As we think about simplicity and gene editing trying to make the Allo approach more like a drug, one thing that's been on my mind recently as we're getting more sophisticated ways of dealing single cells and Allo cells, we're getting a better appreciation of the need for a heterogenous population. As we're looking at clonal or polyclonal expansion do we run the risk of oversimplifying it and eliminating some of that heterogony and polyclonality that we actually think we need in CAR-T to be effective and is that going to be more of an issue in solid tumors.

Mark Gilbert: There's two pieces of general data I would bring in on this conversation, the first has to do with the success I'll claim on till therapy and the association with heterogeneity, more heterogeneous responses until being more likely to have a favorable outcome. Some heterogeneity may be a good thing, if not the responses themselves, the cell types, what have you. The second piece is that as we learn more about engineering for example iPSC's and trying to conceptually make this a homogeneous phenotype or cell type, what you begin to realize is our assay techniques are sensitive enough we can measure heterogeneity in all of these products. The real question is which of them matter within that, and that needs clinical experience in order to determine that, and quite frankly I don't feel like we're there yet for sure, but there are being end roads being made to better understand what may be the critical pieces to be more consistent versus allowing heterogeneity, not so much on specifications but on product attributes within that.

"So, we in general, want a product, specifically a commercial product to have some amount of homogeneity, it should be the same thing every time. Now that is impossible if you're making each product from a different donor because it's an autologous product, and it's even more difficult when you think about that with till. Because in fact what you're trying to do is harvest cells that are uniquely suited to the tumor you are trying to address."

Christopher Heery: Mark actually keyed in on something that does directly go to your question which is the till experience. You have a bit of a conflict right now in the world of cell therapy from a regulatory standpoint. So, we in general, want a product, specifically a commercial product to have some amount of homogeneity, it should be the same thing every time. Now that is impossible if you're making each product from a different donor because it's an autologous product, and it's even more difficult when you think about that with till. Because in fact what you're trying to do is harvest cells that are uniquely suited to the tumor you are trying to address. By definition they should be different from each other, so that heterogeneity between patients but also between the cells. I think that is enormously complicated, and my biggest concern right now is, we all heard Iovance is going to have this delay in the review process. I think there needs to be a broader strategic conversation with FDA and sponsors about what is actually the best, and probably KOLs in the field and treating physicians about, what are we actually trying to achieve and does this always have to be the same, and does a potency assay really tell us the answer to that when we know that the potency assay with the CAR-Ts don't really predict outcomes on a one to one patient basis that well. I think that those are all really important questions that unless we want to take them head on we are not going to get these therapies as to as many patients as could benefit from them as quickly as we could. But to answer your question if you made the same cell every single time like an IPSC and you made them all exactly the same I think you'd probably lose something overall, but how much I don't know yet and I don't think anyone knows the answer to that.