Questions from the NPC community regarding the suspension of VTS-270 301 in UK and France:

1. **Why was the trial suspended in the UK and France?**
   The regulatory agencies in the UK & France are of the opinion that a positive efficacy compared to safety (risk/benefit) balance does not currently exist for the study drug. This is related to the lack of a definitive efficacy benefit (no separation between sham and adrabetadex) from Part A/B of the Phase 2b/3 study (Study VTS301). The regulatory agencies cited a specific concern about hearing impairment in children.

   Mallinckrodt believes that the efficacy compared to safety (risk/benefit) balance remains positive based on all available data. Hearing impairment is a known potential side effect of adrabetadex (VTS-270), and no new safety concerns have emerged in Study VTS301 or in any other data on patients treated with adrabetadex. We are hopeful that there will be a determination that the study may resume in the UK and France, however, we cannot predict when any such change may occur.

2. **What does "suspended" mean? Does this mean the study is permanently stopped?**
   Suspension is a temporary halt of the study. This means that patients participating in the Phase 2b/3 study (Study VTS301) in France and the UK cannot have treatment with adrabetadex right now. The regulatory agencies in France and the UK will eventually make a decision about whether the study can continue or if it is permanently stopped in these countries.

3. **What does unfavorable benefit/risk balance mean?**
   It means that the possible side effects, or risks, from receiving treatment are more than the possible positive effects, or benefit. Think about it like a teeter-totter, with side effects on one side and positive benefit on the other side. An unfavorable balance means that the safety side of the teeter-totter is higher than the positive benefit side.

   For the Phase 2b/3 study, the French and UK regulatory agency stated that in their preliminary review there is a lack of a definitive efficacy benefit (no separation between sham and adrabetadex) from Part A/B of the Phase 2b/3 study (Study VTS301) but there are side effects from receiving adrabetadex.

4. **Is the suspension related to the trial design?**
   No, the trial design was not the reason for the suspension. The regulatory agencies in the UK & France are of the opinion that a positive efficacy compared to safety (risk/benefit) balance does currently not exist for the study drug. This is related to the lack of a definitive efficacy benefit (no separation between sham and adrabetadex) from Part A/B of the Phase 2b/3 study (Study VTS301). The regulatory agencies cited a specific concern about hearing impairment in children.

5. **Does the port have anything to do with the suspension?**
   No, the port was not the reason for the suspension of the study. The regulatory agencies in the UK & France are of the opinion that a positive efficacy compared to safety (risk/benefit) balance does currently not exist for the study drug. This is related to the lack of a definitive efficacy benefit (no separation between sham and adrabetadex) from Part A/B of the Phase 2b/3 study (Study VTS301). The regulatory agencies cited a specific concern about hearing impairment in children.

Mallinckrodt believes that the efficacy compared to safety (risk/benefit) balance remains positive based on all available data. Hearing impairment is a known potential side effect of adrabetadex, and there are no new safety concerns that have emerged in Study VTS301 or in any other data on patients treated with adrabetadex. We are hopeful that there will be a determination that the study may resume in the UK and France, however, we cannot predict when any such change may occur.

6. **Does hearing impairment have anything to do with the suspension?**
   Yes. Hearing impairment is a known potential side effect with adrabetadex treatment. The data in Study VTS301 on hearing is consistent with what was seen in the Phase 1/2a study.

7. **For those countries still participating in the trial, is the drug safe?**
   No new safety findings have emerged during the ongoing Phase 2b/3 study. The safety information today is the same as when the study started. Common side effects are balance problems and fatigue that can occur after a dose. These side effects are usually temporary and resolve on their own within a few days. Hearing impairment is another possible side effect that has been seen in the Phase 1/2a study and in the Phase 2b/3 study (Study VTS301). As we saw in the Phase 1/2a study, hearing impairment can be temporary or permanent, and it can be potentially severe. The hearing impairment is, however, correctable with hearing aids.

   Investigators and physicians treating patients with adrabetadex should make a determination on an individual basis about whether or not treatment with adrabetadex should continue based on all available information.

8. **Is there any information from the regulatory agencies or MNK that can be shared?**
   We have shared the information about the study suspension in the UK and France. We are working with these regulatory agencies to address their concerns. We are hopeful that there will be a determination that the study may resume in the UK and France, however, we cannot predict when any such change may occur.

9. **Can this suspension occur in the USA? What can we do to stop this from happening?**
   We have already informed all Phase 2B/3 (Study VTS301) investigators of the suspension in the UK and France.

   By August 9th, Mallinckrodt will be providing a formal report to all regulatory agencies overseeing the conduct of this study. Additionally, this formal report will be sent to all study investigators, and they will be instructed to submit this to their Institutional Review Board (IRB) The IRB is responsible for overseeing the safety of patients participating in clinical research.

   The report outlines the suspension of the Phase 2b/3 study (Study VTS301) in France and the UK, and provides the rationale for Mallinckrodt's determination of a positive efficacy compared to safety (risk/benefit) balance.

   Suspension of a study by any regulatory agency is a serious action. The FDA will evaluate all available information when they receive the report, and make its own determination about the study continuing in the US. Mallinckrodt is hopeful that other regulatory agencies will decide, based on the information provided, to allow the study to continue.

10. As a community, what can we do in support of VTS-270?

Regulatory agencies have an obligation to ensure the safety of patients that participate in a clinical study. At this time, we are working with the regulatory agencies in the UK and France to present the information that supports positive efficacy compared to safety (risk/benefit) for adrabetadex.

For all other countries participating in the Phase 2b/3 study (STUDY VTS301), the study is ongoing. The regulatory agencies in these countries will be notified by August 9, 2019 that the study was suspended in the UK and France. Mallinckrodt is hopeful that when these respective regulatory agencies review the information provided, they will decide that the study can continue.

Mallinckrodt remains committed to the NPC patient and caregiver community and respects the right of individuals to speak out to voice their concerns or to share their stories to help raise the awareness of the devastating nature of Niemann-Pick Type C and the high unmet need.