*Jubilant Biosys*
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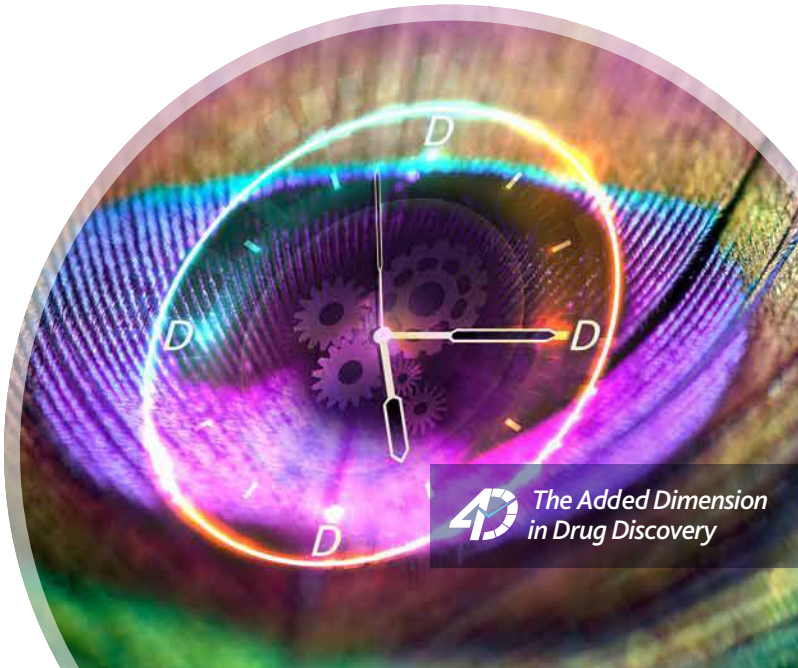
# **Now & Next with Jubilant Biosys:** The Evolution of BioPharma, Drug Discovery, Development, and the Road Ahead

***Saurabh Kapure**, Vice President, Business Development, USA for Jubilant Biosys, recently sat down with **Siegfried Reich**, Ph.D. Co-founder and Senior Vice President, Research, at eFFECTOR Therapeutics. eFFECTOR Therapeutics is a clinical-stage biopharmaceutical company at the forefront of the development of selective translation regulators (STRs) in the treatment of cancer. In an hour- long conversation, they discussed the latest developments in the industry and at eFFECTOR. Dr. Reich also shared his thoughts with Saurabh about his role at the company, the evolution of biopharma, drug discovery, development, and the road ahead. The following Q& A, which has been lightly edited for clarity and length, are key excerpts from their conversation.*

*This is the latest installment in Jubilant Biosys's series, "Now and Next," which highlights select innovators and developments in the biotech industry, and profiles some of the most consequential figures and conversations in biotech and drug development today. To access all available "Now and Next" issues, please visit our website **here**.*



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***Jubilant (Q):** What does eFFECTOR Therapeutics do, and why does it do it?*

**Siegfried Reich, Ph.D. (A)**: Let me start by saying there are so many truly interesting things happening at eFFECTOR right now, it would take us far more than an hour to go through them all. It's a very busy, exciting time for all of us.

Since its inception in 2012, the genesis and basis of eFFECTOR Therapeutics has been to dive deeply into a new area of biology specifically with a view towards cancer therapy. We're a clinical-stage biopharma company focused on discovering and developing new, small-molecule cancer therapeutics.

***Q:** How are you doing that?*

**A:** In a number of ways. But at the highest level, we're pioneering the discovery and development of a whole new class of oncology drugs known as "STRs," or selective translation regulators.

Cancer is a daunting disease and very challenging to treat therapeutically. The reality is, cancer treatment is in dire need of fresh thinking and approaches beyond what has been done during the past 20 or 30 years of cancer drug discovery, development and treatment, despite the amount of progress made in that time.

One of the things we're focusing on at eFFECTOR is a specific area of biology which hasn't really been directly addressed or drugged, per se. To date no one has really put into the clinic, nor brought to market, in a meaningful way, drugs that specifically address RNA translation, or that control RNA translation. This is a key area of work for us.

***Q:** Can you say more about this?*

**A:** We've concentrated our efforts on control of mRNA translation as a central point of therapeutic intervention, providing potency and selectivity while also effectively inhibiting the growth of cancer cells. We have designed and are developing selective translation regulators - small molecule drugs - to selectively block dysregulated protein translation by acting on the components that control it, and ultimately impacting tumor growth and survival.

This is a truly novel approach, and it's an approach which provides a wealth of potential opportunity to bring innovative new medicines to market and, most importantly, to the patients who need them.

***Q:** Let's take a step back to briefly define a couple of terms. What do you mean by "translation" and what do you mean by "transcription" in this context?*

**A:** It's a good question. The difference goes to the very core of what we're doing. "Transcription" is the copying of DNA sequences into mRNA. It, along with specifically targeting oncogenic pathway inhibition, has been pursued in cancer

drug discovery and development for years and rightfully became the status quo. While the regulation of transcription - its mechanics and dynamics - is understood, drugging actual transcription directly has been difficult. Our focus at eFFECTOR is more on "translation." Translation refers to the conversion (translation) of mRNA sequences to specific proteins.

A couple of other useful points to refresh ourselves with - DNA gets transcribed to RNA (mRNA), and then RNA gets translated to protein. Our normal functions are dependent on that translation.

Now, what really wasn't fully appreciated before in our field is just how tightly controlled this translation of (m)RNA to protein can be – that it's reserved for only very select RNAs, and very select proteins. For various reasons, there was long-standing and, as it turns out unfounded, belief within our field - to the point where it became dogma - that if you mess with these biological control mechanisms - the translation machinery - you're going to have untoward effects on all of your normal cells as well, you're not going to be safe. I intentionally use the term "dogma," assumptions that people lived with and worked around for so long that the assumptions were beyond reproach. But as we now know, that turned out not to be true.

While translation itself has been understood for more than 50 years, for various reasons like portfolio constraints, aversion to taking risks, etc., no one really tried to go after it until only the last decade or so. Some companies including large pharma have tried to drug some of the same targets we have worked on, but ultimately were unable to get to the development of a drug-like molecule and couldn't rationalize the investment of time and financial resources that were necessary to crack these targets. eIF4E for example has been deemed "undruggable". In contrast, our view at eFFECTOR is translation is an area of immense potential, and one that's definitely worthy of focus and investment. It represents entirely new ways to treat cancers specifically because tumors are so dependent on dysregulated protein translation.

### *Q: Can you say more about translational control and targets?*

**A:** The targets we're talking about, that are involved in translational control, I characterize as "non-trivial targets." What I mean by that is they're hard to drug with a small molecule. While some pharma companies might have looked at these targets in the past, they weren't successful getting to 'a drug-like molecule.'

In a small company like eFFECTOR, we don't have a large portfolio. That is by our design. Because we're narrowly focused, a central question for us is how can we be successful on these targets rather than deciding mid-stream to go find some new targets that might be more tractable. We don't have the luxury of thinking, "This target is hard. We'll try it but we're going to back off if there's any question at all about whether it will be successful, or things are moving too slowly." It's ultimately a test of perserverance. But we always required that there be a positive trajectory on the programs, to ensure we weren't spinning in circles and wasting our precious funding.

eIF4E is one of the programs we've pursued where we know several pharma had looked at and took a pass for the reasons I just described. That happens sometimes. A pharma company might try to do a drug discovery program but there's a failure to progress, and a defined limit of how long to work on a particular target in a large portfolio. For us, however, it's a different story. There's an interesting dynamic that reaches across the entire industry – how perserverant can a team or company be with a given target, particularly in a new area of biology and drug research?

By the way, eIF4Eis one example of several projects that we've done in partnership with Jubilant Biosys. For this particular project, we've been collaborating for over five years.

***Q: Let's shift gears. Tell us about your role at eFFECTOR Therapeutics as head of research and how your work fits into the overall context?***

**A:** The first thing I want to say is that I love my job and it's an incredible opportunity. I've felt like this since my first day. For context, I've previously worked at both small biotech and several big pharma companies in my career. But more importantly, we've attracted amazing talent, to all areas of our organization, and they are the ones who have made the difference.

My job at eFFECTOR is multi-faceted, which I is another thing I love about it.

My responsibilities often include monitoring and managing (at a high level) the progress of our key drug discovery projects. We have excellent, highly experienced project leaders who do the real nuts and bolts work on this, but I help ensure that certain key timelines are on track and remain on track. We're on the aggressive side of timelines in the biotech sector.

I also help our teams define and then keep their eyes on the larger goals for each of our major projects. Helping set and achieve the various visions. Metaphorically, I function almost like glue at times – helping hold things together, bring cohesiveness and keeping everyone focused on the goals.

Part of my job is to provide a sense of stability amidst all the inevitable chaos of extremely sophisticated research, dealing with huge amounts of data jumping around, and at times daily setbacks. When I say stability, what I really mean is reinforcing the belief and inspiration that we're going to slay this dragon – not in a blind faith sort of way – but rather, in the form of facilitating things like coherent discussions with everyone on the team as we're moving through some difficult, and some less difficult things.

In that way, my role is to be a reminder to the team that we are progressing, and that we will ultimately succeed. So, it's also about inspiring the team and helping everyone stay focused and at times get re-energized. Certain projects require this more than others.

A very important aspect of my job is that I am part of the leadership team at eFFECTOR. This is particularly interesting for a number of reasons not least of which is because I'm also very much down in the trenches of our research work every day. I still love to design compounds on various projects because I'm a chemist and I love to do that. I'm fortunate that I still get

to do some of the more-in-the-weeds kind of stuff. A related challenge this brings though is I also have to be something of a liaison between the leadership team, which of course is trying to keep the ship going in the right direction, keep the lights on, etc. – and the research group, the scientists I work with on the ground level where the real teamwork and progress actually happens.

So, there's also an important continuity aspect to my job too which is successful only through clear and frequent communications to the research group as well as throughout

the whole company. Good communication is one of our single most important challenges and tools.

Possibly the most challenging, and certainly interesting responsibilities I have is to help figure out and implement, solutions to truly critical issues like how to function most effectively as a team. eFFECTOR's success is ultimately a product of the full project team, and every individual is critical to our success. Thankfully, we've built a really great team here, but this is an ongoing task due to challenges and the inevitability of set-backs in our work, organization changes, competitive changes, etc.

### *Q: What makes a strong drug discovery team, or what are some of its characteristics and requirements?*

**A:** Drug discovery is not for the impatient nor the thin-skinned. I often describe drug discovery as a process of one step forward, and two or three steps back. And that's being optimistic. In drug discovery, you better love science, and you better love difficult problems, because there's going to be a lot of uncertainty and a lot of difficulty. If you're up for it, it's a blast.

What makes a strong drug discovery team, like the one we've built at eFFECTOR, it's an assembly of incredibly talented scientists, most of whom have their PhDs and quite a lot of years of experience. It's a team of highly trained, very accomplished specialists, which of course is a requirement in our field since in all our projects we're trying to do things that are at the leading edge of science – at times very complex and challenging. While some of this might sound like hyperbole, it's not. In fact, if anything, I'm understating.

I sometimes describe a highly functional drug discovery team by the term "humming." As a group, they're actually almost humming in the way they're coordinated, anticipating and receiving key information from one another – insights, data and more. This is what it takes to crack the really hard problems and targets we're tackling every day.

Another aspect of this is, as I look back at the groups I've been a part of, there's just nothing like when a team comes together, and is really cohesive, to crack a difficult problem. It's a sublime experience.

In drug discovery, and particularly so at eFFECTOR, it's all about the project all the time. Everyone on the team is doing everything they can, as a team, to move the project forward. It's not about the individual, it's never about individuals taking credit. If people are being egotistical or losing focus, you don't have a chance. This is really critical.

In a high-functioning team, you don't see any of that, there's just no room for it. It's not tolerated. For a drug discovery team functioning well, functioning as it should, you get a neat combination of skills and personalities that blend and unify in wonderful and unexpected ways. And the end result is progress and ultimately success.

***Q:** How do you and Jubilant work together, and what does Jubilant bring to the table for your company and your research work?*

**A:** Everything we've talked about so far is relevant for the role Jubilant has played and their impact on our work. We've been working with Jubilant now for 7 years or more. I was just describing the value of "team" in the field of drug discovery, and at eFFECTOR. Jubilant is an integral part of our team and of so much of what we've done and have accomplished to date. It's a true team effort.

Geographically we might be separated, but we never feel separate. They always function like they're right here within our walls. They are just a super partner.

They've consistently shown the highest levels of engagement and problem solving for eFFECTOR, and they've repeatedly demonstrated that our short timelines are their short timelines. They've bent over backwards to deliver for us on all of our projects, and they've literally never failed. And they are excellent at working with us to solve difficult synthetic challenges.

Just like eFFECTOR, Jubilant brings a real sense of camaraderie - almost a selflessness - to do what's best for every project. Every one of our projects - all the way from the inception to the very large-scale synthesis, which Jubilant is helping us with tremendously. They're doing all the large-scale stuff for us right now up to kilogram quantities material, and have done so for our more advanced programs They just continue to do phenomenal work for us, and they're highly effective and highly efficient as well.

I interact with a lot of people out in the larger industry, and I've worked with lots of different CROs. There are some good ones out there. But Jubilant has been special for us. The level of daily interaction, feedback and trust that have been established between our organizations is just phenomenal. They're also really great people, too, kind and easy to work with, which really helps. It's all about the relationship that we've been able to build and forge with them.