PODCAST 4:

What's next, with your research?

As I mentioned we've take a couple of different approaches for therapy development. I would say we have a very targeted approach, this idea of looking at the PI3P - the zip code - and seeing if we can improve the way that that signaling happens using a very targeted therapy. In that case, it's the PIK3C2B inhibitor. Whether it's wortmannin, or a drug that is more efficacious that we're going to be able to find, that's one element of things. We have our anti-cancer drug, from a very serendipitous finding, which we think seems to be acting in a slightly different way.

Then, as I mentioned, we've been doing non-biased approaches to try to develop therapies. To do this we've been taking our zebrafish model, which has several obvious abnormalities when you just look at the fish, and we've been screening for drugs that make those abnormalities go away. We've got several different hits from our screening - we did a screening of about 1200 compounds, all of which had been used in patients before - not MTM patients - but had been used in people before. We found 6 hits and we've been really focusing on one of them because it's a drug that's been used quite frequently in paediatrics: and we think it works by yet a different way.

So when you think about 3 different drugs that seem to work in 3 different ways, the idea of bringing them all together, to me, makes a lot of sense. Especially because no single one of them by themselves seems to fully promote rescue in the animal. If we could put them all together then that might be a very powerful way of addressing the disease [MTM]. You can imagine: well if I can improve 3 different things, they could all add together to some much more robust improvement. So that's our thought. So what we're working on now is really trying to test this idea by looking at the 3 different things. To do that we also need to better understand why these things are working, because while you think they might be different - but if they are redundant, then you might predict that this combination wouldn't be successful - so understanding that as well. I think also, it will give us some insight into maybe there's some even better targets than can be put together, as we refine the pathways.

I think it's a kind of concept that in rare disease has not been given as much consideration - something that we take for granted in other diseases: cancer; diabetes; hypertension. A lot of people are on multiple drugs …you could think of here - if you have high blood pressure and high lipids, you might be on a statin, and you might be on another drug - you take them in combination all the time. But for some reason we have this idea in rare disease there has to be single thing - there's got to be some magic bullet that's going to make everything better, and which I don't know

why we think that. It's how I was brought up to think as well. Now I've come around to this idea that if we can do several things in combination that can incrementally improve it: those are the kind of things that could really be put together and make a huge benefit. I think that we have the opportunity now, because of these different avenues we've been doing, to develop this for x linked myotubular myopathy.