Rough Script: FDA Clinical Trials 2020 – version 3

INTRODUCTION

The introduction section will be a narrative shot in front of a green screen. The green screen will be used to provide a "whiteboard" background to add written content emphasizing certain points in the introduction.

Hello, I'm Justin DeMoss, Chief Philanthropy Officer at Hough Ear Institute.

In the early 1980s, Hough Ear Institute was formed with the primary focus of bringing innovative treatments to those suffering from hearing loss. We did just that with cochlear implants. So, what's next?

Discovering a pharmaceutical medicine for millions of people who suffer from acquired hearing loss and tinnitus.

Our researchers are working tirelessly to accomplish these goals originally set forth by our founder Dr. Jack Hough.

You probably know someone who suffers from hearing loss or tinnitus. You understand how this can strain relationships, separate people from the world around them, and make them feel like their possibilities are limited.

A major key to bringing hope, help, and healing to your loved ones depends on successfully delivering these medications to the public. And to do that requires the skillful navigation of the complicated road to FDA drug approval.

Drug development is done in essentially three stages. Initial research, pre-clinical research, and clinical trials for FDA approval. Let me walk you through how that works.

INITIAL PRE-CLINICAL RESEARCH

This section will begin the whiteboard narrative explaining initial research and then the 3 primary phases of the FDA clinic trial requirements. Caricatures, written content, and animation will be used to explain the steps in this process.

Before any medicine makes it to FDA testing or into the pharmacy, scientists must conduct initial research to create compounds that they believe will achieve their goals. This initial research starts with analyzing reactions in the test tube and testing new drugs in cell cultures to discover if the compounds achieve the desired results.

Next, research moves to laboratory animals to prove the researchers' hypothesis that it will achieve a desired beneficial effect. All pre-clinical research follows many strict ethical guidelines put into place for animal testing. They are deciphering whether or not the drug will work together effectively to treat a specific ailment. This initial research can take up to 3-7 years and costs approximately $5-10 million.

Now, additional pre-clinical research is required. These studies test drug toxicity on two animal species. Results of this testing must show, above everything else, that the drug is not toxic in animal models. During these studies, dosing and formulation are also tested.

Should all the pre-clinical research be successful, the drug is then ready for FDA clinical trials. To begin this, an Investigational New Drug Application is submitted to the FDA. This application contains information about the drug's composition, manufacturing, and plans for testing the drug on humans. The FDA then reviews the application and chooses whether or not to allow the testing to move ahead to clinical trials.

CLINICAL TRIAL PHASE ONE

This section will transition from initial research into phase one.

Now that extensive research has been done to test the lack of toxicity and efficacy of this drug on animal models, it is time for it to be tested on human subjects for FDA approval.. FDA clinical trials are composed of 3 phases. Once these phases are completed successfully, a drug is considered safe, effective, and approved for distribution.

One critical element of these human trials is that they must be done within very strict ethical guidelines. To accomplish this, each study must be approved by an Institutional Review Board composed of scientists, physicians, ethicists, lay persons and others. They apply research ethics by reviewing the methods proposed for research to ensure that they are ethical. Such boards are formally designated to approve (or reject), monitor, and review biomedical and behavioral research involving humans. The purpose of the IRB is to assure that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in a research study.

Phases 1, 2, and 3 require many years and millions of dollars for the rigorous research, development, testing, and validating of results. Here's what each specific phase looks like.

Phase 1 studies focus on the drug's safety in humans.
Prior to moving to Phase 2, the FDA requires that the research team prove their drug is safe for human use and is well-tolerated.
In order to do so, phase 1 includes/requires 20-80 healthy test subjects who are exposed to the maximum dose of the drug being tested. During this process, subjects are very closely monitored in a hospital setting to be sure there are no adverse effects from the drug. .
Phase 1 can take anywhere from 1-2 years to complete and cost up to $2 million.
Phase 1 strictly focuses on safety and not on efficacy because normally the sample size isn't large enough with only 20-80 individuals to get accurate results. In other words, the test pool isn't big enough and doesn't have a wide enough variety of patients. Also, it would cost a substantial amount of money; therefore, efficacy tests are left up to Phase 2.
Once the product is deemed safe initially in human, it is allowed to move to phase 2.
During the drug development process, a drug company can apply for Fast track designation. In order for a drug to get placed on this route, it must meet a pertinent medical need. Should a drug get approval to be on the fast track, accelerated approval and priority review as well as additional communication between the FDA and drug company are among the benefits.

CLINICAL TRIAL PHASE TWO

This section will transition from the requirements of phase 1 to those of phase 2.

Phase 2 requires up to hundreds of new test subjects who suffer from what the drug is designed to treat.
These test subjects are divided into two groups: the "experimental" group, and the "control" group.
The "experimental" group is administered the drug while the "control" group is administered a placebo.
The experimental group will receive various dosages of the drug to see how various amounts affect what the pill is designed to treat. Safety is closely monitored at all times.

Data is derived from the "experimental" group and then analyzed to determine drug safety, appropriate dosage, and how well the medicine works compared to the placebo group.
Phase 2 can take up to about 2-3 years of testing and up to $10 million.
Once the FDA has reviewed this data and deems the product safe, it is then allowed to move to phase 3.
Advancing to phase 3 is a very encouraging step, yet it still has its challenges.

CLINICAL TRIAL PHASE THREE

This section will transition from the requirements of phase 2 to those of phase 3.

Phase 3 is similar to phase 2 in what is being tested; however, the test subject group is increased to thousands of individuals. Testing how the drug interacts with other various medications is also a part of this phase.
As the drug is administered to the new test subjects, the research team reviews an immense amount of data even more deeply to determine appropriate dosing amounts, drug interactions, safety, and effectiveness.
Once the data is collected, the final results are submitted to the FDA.
Phase 3 can last 2-4 years and may require $50-$100 million to complete.
When the FDA agrees with the researchers' findings, the drug is finally approved for distribution.
This is a rigorous process that helps ensure your medications will safely and successfully treat your ailment with limited side effects.

CLINICAL TRIAL SUMMARY

This section will summarize the highlights of phases 1 – 3 in a very quick synopsis prior to transitioning to the explanation of the HEI business model

As you can see, this is quite a long and complicated process. Let's recap!
It takes a **minimum** of 8 years for a compound to move from initial research to distribution.
FDA clinical trials take a **minimum** of 6 years before the drug is approved for patients.
A medication can only be fast tracked if there is a **pertinent medical need.**
The testing period requires the expertise of **dozens** of researchers and medical professionals.

Participation is needed from possibly up to **thousands** of test subjects.
All this has to come together before the drug can be deemed safe and effective.
It's a daunting task, but we have hope!
Hough Ear Institute has developed a business model to help navigate this process, and we are making great strides toward our goal.

THE HEI BUSINESS MODEL

This section should illustrate the HEI business model, how it is designed to accomplish the goal of generating revenue and finding medical solutions.

This business model has proven effective and is advancing!

As a nonprofit medical research institute, HEI conducts initial and pre-clinical research, and possibly even early stage clinical studies. All of this with the goal of attracting pharmaceutical partners that will take a drug through remaining, most expensive, clinical studies and into the market.

Researchers from HEI and our pharmaceutical partner, Auditus LLC, a wholly owned subsidiary of Otologic Pharmaceutics, Inc., conducted initial, pre-clinical, and early stage clinical studies for its hearing loss pill. A biotech company, Oblato Inc. recently signed an agreement to take the drug through the remaining clinical trials and into market.

HEI continues to advance this drug to test its ability to treat tinnitus among other ailments while it progresses through the clinical trials. HEIcontinued to conduct research, where it was discovered that the pill not only soaks up harmful toxins, but also that it has the ability to regenerate and reconnect damaged nerve endings on surviving hair cells, which was once thought to be irreversible.

HEI researchers have also come up with a separate technology, inner ear injection that has proven the ability to re-grow inner hair cells – this is now moving towards formulation and toxicology studies to be poised for Phase 1 clinical trials. We will continue to use the proven business model to advance this research.

Additional research that is being conducted includes an inner ear drug delivery approach that could help with hearing loss caused by genetic mutations. Genetic mutations/ hearing loss is incredibly tricky when it comes to finding a treatment. Our researchers believe they may have found a way to speed up the process of infusing medication quickly and efficiently into the inner ear. We are so excited because that means hope is in store for many individuals who suffer from even genetic hearing loss. If our theory is correct, this technology could help those suffering from over 150 genetic disorders that lead to hearing loss.

These are just a few of many answers we continue to seek on the path to restoring hearing worldwide! Because the brain is involved in hearing and there is overlap between hearing and pathologic

Tau proteins, our hope is to investigate our therapeutics' effects on neurodegenerative disorders like Alzheimer's, Parkinson's, ALS, etc. We also hope to run additional studies to test the effects on hearing loss caused by Meniere's disease.

THE HEI STATUS UPDATE

This section will demonstrate the progress already made, and the work yet to be done. This is where we'll define the amount of money needed, the things that will be done with the money, and the call-to-action for raising funds.

We have already concluded initial, pre-clinical, and phase 1 trials on our hearing restoration pill. We are now ready to move to phases 2 and 3.

Learn more about Hough Ear Institute's research to advance medications that will restore hearing at www.INSERTLANDINGPAGE.org.