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AN AUDIENCE WITH…

Yong-Jun Liu


Sanofi

Yong-Jun Liu is a drug discovery veteran with a career that has spanned both academia and industry. Since 2002 he has overseen drug discovery programmes at the University of Texas MD Anderson Cancer Center, Baylor Research Institute and AstraZeneca's biologics company MedImmune. He added another large pharma firm to this roster in 2016, when he joined Sanofi as head of research. Sanofi's president of global R&D Elias Zerhouni prioritized the development-stage pipeline during the first years of his tenure at the company, but brought Liu on board last year to refocus on the internal early-stage drug discovery efforts. Liu spoke with **Asher Mullard** about his first year at Sanofi and the company's emphasis on multi-targeted therapeutics.

What have you been up to in your first year at Sanofi?

I joined Sanofi at a time when the company was transitioning from 'R&D 1.0' to 'R&D 2.0'. It has been 6 years since Elias Zerhouni joined Sanofi as the president of R&D. His strategy initially focused on development, to fill the pipeline with candidates that could be launched within a 5-year time frame. And he has been very successful in this. With R&D 2.0, one of the major goals is to refocus on internal research, moving molecules from the bench into first-in-human trials. I was honoured and fortunate to be recruited to implement this strategy. I feel very excited to be at one of the world's top pharma companies, with a very clear message that it wants to invest in early discovery and early development. We have more than 2,000 scientists in our research organization, and I want to reinvigorate this organization as a powerhouse for innovation. That means we are going to generate a lot of targets and a lot of projects internally.

I believe that in 5 years from now, two-thirds of our late-stage preclinical projects will be generated internally. We also expect a number of new drug candidates from our internal portfolio to enter clinical testing in 2017 and 2018.

That said, you cannot fully separate internal and external R&D. If you want to bring in the seeds of transformative medicines, you need to have good judgement and talented scientists who know where to look and you need a good network of contacts in the scientific community. And, sometimes it is very difficult to define whether a project is internal or external. Many of the projects that we are working on are brought in at a very early stage, when we only have a target. We put a lot of effort into lead generation, optimization and preclinical studies.

Will you get more resources to boost your internal capabilities?

No. The headcount is flat and the budget is flat. Our aim is to increase the productivity 2- to 3-fold in 5 years. My focus is on the science and operational efficiency.

To achieve this, I've been busy doing deep dives of the company's portfolio. We have gone through each therapeutic area and each technology platform, bringing all the smart scientists from a therapeutic area or technology platform together and reviewing all of their current projects. The first step is focus. To give you an example, some of the therapeutic areas had 30 projects. At the end of a deep dive, maybe only 5 projects are selected as top priorities. But we will double or triple the resources for these projects, to accelerate the path to the clinic. Then we look at the big, blue-sky science in this area and identify new projects that could become breakthrough drugs. In some areas we have added up to 10 new projects. And then the third thing that we do is build a project team and an implementation strategy.

I tell our teams that they need to be bold and they need to be winners. But they also need to be very patient. There is no such thing as a quick win in this business.

What general trends have emerged from your deep dives?

Sanofi has traditionally been a small-molecule company, but if you look at our current pipeline we are very rich in biologics these days. We still need to improve our ability to discover, develop and manufacture biologics, and one of our strategies is to continue to transform in this direction.

A second trend in our strategy is what we call multi-targeting, by inventing therapeutics that can do not just one thing at a time but a number of things. The best example of this is dupilumab, an antibody that we co-developed with Regeneron that blocks both interleukin 4 (IL-4) and IL-13.

To give you another example, we know that the PD1 axis is important in oncology. But many patients don't respond to PD1 inhibition. We believe in the effectiveness of Regeneron's humanized monoclonal antibody (mAb) platform, and intend to leverage our co-developed anti-PD1 mAb as an initial building block, leapfrogging into the combination space with candidates that include the anti-CD38 mAb isatuximab.

Our in-house scientists have also done beautiful work into the mechanisms of resistance to anti-PD1 therapy, and have found something very exciting. I cannot disclose what it is yet, but we have a molecule that will be in the clinic by the end of this year targeting a PD1-resistance mechanism.

When you think about your multi-targeted projects — whether they are multivalent antibodies, small molecules with pleiotropic effects or combination strategies — how many targets can you go after with a therapeutic?

Whether we are going after two or three or four targets, I think that in the future technology will not be the limiting factor for multi-targeted therapeutics. The limiting factor is going to be the precision medicine. Exactly how many major molecules are really causing the trouble for a given disease subpopulation? This multi-targeting approach has to go hand in hand with strong translational science.