm not just talking about molecular genetics. Modern medicine encompasses many different fields, different technologies, different procedures, medications, and tests. What we need to do in the general sense, and, especially in molecular genetics, is approach the payers with both components.

"For us, it all comes down to integrity, responsibility, and ethics. It just comes down to that. Why? Because there's a patient behind the testing. You must do the right thing for the patient, period."

We acknowledge that payers. including government organizations, act as a kind of financial institution. They do have a bottom line and a financial responsibility to the company to minimize costs. We, on the other hand, need to keep the patients first and show that there is a clinical benefit of the tests; but we also need to show the economic benefit of being precise with each patient in a way that allows for the best outcome in the shortest time, specifically by recommending the most appropriate next steps, which is faster than using trial and error with the patient. Trial and error approach is not the right way only for medications, but also for diagnostics. For some tests depending on the patient's holistic current and future benefit, we must move away from "Let's do test A, and if test A comes back negative (or even positive), we do B, C, D and such." Same thing with procedures. This model is still useful but only in instances when the clinical benefit and the cost-effeteness of the tests suggest this approach.

We need to reduce trial-and-error approach as much as possible because it has a cumulative greater cost than getting the correct, most appropriate, and most useful information from the start. The way to approach generating results for a patient is by doing the proper laboratory analytics and data analysis, showing a clinical, health, and economic benefit for the patient. You could have a patient coming in that is taking the "correct" medication for the condition; unfortunately, it may turn out that the patient happens to have an uncommon gene variant that produces a severe adverse drug reaction.

Something that could have been easily resolved ends up putting the patient in the hospital with a life-threatening adverse drug event or reaction that costs twentyfold what the medication originally cost. You can have a patient paying, say, $50 or $60 for a medication and end up with a $100,000 bill for the health institution, the system, the insurance, etc. We avoid that scenario by using one test that costs a fraction of the outcome that allows us to switch the patient to another medication. Precision medicine is not just about medications. We see the same thing with medications, diagnoses, and procedures. The best medicine is preventive medicine, precision medicine is preventive medicine.

Q. Your point about finding a potential adverse reaction to a drug is exactly to the point. What's the process for engaging in those dialogues? Do you compile evidence and present it to the payer to switch medication case-by-case, or do you have some means of holistically approaching the payers?

A. You have to approach payers holistically, but you do need the evidence to show what we just mentioned. You have to show the facts of clinical and health economic benefit, that there is a financial benefit for the patient, for the institution, for the payer, for the network. We are responsible as healthcare providers to make sure that one provider (MD, RN, PharmD, or GC) is overseeing patients, and one provider (MD, PhD, PharmD, or GC) in the laboratory oversees the types of procedures or test types , to establish the correct connection in a responsible way to address the patient's needs.

It's our responsibility, and it's a legal duty, to make sure that we always use what is correct for the patient and to produce the best outcome. In that way, we show the payers – by facts – that something they're not covering today will produce not only a clinical benefit for the patient, but also a financial benefit for the organization. We are responsible for making the case that they should be spending X amount of money upfront that is a lot less than the undesirable outcome of choosing the wrong test, the wrong medication, the wrong procedure. Simply, you must show the facts.

Q. How do you position your discussions

with healthcare providers or healthcare system leaders about the value that IGx brings to testing and the subsequent data and information?

A. We are constantly in conversation with healthcare providers and leaders. We have ongoing discussions with them to approach them about what we do, the way we do it, the value that it has, how it differentiates us in general, and to show that what we are doing is not only correct, but it is substantiated by evidence.

Again, I can tell you that it's not an easy or fast process. It's a very slow multistep, long-term process, but the outcome is worth it because the outcome is simply better care for our patients. The process may be painful for as long as it may last, but it is worth it because the outcome is the benefit for the patient.

Q. In our preliminary discussions, you emphasized that the quality of a test is its ability to provide actionable clinical utility. To what extent has IGx been able to close the loop and access data for test results to determine the impact of the test on patient treatments and outcomes? In other words, do you find out the clinical utility of what you've recommended to patients?

A. That's very important to us because even changes in regulation now require, at least for pharmacogenomics, that laboratories establish a continuity process that starts from ordering the test, performing the test, producing the test. Now, here's the part I like, and many people do not appreciate, is the need to follow up and ensure that pharmacogenomic testing and the resulting recommendations are timely implemented per provider's consideration. I love that part because many tests, including pharmacogenomics, may be ordered and carried out but reports end up in the drawer. These reports are put together well and have an amazing wealth of information, but the recommendations are never implemented.

The most common reason is that providers do not feel confident enough to interpret and act on pharmacogenomics results. The key point here is about interpreting pharmacogenomics results – we do not look to providers to interpret results, we interpret the results and offer them in clinically useful, safe statements so providers can act on them.

More to the point – we establish a process through a stewardship program in which we follow up with the providers to assess whether they need any support. You cannot be a laboratory or a healthcare institution that produces a result and then forgets about the provider – remember, there's a patient behind the test. You must follow up with them. Medicine is complex enough that it requires multidisciplinary teamwork. You need to work with the team to get to the patient, to do the right thing for the patient. That's why our organization has a team of PharmDs and Genetic Counselors (GCs) that will follow up with the provider. They are trained about our tests, so they understand the results, they understand the different components of the report, how to use it, how to implement it. We will provide all the supporting forms and documents to use to make that process easier.

And while it may be true that pharmacogenomics is disruptive, I mean it's not just the technology itself but also the process. It requires pre-testing assessment, post-testing assessments. You potentially may have to see the patient more than one time to use all the information. Remember, just because a test tells you which medication is most likely to work on the patient in a clinically useful and safe manner, that doesn't mean the patient is going to respond to them overnight. You need to monitor the patient and assess if you have to change or adjust medications again based on the clinical information from the follow-up visits – you get to fine-tune what the patient needs using the test results, providers, knowledge, experience, and clinical judgment. That's the nature of personalizing. It's not just black and white or that immediately, you get the best outcome. You still need to work with the patient, and we provide support for that.

Q. So, it's not just trial and error – it's more iterative, learning as you go?

A. Yes, and using the data correctly to "retrofit" what the providers are finding in the course of treatment. That feedback is crucial for us. We take all feedback into consideration, whether it's instruction on a form, whether it is the way we report, whether it's the layout, whether it's the language, everything, everything.

Sources keep changing and we keep up with all the sources. Sometimes a provider checks the data and tells us, "Hey, this source has been updated. Can you make an update to the report?"

We are establishing all these processes to make sure that changes are identified as fast, often, and automatable as possible. However, we still need to assess the change to evaluate if it grants changes to gene-drug pair interactions or if they go all the way to suggest changes to our assay. All that is taken into consideration.

Q. IGx offers a genetic counseling service to patients and physicians to help understand test results and answer any questions through throughout the process. Can you discuss how you came to offer this service and what value this service has added in terms of providing patient care?

A. That is an important point because we cannot assume that the interpretation of laboratory results for genetic testing simply be left to the provider; of course, certain providers are more than qualified to read and interpret even raw data depending on their training, but the vast majority are not.

The whole point of personalized medicine is to become the standard of care, which means that it's not going to only be used by the specialist only, but the general provider, the general practitioner, the primary care provider, and the family doctor (who has a very good knowledge of everything but may not have the depth of knowledge to interpret genetic results, however, some do).

We play our part, not only by providing the clearest reports possible, but also by supporting healthcare providers with our laboratory stewardship program which includes GCs, PharmDs and infectious disease specialists.

For a genetic diagnostic test only, a genetic counselor is the most appropriate person for follow-up. For a genetic test associated with medications, a PharmD and a genetic counselor are the right team to approach the provider or the patient. For infectious diseases, an infectious disease specialist or a PharmD would be best because you're treating a pathogen.

We do this for the providers and for the patients when required. Usually, when you give this assessment, this aid to the provider, they can handle the work and pass it on to the patients. Few of them will require us to have a three-way conversation with the patient and the provider to make sure that they all hear the same message. We explain things to them the same, so there's no loss in translation or the message is changed from what we have to say.

So that's how we handle it – the provider is there, our counselor or PharmD is there to make sure that they all hear the same message. The provider and counselor need to be present in case the patient asks questions that may be related to the test or the treatment, but they may also ask questions related to pharmacogenetics. We don't treat patients. We don't suggest any treatment. We only supply information for the provider to use, to act on for the patient's benefit.

Q. You shared data results with the genetic counselors, but do you also share with them any lessons learned that you've been able to glean from having worked with genetic counselors before?

A. Yes, we do. During our educational series (currently in preparation) we will use a "ground rounds" format or a morbidity and mortality (M&M) case analysis in which we will basically

teach what we've done, how we done, what we've learned. That is actually very important to do because that's how you evolve in a positive way.

We recognize that all labs will have imperfect results at some point. Sometimes it could be human error. Sometimes it could be a technology error; sometimes it could be a product error. Remember, we use things that are manufactured for us. There could be a manufacturing process problem that isn't performing correctly, could be a timing problem that the person didn't put the right time for whatever process it was. We do learn from all those processes and establish the procedures to prevent that from happening again. Many people do not like to talk about that, but one has to acknowledge and address those facts to positively evolve. If any lab tells you that they have never ever had a quality reportable incident (RQI), run away from that lab as fast as you can, ha! I am not joking!

It's an important responsibility of the testing lab to learn from its shortcomings and, while such shortcomings may be few, we have to learn from them. That's the only way we evolve. How you inform, how you correct, how you act, and how you produce a corrective action for whatever happened – what you do and how you do it is what makes the difference.

Q. Have you put together, say, a list of frequently asked questions or case histories that you share with genetic counselors?

A. Yes, that is part of the program that we have. The frequently asked questions come from all different areas – infectious diseases, genetics in general, pharmacogenomics – and we put them either as FAQs or as a glossary, so they understand the concepts or what we're talking about and what we do.

Things that may be very simple for us may not be simple for others, so we make sure that we put reports in a way that the final understanding is the same. You may not know the process, but you understand the same from it.

Q. Have any lessons learned from the genetic counselors been used and fed back to the development teams or the testing teams that has caused them to do something different?

A. That always happens. It's not just the GC. We learn from our GCs, the pharmacists, our amazing sales team. We get feedback from all levels. All the information is used for the next version of what we offer. We are always moving forward and integrating all that feedback into all parts of the process. As I said, most labs only focus on the assay. We don't. We do everything. We incorporate and consider everything, including supporting the documentation to help providers identify patient eligibility for their corresponding payers.

Once the test results are produced and our team talks to a provider or a patient together, recommendations may include, believe it or not, test that we do not perform or a test that maybe at that time point better than our test. That's very important because we want to be an unbiased laboratory. We will recommend whatever is necessary for the patient's better outcome.

Q. Last point and we'll wrap up. Do you have any final comments on plans for molecular diagnostics at IGx or any other point you would like to raise?

A. We are a 100% patient-centric organization. That comes from the top – that's the view of our CEO, that's the view of our CFO, that's the view of our CBO, that's the view of myself, the CMO, and that's the view throughout the organization – the needs of the patient comes first.

I'm a stickler to that view because I was trained at Mayo Clinic and that's exactly their motto. It's deep within me, even before I was at Mayo, that's the way that it is. If you are in any way in healthcare, not just a physician, you have to have the needs of the patients first, period. There's no other way around.

We are in a very exciting time in IGx history. We are just about to produce one of the most exciting, comprehensive, and clinically useful pharmacogenetic offerings, and then we're moving immediately to other areas with the same approach. So many things to come – and not only limited to molecular genetics. We will expand into other areas that complement molecular genetics and vice versa. It's always necessary to expand the test menu to produce clinically useful tests that complement what you already have to provide a more complete assessment for the patient.

But again, because we are starting from zero with many of these tests, we can seize the opportunity to create, build, produce, report diagnostics correctly, taking all into consideration – the technology, the clinical aspect, and the payers' aspect of the test. We are at a very exciting but crucial time for IGx. We believe many good things are still to come. For us, it all comes down to integrity, responsibility, and ethics. It just comes down to that. Why? Because there's a patient behind the testing. You must do the right thing for the patient, period.

JPM: That's an important message. Thank you again. JoPM

Lessons Learned:

- Responsible Genetic Testing – Test what is holistically clinically useful for the patient today and tomorrow.
- Comprehensiveness and Cost-effectiveness are not mutually exclusive.
- Patient care in all its forms is a delicate privilege that comes with responsibilities that need to be closely guarded and continuously improved.

About IGx

Innovative Gx Laboratories, a Texas-based CLIA certified and COLA accredited advanced molecular diagnostics company, specializes in developing personalized medical solutions using real-time RT PCR and DNA sequencing. The company is a leader in applying molecular genetics to provide more accurate and faster testing for Respiratory Pathogens, Infectious diseases, COVID-19, and DNA-based Pharmacogenetics (PGX) to improve patient outcomes. Founded in 2019 by a team of career medical diagnostic scientists with a combined 30+ years of experience, Innovative Gx is dedicated to providing the highest-quality clinical testing services through high-accuracy testing, ship-to-home diagnostic kits, in-office support, and rapid results for its physicians, hospitals, and clinics nationwide.

Dr. Ruben Bonilla-Guerrero

Ruben serves as Innovative Genomics (IGx) Laboratories' Chief Medical Officer. He is a laboratory professional, who is Mayo Clinic trained in Clinical Pharmacology, Clinical Biochemical Genetics, and Molecular Biology, a Fellow of the American College of Medical Genetics, the American Association of Clinical Chemistry, and is an active member of several distinguished professional organizations. Dr. Ruben Bonilla-Guerrero board certified in Clinical Biochemical Genetics by the American Board of Medical Genetics (ABMG) and in Molecular Biology by the American Society for Clinical Pathology (ASCP), with expertise in clinical pharmacology, inborn errors of metabolism, genetics, vaccine development, and clinical pharmacogenomics. Having authored several peer-reviewed medical publications including book chapters, Dr. Bonilla-Guerrero is also the winner of the Henry Christian Award from the American Federation for Medical Research (2002) and the Mayo Clinic Department of Internal Medicine Outstanding Research Fellow Award (2003). Previously, Dr. Bonilla-Guerrero simultaneously served as Laboratory Director, Associate Medical Director, and Medical Director of Medical Affairs for the department of Genetics at Quest Diagnostics, as well as concurrently served as the Medical Director and Vice President of Medical Affairs at Admera Health. He is responsible for the clinical genomic-based testing at Innovative Gx Laboratories and leads the Medical Affairs team.