CEO Update: Interview with Lumos Pharma's Chief Medical Officer, David B. Karpf, M.D.

July 26, 2022

Lumos Pharma CMO, David B. Karpf, M.D., walks us through his background and perspective on LUM-201.

Q: When did you know you wanted to go into medicine – what drove you to that profession?

A: My dad was an exceptional doctor, so I knew at age 5 that I wanted to be a physician. Also, being a twin meant that I was never in doubt of my decision because there was always someone who would validate my world view. I had friends in college who were smart but grew up in rural San Bernadino so never thought that way; they never had the validation I had from being a twin. I shared a room and a womb with Jonathan (my twin). The biggest impact on my going into medicine was having a monozygotic twin and having a father as a physician.

Q: Tell us a bit more about your educational background.

A: I went to UC Berkeley for my undergraduate degree, double majoring in molecular biology and psychology. I went to UC San Diego (UCSD) for medical school, then to UCLA Cedars Sinai for my internal medicine residency and endocrine fellowship. After that, I wanted to be trained in metabolic bone disease, so I subsequently did a 2-year fellowship in endocrine diabetes at Cedars Sinai and then accepted a post-doc fellowship at UC San Francisco (UCSF) in their bone group where I became a faculty member in 1991. There I was doing clinical research, teaching, and seeing patients. In addition, I worked at various free clinics in Los Angeles, San Francisco, and Berkeley to help those who couldn't afford fee-for-service medicine.

Q: Tell us about your work experience and your path to clinical development in the pharmaceutical industry.

A: While I was on faculty at UCSF, my first child was born, and my wife wanted to stay home with the baby. To support my growing family, I looked around for other opportunities and was recruited by University of Southern California (USC) and the University of Minnesota. I was close to accepting a position at the University of Minnesota when I got a call from a headhunter who presented an opportunity at Merck because of my prior work on the parathyroid hormone (PTH) receptor. I was recruited to run the Fosamax project at Merck. It was a great opportunity, so I joined Merck where I advanced the Fosamax program to the drug's launch.

Because of that experience, at the end of 1996, I got calls from noted pharma companies and received an offer from Roche. My wife and I missed California, so I accepted the offer, and we headed back west.

When I started at Roche in 1997, I got my faculty appointment at Stanford where I worked as an adjunct clinical professor of endocrinology. I have been very lucky to be able to pursue my work in clinical development while also seeing patients. It is unique to be able to work in drug development and be able to continue the hands-on experience of practicing medicine. For those of us who are on faculty, seeing patients brings a different perspective to these clinical programs, enabling an enhanced relationship with investigators. Merck encouraged academic hires to continue faculty appointments (practicing medicine), as have the companies where I've worked since, including Roche, Metabolex, Virobay, Ascendis, and now Lumos Pharma.

Q: When you worked at Merck, were you aware of LUM-201?

A: While running the Fosamax program at Merck, I was aware of the MK-0677 (LUM-201) program. It was a huge accomplishment from a scientific drug development perspective. You could give it once a day morning or night, with or without food, and it would augment GH production during the day. It was a miraculous drug, but Merck was having trouble finding an indication for it. At that time, Merck was all about once-a-day pills for big indications: hypertension, osteoporosis, hyperlipidemia, asthma, and diabetes. Merck wanted MK-0677 to treat frailty of aging, (aka age-related disorders like sarcopenia). That was a big indication, but the FDA didn't view it as an actual disease – that was the main reason it was put on the shelf although data from those adult trials supported that indication. Merck never intended to treat PGHD – PGHD was really an after-thought for Merck, where trials for MK-0677 erroneously included organic severe PGHD patients who wouldn't respond to the drug as the drug only works in idiopathic PGHD patients - patients who have a partially functioning pituitary. Luckily, Michael Thorner, MB, BS, DSc, recognized the value of this molecule, so he formed the company Ammonett and licensed it from Merck, and Lumos licensed it from Ammonett. Michael remains an advisor to Lumos Pharma.

Q: When you were asked to join Lumos, what interested you in this opportunity?

A: It was really my prior knowledge of MK-0677 that originally piqued my interest. I had recently retired from Ascendis where I had taken Skytrofa® from Phase 2 all the way to its BLA filing. After that, I went back to consulting and practicing at Stanford. Then Rick called and offered me a full-time position as Chief Medical Officer. The only reason I left retirement – in addition to the fact that Rick came across as an excellent CEO – was that I knew the drug, LUM-201. I had developed 3 ½ drugs that met unmet medical needs – Fosamax, Boniva, Skytrofa, and most of TransCon PTH. I thought, "Wouldn't it be great, after having gotten approval of a PGHD therapy that reduced 7 injections/week to 1 injection/week, to develop a needle-free option for the majority of PGHD patients?" So that's why I joined Lumos. I thought this would be a wonderful bookmark for the end of my clinical development career and for patients, so I am going to do everything I can to help Lumos develop LUM-201.

Q: What do you think LUM-201's key advantages are compared to current therapeutics for PGHD (daily & weekly injectables)?

A: A key difference is, of course, that LUM-201 is administrated orally and, therefore, requires no needle sticks, lessening the pain and logistical burden experienced by patients and their families.
As a physician, I prefer to prescribe treatments that more closely resemble the physiological functioning in healthy individuals. Daily injections give ~6 hours of increased GH vs the 23-25 peaks of GH that people normally secrete across a 24-hour period. Weekly injections also provide a prolonged period of increased GH.

Prior studies with LUM-201 indicate it amplifies the peaks of GH that would normally occur. Additionally, this physiological mechanism of LUM-201 provides protection from overtreating a child with growth hormone deficiency given that the IGF-1 SDS should never go above 2 due to the natural feedback loop that exists along the GH endocrine pathway.

Q: What do you see as LUM-201's other opportunities beyond PGHD?

A: LUM-201 has the potential to treat other indications in the $3.4 billion worldwide growth hormone deficiency (GHD) market, as well as NAFLD where Mass General Hospital's Dr. Dichtel is evaluating LUM-201 in the clinic.

Q: How do you see the PGHD therapeutic market in 5-10 years?

A: I believe that the daily injectable market will eventually be replaced with long-acting therapies for patients with organic PGHD and LUM-201 for patients with idiopathic PGHD. In my opinion, the organic – or more severe – PGHD market will probably be split between a limited number of long-acting GH therapies (assuming efficacy, safety, and out-of-pocket costs to patients are equal). I also believe that LUM-201 will be well received in the idiopathic – or more moderate – PGHD market. I anticipate the clinical data will show that patients have a choice between 2 compounds with the similar efficacy, tolerability, and cost. Given that choice between recurring injections and a small pill, I anticipate patients and their family will strongly prefer the daily oral regimen of LUM-201.