Questions from Webinar

"Avances en la Investigación de la Enfermedad de Huntington - Estudio PIVOT-HD"

(https://www.youtube.com/watch?v=DgPjuxBL_bw)

- How long will it take to finish Phase 3?
    - *PIVOT-HD is a 1 year Phase 2 trial, and completion is expected later in 2024. We won't know how long a Phase 3 trial will need to be until the data from the Phase 2 are available.*
- How long will it take for the health authorities to evaluate the results?
    - *Once the results are available, it typically takes 1 year from submission for regulatory authorities (European Medicines Agency – EMA) to approve a drug. There are instances where trial results may be reviewed sooner, and PTC will pursue these options should they become available. Following EMA approval, individual countries may implement a separate review process such as a Health Technology Assessment.*
- Can you explain the distribution process?
    - *Due to the early nature of the development program (Phase 2), distribution is not something that we can comment on. However, after country approval, there is a country specific launch date which is dependent on individual country's laws and regulations.*
- Will you try to increase the dose until you can decrease the protein by 100%?
    - *No, PTC518 lowers both normal HTT and mutant HTT, so lowering to 100% HTT is not planned.*
- Are patients diagnosed with Huntington's disease but with no visible symptoms, who have not yet developed the disease, eligible for this type of trial?
    - *If patients have motor signs but no symptoms, depending on their doctor's evaluation, they may be eligible for this type of trial. Patients must meet the clinical trial eligibility criteria.*
- Can patients with substance use or abuse such as cigarettes, alcohol and marijuana be included? Which recreational drugs of abuse would be excluded?
    - *Recreational drugs that are legalized are not excluded, including alcohol and cigarettes. However, some exclusions for excessive use may apply.*
- Do you think there is any possibility of carrying out these trials in Argentina, taking into account that other companies have already done so with good professional results?
    - *It is possible that a Phase 3 study may be opened in Argentina.*
- Do you think there is any possibility of doing the trials in Brazil?

- *It is possible that a Phase 3 study may be opened in Brazil.*

- Do you think there is any possibility of doing the trials in Colombia?
  - *It is possible that a Phase 3 study may be opened in Colombia.*
- My question is, how does the false exon target this gene and not the rest of the genes?
  - *This is a great question. The scientists at PTC spent nearly a decade making sure to find a compound that would only target the HTT gene.*
- Where can I read about this trial?
  - *This study is listed at clinicaltrials.gov, clinicaltrials.ptcbio.com, and ClinicalTrialsRegister.eu.*
- Is this study going to continue with these patients or is the idea to stimulate other countries to participate?
  - *The study is currently recruiting in many countries. A Phase 3 study may be open to other countries, as well.*
- At what stage is the research?
  - *PIVOT HD is a Phase 2 study*.
- My question is: if all goes well with this trial, after the evidence and if it proves to be viable (hopefully yes) when could all of us patients benefit from it?
  - *PTC is committed to bring PTC518 to countries as soon as possible with all needed studies, regulations, and regional and local approvals.*
- Once the research has been concluded with favourable results, how long will it take to make the drug available outside Spain?
  - *Once the results are available, it typically takes 1 year from submission for regulatory authorities to approve a drug. There are instances where trial results may be reviewed sooner, and PTC will pursue these options should they become available. Following regulatory approval, individual countries may implement a separate review process such as a Health Technology Assessment.*
- Once the study is completed in about 12 months (or more) and if positive, how long would it take for the regulatory agencies to authorize the sale of the drug?
  - *PIVOT HD is a Phase 2 study and may need to be confirmed with a Phase 3 study before submission to regulatory agencies. Once all results are available, it typically takes 1 year from submission for regulatory authorities to approve a drug. There are instances where trial results may be reviewed sooner, and PTC will pursue these options should they become available. Following regulatory approval, individual countries may implement a separate review process such as a Health Technology Assessment prior to approving reimbursement for a drug.*
- Is PTC518 specific for the mutated HTT gene? Please, it's not clear if it also decreases normal huntingtin.
  - *PTC518 does decrease normal HTT as well as mutant HTT.*