VTESSE --

1. **Commitment to the Niemann-Pick C (NPC) community** – We at Vtesse have consulted with key members of the NPC community. We have taken their counsel and have done our best to incorporate feedback into the trial design in order to best satisfy physician input, parent/patient input, and regulatory agency requirements.

2. **Our priority** – We are focused on gathering data on the safety and efficacy of VTS-270 through the execution and completion of the pivotal clinical trial, VTS301 (The NPC Study).

**Study of VTS-270 (a unique formulation of 2-hydroxypropyl-β-cyclodextrin) to Treat Niemann-Pick Type C1 (NPC1) Disease --**

1. **Some considerations that parents/patients should think about when deciding if this trial is right for them:**
   - The purpose of the study is to evaluate the efficacy and safety of VTS-270 (a unique formulation of 2-hydroxypropyl-β-cyclodextrin) in patients with neurologic manifestations of Niemann-Pick Type C1 (NPC1) Disease
   - The trial is designed to be scientifically rigorous and to deliver a robust clinical package to regulatory authorities
   - The double-blind trial is 12 months in duration, with an open-label extension after the double-blind portion
   - The rationale for and the design of the trial are based on a set of preclinical and clinical data that are specific to VTS-270. Put another way, these data should not be used to measure the effect of any other cyclodextrin-based treatments, investigational or otherwise
   - Preclinical animal models studies show that VTS-270 increases the life expectancy in animals (mice and cats). We have not conducted studies in humans assessing the impact of the drug on overall survival
   - VTS-270 is a unique formulation of 2-hydroxypropyl-β-cyclodextrin and is the same drug that was studied in the Phase 1 study at the National Institutes of Health (NIH)
   - Possible benefits of the trial need to be considered along with the potential risks (see below for further discussion)
VTS-270: Potential side effects – The primary objective of running any clinical trial is the safety of the participants, and all study participants will be closely monitored. There is a dedicated team of drug safety experts who will have all the ongoing data from the trial, and make independent recommendations regarding whether a dose level for a particular subject should be reduced or discontinued – or even the entire study stopped – if significant safety concerns are observed.

Overall, based on current data, including those from the NIH Phase 1 clinical study, the most common side effects seen are:

- **Impact to hearing** – difficulty hearing or understanding high-pitched voices of women and children is one of the first symptoms. High-frequency hearing loss distorts sound, which can make speech difficult to understand even if it can be heard. Most of the events reported to date regarding impact to hearing are related to the high frequency range, though some impact to mid-range frequency has also been seen.
  - The impact to hearing seen with VTS-270 treatment can be treated with hearing aids
  - No one receiving VTS-270 in the Phase 1 trial at NIH and through iINDs has reported profound deafness
  - The impact to hearing observed to date does not appear to be dose related

**PHASE 2B/3 CLINICAL TRIAL**

1. **Patient enrollment** – With the support of the NPC community, we plan to enroll 51 patients in the trial. The overall design of the program is based on one global pivotal study that can support regulatory approval. Patients completing 12 months in the double-blind portion of the clinical trial will be provided study drug (in an open-label extension) up until the point of a regulatory decision or program termination. This open-label extension is subject to local and national limits on such activities and may need annual authorization to continue.

2. **Sham control** – We recognize that all parents and children would wish to be placed on study drug as soon as possible. A sham control trial is the quickest path to an answer about whether VTS-270 works. In other words, a controlled,
randomized trial is the gold standard of scientific and regulatory evaluation that provides for us a single protocol worldwide. We are conducting a single study to ensure speed towards potential regulatory submissions with the highest scientific rigor, the best chance of success, and the potential to deliver this drug to market as quickly as possible.

3. **Dosing** – We are starting to see positive trends in efficacy with VTS-270 administered intrathecally at the current dosing levels in the Phase 1 study. In Part A of Phase 2b/3 trial of VTS-270, three doses were studied against a sham control. Upon completion of Part A, the independent dose selection committee chose the dose of 900mg every two weeks to be the dose in the active treatment arm for the duration of the trial. The dose was selected based on safety and tolerability data gathered during Part A. It is important to note that the dose is based on brain weight, not body weight. Thus, dosing is scheduled to be at consistent levels across all ages of patients in the trial. This is because a human brain is nearly fully developed by the age of 4.

4. **Lack of dose escalation** – Early in clinical development, doses are often escalated slowly in order to ensure patient safety while at the same time find a dose that offers the best potential for benefit while minimizing risk. We tested VTS-270 via dose escalation up to doses of 1200mg during the Phase 1 trial at NIH. Based on what we know now, starting patients at a dose of 900mg every other week seems to offer the greatest potential for benefit while minimizing side effects. Also, note that VTS-270 washes out from a patient’s body within 24 hours; in other words, the dose does not appear to accumulate in the body over time.

5. **Exclusion criteria** – We want to do what’s best for the NPC community as a whole through this clinical trial. Because the disease is extremely heterogeneous in onset and progression (meaning, it takes a number of different forms in how it shows up in one patient or another) it is difficult to measure an effect if each patient has a different “presentation” of the disease. We wish to study as homogenous a patient population as possible within the NPC community to see and measure the treatment benefit to ensure the greatest chance for success in seeing an efficacy signal. We want to identify the areas of greatest need and build upon the positive effect. We need to clearly see where VTS-270 works and where it doesn’t as we build a foundational data set for future research and development into the disease.
6. **Mode of Administration** – There is an urgent need among patients with NPC1 to have access to a drug that has an impact on neurological symptoms. VTS-270 is delivered to the brain through intrathecal (IT) administration. IT drug administration delivers drug to the cerebrospinal fluid (CSF). IT delivery involves the direct injection of the drug into the CSF within the intrathecal space of the spinal column. Intrathecally-administered drugs are confined within the CSF circulating in the spinal column and the brain ventricles. Some drug needs to be given this way to cross the **blood brain barrier** because drugs given orally may not be able to pass through the blood brain barrier and into the brain. IT delivery is thought to be the best way to get VTS-270 to the brain with the goal of achieving efficacy on neurological impact of the disease.

**Q&A**

1. **How does VTS-270 work?**

Data suggests that VTS-270 may target important chemicals stored in cells, such as cholesterol and sphingolipid. In patients with NPC1 disease, the NPC1 pathway in the cells doesn’t work properly, so cholesterol builds up in the brain cells and, over time, can damage and even kill these cells. This leads to the severe neurological problems in patients with NPC1.

Preliminary studies suggest that VTS-270 may help cholesterol bypass the broken NPC1 pathway, promoting transport of the cholesterol that would normally accumulate in the lysosomes of cells that have the NPC1 mutation.

2. **What results/effects have you already seen with VTS-270?**

In preclinical animal models of NPC1 disease, VTS-270 delivered into the cerebrospinal fluid surrounding the brain prevents NPC symptoms, such as ataxia (balance disorders), and prolongs survival of the animals.

In August 2015, Vtesse announced preliminary results from an open-label Phase 1 clinical trial of VTS-270 conducted in NPC1 patients. The 12-month analyses suggest that the rate of disease progression had slowed down (based on a standardized measure) in children dosed with VTS-270 in the Phase 1 trial (conducted at NIH) as compared to the rate of disease progression in age and disease severity-matched
patients observed in a separate natural history study of NPC1 patients. The analyses also show that children dosed with VTS-270 demonstrated improvement on several aspects of the disease, such as cognition, speech and fine motor skills. The 18-month analysis showed continuation of the trends seen in the 12 month data.

While these results are promising, these are preliminary data. This is why Vtesse is conducting a pivotal (Phase 2b/3) clinical trial with a rigorous scientific design that has been selected in order to be able to clearly evaluate the safety and efficacy of this compound in the shortest time that is scientifically feasible. The regulatory authorities in the US and Europe (the FDA and EMA) have endorsed this study design.

Based on preliminary data, the most common AEs experienced by subjects were of the ear and labyrinth systems. Other AEs occurring in 2 or more subjects included:

- headache, post-LP
- emesis
- elevated liver enzymes - pre- and post-drug
- fatigue after IT administration
- change in seizure pattern or frequency
- fever
- tingling hands
- proteinuria
- urobilinogen
- discomfort at LP site
- fecal incontinence

Except for sensorineural hearing loss and aspiration event during anesthesia, all of the most frequently occurring AEs previously mentioned were grade 1 or grade 2, as were most of the AEs reported during the study.

3. What can you tell us about the study of VTS-270 for NPC1?

The NPC Study is a Phase 2b/3 randomized, sham-controlled clinical trial designed to evaluate the efficacy and safety of VTS-270 for the treatment of children with Niemann-Pick Disease Type C-1 (NPC1). The primary objective of the trial is to evaluate the impact of VTS-270 on the progression of the neurologic manifestations of NPC1 in children.
The study will be conducted at multiple sites worldwide. The study began in September 2015. We will evaluate patients between the ages of 4 and 21 years of age who have been diagnosed with NPC1 and meet all the study entry requirements.

The study will be conducted in three parts. Part A enrolled 12 participants that evaluated the safety of three doses of VTS-270 as compared to a control group in order to determine the dose to be used in Part B for up to 12 months. In Part A, nine participants received one of the three doses of VTS-270 and three participants did not receive VTS-270 (these patients underwent sham treatment). The dose selected from the data in Part A was 900mg every two weeks. Part B will enroll 39 additional patients and will employ the VTS-270 dose of 900mg. 26 of the 39 patients will receive 900mg of VTS-270 every two weeks and 13 patients will comprise the control (sham) group and will not receive VTS-270.

Patients in both Part A and B will be in the study for a total of 12 months. After completing 12 months of the study, patients will be allowed to enroll in Part C of the study where all patients will receive 900mg of VTS-270 every two weeks. Part C will continue until the regulatory agencies make their decisions on whether they will approve VTS-270. In addition, any participant who shows unexpected, significant disease progression, assessed by specific criteria, at any time after six months from their first study dose will be removed from Part B and allowed to enter Part C, the open label part of the trial where they are guaranteed to receive VTS-270.

4. How will VTS-270 be administered in your study?

Participants randomized to receive VTS-270 in this trial will receive VTS-270 intrathecally, which was found to be the most effective administration method in animal studies, through a lumbar puncture. The patients randomized to the control group will undergo a sham procedure consisting of a needle prick that does not penetrate beyond the top layer of skin. The group receiving VTS-270 will receive conscious sedation or general anesthesia (as determined on a case-by-case basis). Sham patients will receive conscious sedation. Conscious sedation is a minimally depressed level of consciousness that retains the patient’s ability to independently and continuously breathe and respond appropriately to physical stimulation or verbal commands. Conscious sedation is produced by a pharmacological method (using drugs) or a combination of methods.
5. Why are you running a controlled trial with a sham control?

We recognize that all parents and children would wish to be placed on study drug as soon as possible. A sham control trial is the quickest path to an answer about whether VTS-270 works. In other words, a controlled, randomized trial is the gold, regulatory standard of scientific evaluation that provides for us a single protocol worldwide. We are conducting a single study to ensure speed towards potential regulatory submissions with the highest scientific rigor, the best chance of success, and the potential to deliver this drug to market as quickly as possible.

Importantly, this rigorous study design will establish a foundational data set for the NPC community. This not only allows for the possibility of approval by regulatory agencies, which means access to the broader NPC1 community, but this also allows for the future development of drug cocktails, which may have even better efficacy than VTS-270 alone.

6. How will the sham control work in this trial?

The sham procedure consists of a needle skin prick at the same site where a lumbar puncture would occur in patients on active drug, the needle will not be inserted and no lumbar puncture will be performed in sham control patients.

For this trial, patients enrolled in Part A of the study were randomly assigned in a 3:1 ratio to receive either intrathecally administered VTS-270 or a sham control procedure. This means that for Part A, there was a 75 percent chance that participants will receive VTS-270 at one of three doses. In Part B of the study participants will be randomly assigned in a 2:1 ratio to receive either intrathecally administered VTS-270 or a sham control procedure. This means that in Part B, there is a 66 percent chance that participants will receive VTS-270 at the dose determined from Part A.

It is important to note that all participants, including those randomized to sham, will be allowed to enter Part C of the study after 12 months where they are guaranteed to receive VTS-270. To be clear, that is 12 months for each individual participant. For example, if one patient starts in October 2015 in Part A, they may enroll in Part C in October 2016. If a patient starts in January 2016, then they may enter Part C in January 2017.
7. Why is a blinded (or double-blind) trial necessary?

A blinded or double-blind trial is a term used to describe a study in which both the investigator or the participant are blind to (unaware of) the nature of the treatment the participant is receiving.

In other words, blinding is a way of making sure that the people involved in a research study — participants, clinicians, or researchers — do not know which participants are assigned to each study group. The intention of the sham procedure control group is to provide the most unbiased assessment of the efficacy and safety of VTS-270 in patients with NPC1. If parents or physicians were to know whether or not a child received study drug (i.e., if they were unblinded), they may treat the child differently, which would impact the validity of the study results.

8. Are there side effects from VTS-270?

Early research has helped us start to understand side effects, and we are very grateful to the parent-scientists who have shared their data. Overall, based on current data – including that from the Phase 1 clinical trial.

The primary objective of running any clinical trial is the safety of the participants, and all study participants will be closely monitored. There is a dedicated team of drug safety experts who will have all the ongoing data from the trial, and make independent recommendations regarding whether a dose level for a particular patient should be reduced or discontinued – or even the entire study stopped – if significant safety concerns are observed.

Please refer to page 1, topic “VTS-270: Potential side effects” for additional information.

We will continue to carefully assess the risk/benefit profile of the drug and carefully consider the needs of each individual patient. The dose of 900mg every two weeks was selected by an independent committee of experts and was based on the safety and tolerability data from Part A.

9. What can you say about impact on hearing in patients using VTS-270 to date?
We have observed some impact on patients in terms of high-frequency hearing loss with some loss in the mid-frequency range. In what has been observed to date:

- **High-Frequency Hearing Loss** - difficulty hearing or understanding high-pitched voices of women and children is one of the first symptoms. High-frequency hearing loss distorts sound, which can make speech difficult to understand even if it can be heard.
  - High to mid-frequency hearing loss can be treated with hearing aids
  - No one receiving VTS-270 in the Phase 1 trial at NIH and through iINDs has reported profound deafness
  - The high to mid-frequency hearing loss observed to date does not appear to be dose related

More specifically:

Hearing changes on audiologic testing were noted among some participants in the NIH Phase 1 trial. Some of the change is transient, but some (variable among patients) permanent high frequency hearing loss has been seen. No one has become deaf. We don’t yet fully understand the patient variability (nor how to predict it), the total amount of hearing loss one can get (again, no one has become deaf), or what the impact that hearing loss that occurs as part of the NPC1 disease itself may have on this process.

It is unclear to what extent hearing changes may be related to dose, duration of dosing or the patient, especially as many patients started the study with some level of hearing impairment and even hearing aids. Therefore, the long-term effects on hearing loss are not known at present. Hearing aids may be required to compensate for the high frequency hearing loss. If the patient needs hearing aids during the study, Vtesse will supplement costs to a prespecified limit, not covered by the National Health Service (or private insurance), associated with the purchase of an initial set of hearing aids for the subject.

10. **What about eye movement issues observed in some participants in the Phase 1 trial?**

Preliminary 12-month data from the Phase 1 trial showed an impact on vertical eye movement. There was no impact on eyesight, only on eye movement. This signal was no longer present in 18-month data. We will continue to evaluate any impact on eye movement.
11. How were the dose levels in the trial selected?

We are starting to see positive trends in efficacy with VTS-270 administered intrathecally at the current dosing levels in the Phase 1 study. We expect to see more efficacy if we go higher with the dosing, as was observed with preclinical study. If the dose selected is too low and clinically suboptimal, then participants are exposed to risks without receiving the full potential benefit of the drug. The converse is true if the dose is too high. The doses we are using in our Phase 2b/3 study are not the lowest nor are they the highest doses that could be given in humans based on the animal models. They are in the middle of the range.

In addition, it is important to note that since VTS-270 will be administered intrathecally, the participant’s actual weight is not the key factor regarding dose levels. That is, the weight of a 4 year old is much different than the weight of a 21 year old. If the dose were to be given IV, then the actual weight of the participant would likely determine the dose. In this case, what matters is the brain weight. The brain weight of a 4 year old is very similar to the brain weight of an adult. Therefore, the doses of VTS-270 do not need to vary based on the weight or age of the participant for patients to be included in this study, 4 to 21 years old.

12. What can you tell us specifically about the dose levels used in animal studies of VTS-270 and how this provides rationale for the dose levels you are using in the Phase 2b/3 trial?

VTS-270 has been administered in animal models of NPC at doses up to a human equivalent dose of 4,800 mg administered intrathecally. In Part A of the study, doses of 900 mg, 1,200 mg, and 1,800 mg were evaluated. The dose levels were in the middle of the range where preliminary efficacy and safety was demonstrated in animal models. Upon completion of Part A, the independent dose selection committee chose the dose of 900mg every two weeks as the dose that should be used for the duration of the study. This was based on safety and tolerability data from Part A.

13. What can you tell us about the dose levels used in clinical testing to date and how this provides rationale for the dose levels you used in Part A of the Phase 2b/3 trial?
In the Phase 1 trial, multiple doses have already been administered at the 900 mg and 1,200 mg levels. Dose increases are often more related to percentage dose increases than they are to absolute dose increases. For example, the 1,800 mg dose is 1.5 times the 1,200 mg dose. To put this in perspective, the dose increase from 1,200 mg to 1,800 mg is the same as going from 200 mg to 300 mg or going from 400 mg to 600 mg.

It is common in drug development for the dose to be doubled for each step in the dose escalation process. We at Vtesse decided to limit this to a 50 percent increase. Based on the pre-clinical data, we believe that we are operating in the middle of the possibly effective range.

Regulatory agencies, FDA and EMA, agreed that there is sufficient human evidence and rationale that a step up to 1,800 was an appropriate approach to ensure that a dose that is sufficiently different from 900 and 1200mg, could be selected from Part A of the study that provided the right balance of benefit and risk for the participants.

14. Why did Vtesse decide not to dose escalate in the Phase 2b/3 trial and immediately expose the patients to the target dose?

The dose levels for this study are not the lowest nor the highest dose that could be given in humans based on the animal models. It is in the middle of the range. Early in clinical development, doses are often escalated slowly in order to ensure patient safety while at the same time find a dose that offers the best potential for benefit while minimizing risk. We tested VTS-270 via dose escalation up to doses of 1200mg during the Phase 1 trial at NIH. Based on what we know now, starting patients at a dose of 900mg every other week seems to offer the greatest potential for benefit while minimizing side effects. Also, note that VTS-270 washes out from a patient’s body within 24 hours via urine. The half-life is only about 4 hours, which means that within 24 hours it is out of the body. No cumulative effect or built up “tolerance” in terms of side effects to VTS-270 have been observed. There is no evidence to date to suggest that dose escalating will either benefit the patient or alleviate any potential side effects.

Many people have heard about dose escalation from the design of the Phase 1 trial. Phase 1 studies are designed to provide different answers than a Phase 2/3 study. Phase 1 studies give us information as to what doses are feasible to study in later
trials and address questions related to research. Phase 1 studies may also, as in the case of the NIH Phase 1 study, show signals of possible efficacy.

It is important to differentiate between escalation of doses given to an individual patient (as was done in the NIH phase I trial, where a patient receives doses that increase over time) and the more common dose escalation design where each group receives one dose level multiple times (multiple ascending dose). This latter design allows a more clear assessment of each different dose for both safety and efficacy. In fact, most Phase 1 trials do not escalate the doses given to any given patient, they are dose escalation trials that evaluate groups of patients’ receiving a given dose before the dose is escalated to another group of patients receiving a higher dose. These trials give us information on what doses might be studied in larger efficacy trials. It is common to dose escalate from one patient group to another patient group during Phase 1 and then not dose escalate in Phase 2/3.

Specifically regarding VTS-270, it is important to emphasize that the intra-patient dose escalation for the Phase 1 trial was employed in order to assess any side effects of various doses in a controlled clinical setting. By doing that, researchers can determine if dose escalation is necessary moving forward in the clinical trial process or not. This escalation process is not necessary in the Phase 2/3 trial because the evidence gathered from the Phase 1 study identified that the likely side effects of treatment with VTS-270 would not be alleviated based on any dose escalation process. Therefore, there is no evidence that starting a patient in the Part A doses poses significant safety risk.

High to mid-frequency hearing loss to date has not been dependent on the dose level. This means, the evidence we have to date shows that we can expect some level of high to mid-frequency hearing loss and other side effects no matter if the dose is escalated or if it is started all at once.

Therefore, the clinical and medical experts designing the trial decided that the best approach was to move directly to the doses being tested without any intra patient dose escalation.

15. How did you set the age range for your trial? My child is 3.5 years old or 21.5 years old; why can’t he or she participate?
We want to ensure the greatest potential for achieving clear and interpretable results in our trial with the highest likelihood of achieving regulatory approval. We understand the urgent need to clearly understand the potential benefit of VTS-270 and if positive, bring an approved drug for the treatment of NPC to the marketplace. With that as a goal, we have to set cut off points for age that allow a relative uniform patient population to be enrolled in order to enable the interpretation and analyses of the data. The focus of this trial is on juvenile onset NPC1. For a clinical trial to be successful, it is important that the participants are as similar in progression as possible. This is quite a difficult task in a heterogeneous disease such as NPC1.

Based on the natural history study data, it has been determined that patients age 4 to 21, with onset of neurological problems by age 15, will provide a group of patients that are as uniform in their disease presentation and progression as possible. Unfortunately, there will be people who fall just below or just above the age ranges.

For patients who are close to four years old, it is important to understand that clinical trials take time to enroll. Therefore, there is a chance that the child may turn four before enrollment is completed. Vtesse and the clinical centers participating in the study will work closely with the parents and caregivers in such cases, if enrollment is still feasible.

Vtesse is also giving the Phase 1 patients an option to enroll in Part C, open-label extension of our trial and activities to help with this transfer from the NIH to other clinical sites that are geographically more feasible are already underway.

We are supporting current iINDs and we are evaluating options for compassionate use as the clinical trial is enrolling and we are gathering additional data.

16. Why can’t patients who have previously received IT cyclodextrin enroll in your Phase 2b/3 study?

It is important that the NPC1 community has a clear picture of the safety and efficacy of VTS-270 for NPC1. Patients who have already been on IT cyclodextrin cannot be evaluated for efficacy or change from a baseline measure. Secondly, if VTS-270 is approved, the vast majority of patients getting it in general clinical
practice will not have previous exposure to cyclodextrin. Therefore, it is important that we assess the efficacy and safety of VTS-270 in patients who have not received cyclodextrin in the past. If we don’t, we could get a false picture of the safety and efficacy of VTS-270 and jeopardize the chances of getting regulatory approval.

Patients who have previously received IV cyclodextrin will be eligible for the trial as long as they have not been using IV cyclodextrin for a minimum of 3 months before their entry into the trial.

Participants in the Phase 1 trial at NIH will be allowed to go into Part C of this trial.

17. **Why are uncontrolled seizures an issue for enrolling in the clinical trial?**

For a clinical trial to be successful, it is important that the participants are as similar in disease status and progression rates as possible. This is quite a difficult task in a heterogeneous disease such as NPC1. Inclusion and exclusion criteria are included in clinical trial protocols in order to help achieve the goal of getting participants that are as similar as possible. In addition, any change in medications or any other clinical procedures that need to be done during the study can also change the way a participant responds to the study drug or it can inhibit the participants' ability to even be in the study. Also, data from clinical trials are gathered by measuring outcomes. Anything that may hinder the measuring of those outcomes can negatively affect the quality of the data.

By requiring seizures to be “controlled”, we are attempting to mitigate the risk of variability in the study. We are also attempting to mitigate the risk of inhibiting the measurement of outcomes. For example, uncontrolled seizures could be a confounder because if VTS-270 is beneficial the neural cells could increase and become more active. This could lead to the need to change anticonvulsants, and those changes could affect coordination, gait, or alertness and thus confound the measurements of outcomes.

Situations can arise during any study where the participant needs to have unforeseen medical intervention. This is not controllable. But by limiting participation to patients who have their seizures under control, we set up the study for the best chances of success.
18. My child does not qualify for the trial (age, seizures), can I get VTS-270 through compassionate use?

We recognize that the complex balancing of factors related to compassionate use programs may create situations that appear deeply unfair to a single patient or family facing the unthinkable. Yet the reality facing companies presented with these situations is whether individualized decisions could delay FDA approval of a drug or therapy for use in a larger number of suffering patients. Vtesse believes that these complex and difficult decisions require thoughtful involvement of the people working in biotech companies, regulators, and representatives of patients and their families.

At Vtesse, we believe the clinical trial process offers the best chance of securing regulatory approval enabling medicines to be available to as many patients as possible as quickly as possible. We hold an ethical responsibility to ensure the quality and integrity of clinical trials and to minimize risk to patients.

While our main focus is ensuring enrollment and completion of our clinical trial, Vtesse is currently supporting expanded access in a limited fashion. We are deeply committed to working together with the patient community and regulators to objectively evaluate and expand this policy as the clinical trial progresses and we gather additional data.

19. Why did Vtesse decide to study IT administration versus IV administration?

There is an urgent need among patients with NPC1 to have access to a drug that has an impact on neurological symptoms. The most effective way to deliver VTS-270 to the brain is through intrathecal (IT) administration. IT delivery is thought to be the best way to achieve efficacy on neurological function in patients with NPC1. Neurological symptoms, in most cases, are what lead to death in this patient population.

It has been shown in pre-clinical animal models that IV administration of cyclodextrin does not supply an efficacious level of cyclodextrin to the brain, as cyclodextrin does not pass the blood brain barrier. The most efficient way to deliver VTS-270 to the brain is through intrathecal administration.

We are focusing on one method of administration to ensure we get the highest
quality data set to submit to regulatory agencies for approval of VTS-270 for patients with NPC1.

20. How is your product different from the various cyclodextrins?

Not all cyclodextrins are the same. From a drug quality perspective, the pre-clinical safety package and quality attributes of VTS-270 have been reviewed by FDA and EMA and have been considered appropriate for a product that will be administered intrathecally to a very vulnerable population. In addition, the clinical data from the Phase 1 NIH trial and the Part A (dose selection phase) of the Phase 2b/3 clinical trial were gathered based on treatment with VTS-270. Therefore, VTS-270 is a unique version of cyclodextrin and the data gathered from the studies done with VTS-270 cannot be extrapolated to other cyclodextrins.

21. How do you plan to successfully enroll enough patients? Can the NPC community support more than one trial enrolling at the same time?

Vtesse has worked diligently to coordinate with the FDA and EMA to align the trial protocol for the VTS-270 2b/3 clinical trial. This protocol mandate a minimum of 51 patient enrollees. Several parent/patient organizations have bonded together to help us achieve this enrollment goal, under the slogan: “51 and Done!” You can contact the National Niemann-Pick Disease Foundation for more information (http://www.nnpdf.org).

In addition, Vtesse is working to recruit patients via outreach through advocacy groups, professional societies, and other means of raising awareness of the trial to those patients who may not be active with patient organizations. If you have interest in the trial, please reach out to your physician or local patient advocacy group or contact our head of patient advocacy, Carrie Burke at carrie@vtessepharma.com or at 301-233-2950.

More information can be found at www.clinicaltrials.gov and searching for “NCT02534844”