

# RARE Film Guide

## Curriculum Supplement—Exploring Rare Disease Research

### INTRODUCTION

This activity is designed to be used with the film *RARE*, a documentary that explores the major issues affecting people living with a rare genetic disorder, **Hermansky-Pudlak Syndrome (HPS)**. Before the film, students explore and share their ideas about general themes in the film by responding to statements in a *Silent Chalk Talk*. Students are then asked to view the film from the perspective of a **stakeholder** in regard to a **clinical trial** testing a new drug for HPS. Stakeholders include Donna Appell, a mother working to find a cure for her 21-year-old daughter who has HPS; Heather Kirkwood, a woman with HPS who is involved in a clinical trial for a drug to treat people with HPS; and Dr. William Gahl, a researcher from the National Institutes of Health (NIH) who works with people with HPS and runs the clinical trial in which Heather is enrolled. After watching the film, students gather for another *Silent Chalk Talk*, and meet in small groups to discuss the film's **ethical** issues from different perspectives.

### FILM BACKGROUND AND ORDERING INFORMATION

*RARE* is a documentary by award-winning filmmakers Maren Grainger-Monsen, MD, and Nicole Newnham. This film guide accompanies the high school version, which runs 36 minutes. A 56-minute version is also available. The film may be purchased at <http://www.rarefilm.org> (the educational use cost is \$40).

### CLASS TIME

One class period of 55 minutes allows time to show the film with minimal remaining time for either a class discussion about clinical trial design and/or the themes in the film.

Spreading this lesson over two class periods allows for viewing the film and going into more depth on clinical trial design, while leaving time for discussion about film themes.

### KEY CONCEPTS

- Clinical trials are designed to systematically test a study medicine or treatment to see whether it is safer and more effective than no treatment at all, or than other existing treatments.
- There may be unique challenges for a clinical trial for a rare disease, such as being able to enroll enough participants for the trial to generate meaningful data.
- **Patient advocacy groups** can create community, provide education and awareness, encourage research, and organize lobbying efforts for their constituents.
- Researchers, participants, and others involved in a trial may feel a conflict between what best serves the trial and what best serves their personal interests.
- Hope can play a powerful role in treating disease.
- Successful clinical trials require community support and participation.

### LEARNING OBJECTIVES

#### *Students will know:*

- A study design for a clinical trial for a rare disease.
- Many stakeholders are affected by medical research.
- Successful clinical trials require community support.

#### *Students will be able to:*

- Discuss ethical considerations that may be associated with a clinical trial.
- Speak about participation in a clinical trial from different stakeholder perspectives.

Vocabulary words used in each lesson are in **bold**. Definitions can be found at the end of each lesson and in the *Master Glossary* in the *Appendix*.

## MATERIALS

Materials	Quantity
DVD of the film <i>RARE</i> and projection equipment	1
Computer with PowerPoint	1
Teacher Resource— <i>Silent Chalk Talk Posters</i>	1
Teacher Resource— <i>Silent Chalk Talk Rules of Participation</i>	1
Teacher Resource— <i>Images for Chalk Talk Posters</i>	1
Student Handout— <i>Post-Film Stakeholder Quotes and Guiding Questions</i>	1 per student
Teacher Resource— <i>Key Phrases and Stopping Points</i>	1
Teacher Resource— <i>Clinical Trial Design for Pirfenidone Study</i>	1 (or more if copying for students)
Teacher Resource— <i>Clinical Trial Design for Pirfenidone Study PowerPoint Slide Set Overview</i>	1
<i>Clinical Trial Design for Pirfenidone Study Slide Set</i> (found at <a href="http://nwabr.org/curriculum/humans-research">http://nwabr.org/curriculum/humans-research</a> ).	1
<b>Optional:</b> Student Extension Handout— <i>InterMune Share Prices and the FDA</i>	1 per student

## NOTE TO THE TEACHER

This lesson is a supplement to *The Science and Ethics of Humans in Research* curriculum from the Northwest Association for Biomedical Research (NWABR). While the film can be shown independently, it is helpful for students to have a background in research with human participants and clinical trial design. In preparation, we recommend completing *Lesson Five—Clinical Trials* from this curriculum before presenting the film.

Another applicable lesson, *Who Should Pay? Funding Research on Rare Genetic Diseases* is *Lesson Seven* of NWABR's *Advanced Bioinformatics* curriculum, *Using Bioinformatics: Genetic Research*. In this lesson, students learn about Leigh's disease and meet in "like" and "mixed" stakeholder groups to identify areas of agreement and disagreement, and to propose a recommended compromise to Congress regarding funding for rare disease research. This lesson can be found at <http://www.nwabr.org>.

## FRAMING THE LESSON

Before viewing the film *RARE*, students explore and share their thoughts and ideas about researching treatment and cures for rare diseases by silently responding in writing to statements, questions, and pictures posted on *Silent Chalk Talk Posters*. Because the conversation is in written (silent) form, conversation cannot deteriorate into shouting matches, all students are given an equal voice, and students feel safe to express their true thoughts and feelings.

Students will view the film through the eyes of one of three stakeholders, sharing their unique perspective in a small group after the film. By personalizing the experience in this way, students have a chance to become aware of differing perspectives and how they may conflict with the intentions of researchers. Afterward, students revisit their initial *Silent Chalk Talk Poster* comments to see how their thinking may have evolved as a result of the activities.

## TEACHER PREPARATION

- Make copies of *Student Handouts*.
- Make posters as directed in the Teacher Resource—*Silent Chalk Talk Posters* and post them around the room.
- For showing the film, prepare the computer and projection unit. **[Note:** If you plan to pause the film at suggested stopping points, make sure you have easy access to the pause button.]

## PROCEDURE

### Activity One: Silent Chalk Talk

1. Tell the class that in this lesson they will be exploring their thoughts and feelings about researching treatments and cures for rare diseases. To begin, students will be able to share their thoughts and ideas in a silent discussion.
2. Point out the *Silent Chalk Talk Posters* you have posted around the classroom. Read through each poster with students and ask for clarifying questions before anyone responds. Be careful not to discuss any opinion or give any information that may change student responses; merely ensure that they understand what each poster addresses. It is important to leave this as vague as possible to allow students to identify their own preconceived notions and/or misconceptions.

3. Post and review rules of participation on Teacher Resource—*Silent Chalk Talk Rules of Participation*.
4. Provide the same color of marker for each poster so that responses are as anonymous as possible. If possible, use the same color of marker before viewing the film and a different color after viewing the film. This will allow teachers and students to more easily see the impact of the film on their thoughts and ideas.
5. Give students about 10 minutes to add their thoughts to each poster, revisiting each poster at least twice. Encourage students to respond at least one time to the primary comment on the poster, but if they have trouble doing so they may choose to respond only to other students' comments.
6. Explain to students that they will be using these posters to continue a conversation at the end of the lesson, but they will not be discussing the posts until then.

## Activity Two: Exploring Rare Disease Research

### Part I: Introducing Clinical Trial Design

7. Tell students that they will be viewing the film *RARE*, which illustrates both the hope and the challenges of enrolling people with HPS into a clinical trial for the drug **pirfenidone**. In early studies, pirfenidone showed promising results in the treatment of a lung condition (**idiopathic pulmonary fibrosis**), experienced by some people with HPS. In the **Phase II** trial shown in the film pirfenidone was given to people with HPS who also suffer from **pulmonary fibrosis**.
8. Show students the PowerPoint presentation about the pirfenidone clinical trial design found at <http://nwabr.org/curriculum/humans-research> (to view copies of the slides see Teacher Resource—*RARE PowerPoint Slides*). Use this presentation to introduce students to the clinical trial design of the trial presented in the film. The pirfenidone trial is a **randomized, placebo-controlled, double-blind trial**.
9. Before moving on, check to make sure that students understand what a placebo is, know the characteristics of a double-blind study, and realize how strict **inclusion and exclusion criteria** can limit participation in some clinical trials. If students have not already completed *Humans in Research Lesson Five*, teachers may wish to present that lesson before this one. *Lesson Five* introduces the purpose and structure of each phase of a clinical trial, as well as the challenges of recruiting participants for a study.

### Part II: Meet the Stakeholders

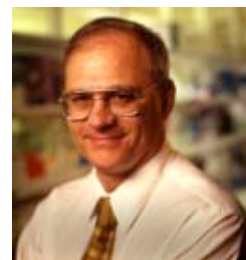
10. Explain to students that the film tells the story of a number of people who are in some way affected by or interested in HPS. These people are all stakeholders in the area of rare genetic diseases. A stakeholder is any person or institution that is affected by or interested in HPS. Additionally, in the situation portrayed in this film, each stakeholder will be affected by the outcome of the clinical trial for a drug to treat people with HPS.
11. Ask the class to come up with examples of as many pirfenidone clinical trial stakeholders as possible. This could include makers of the drug, other people with HPS not involved in the trial, funders of the trial, people with other rare diseases, insurance companies, hospitals, families and friends, and more.
12. Before showing the film, use the PowerPoint slides to introduce Donna Appell, Heather Kirkwood, and Dr. William Gahl. Explain to students that in this activity they will be asked to view the film through the eyes of one of these three stakeholders:



**Donna Appell:** Donna's daughter, Ashley, was diagnosed with HPS when she was a toddler. Donna worked to find others with the condition and founded the HPS Network in 1992. Ashley is now in her 20s and Donna has more than 700 HPS patients in her database.



**Heather Kirkwood:** Heather was in her 20s before a physician suggested she might have HPS, though she had had symptoms all her life. Heather is a journalist, an advocate for people with HPS, and a participant in the clinical trial shown in the film.



**William Gahl:** Dr. Gahl works in the Office of Rare Disease Research at the National Institutes of Health. He is both an MD and a PhD who works as a physician and clinical researcher for rare diseases such as HPS. He is the principal investigator of the clinical trial presented in the film.

13. Have students form groups of three. Match up each of the students in each group with a different stakeholder. Explain to students that they will watch the film from the perspective of their assigned stakeholder. Their job will be to represent the views and concerns of that stakeholder in a discussion after the film.

### Part III: View the Film

14. Pass out to each student a copy of Student Handout 6.1—*Stakeholder Quotes and Guiding Questions*, and give them time to read the film themes and quotes. This information will help students frame their post-film discussion. Encourage students to take notes during the film.

15. Show the film. [Note: You may show the film straight through, or you may choose to occasionally pause it to give students a chance to process the dialogue and take notes from the perspective of their stakeholder. Useful stopping points are outlined in Teacher Resource—*Key Phrases and Stopping Points*.]

### Part IV: Post-Film Discussion

16. After the film, tell students that they will next talk about their experiences as their assigned stakeholder with their group. Share these discussion goals:

- Achieve a deeper understanding of the film as well as the concerns and interests of the three main stakeholders.
- Promote participation in the discussion through the perspective of each stakeholder and/or each student.
- Explore many differing views; *do not engage in a debate* with pro/con stances.

Refer students to Student Handout 6.1—*Stakeholder Quotes and Guiding Questions* and explain that the facilitator role will rotate among the three students in each group for each new theme. You may wish to write the following discussion steps for facilitators on the board:

1. The facilitator reads the quote and the question.
2. The students discuss the question from their stakeholder's perspective, using things that happened in the film (and/or their notes) to back up their statements.
3. The facilitator invites students to discuss the question from their own perspective and makes sure everyone who wishes to speak has a chance to contribute.

4. The facilitator tries to paraphrase what others have said.
5. The group moves on to the next theme. The facilitator for the new theme repeats the steps above.

[Note: Based on the time available, monitor discussion length so every facilitator has the same amount of time. Provide groups with a one- to two-minute warning before moving on to a new theme.]

### Closure

17. After the discussion, use Teacher Resource—*Silent Chalk Talk Rules of Participation* to remind students of the guidelines. Invite students to again make comments on the *Silent Chalk Talk Posters*. [Note: Alternatively, teachers may choose to allow more time for student reflection and wait until the next class session to have students revisit the posters.]

18. Bring the groups back together as a class and ask a few students to share their small-group conversations (and/or *Silent Chalk Talk Poster* comments) with the class.

- a. Ask students to share how the film reflected the themes of: inspiration, harms and benefits, **conflicts of interest, futility**, and hope.
- b. Explain that even though the study reached futility, this does not mean that it was a “failed trial.” Even though the results were disappointing to the stakeholders involved, any study that ultimately answers the question researchers set out to answer is considered a “good study.”
- c. Ask students if they think federal money, which comes from taxpayers, should be used to fund rare disease research. You may want to discuss who is impacted by rare disease research, whether it be financially (taxes), medically (treatments for more common diseases originally tested on patients with rare diseases), or ethically (greater good, etc.).

### CONNECTION TO FORMATIVE ASSESSMENT

Revisit the statements students sorted for the formative assessment. The *RARE* Film Guide should further reinforce that Statement A is accurate and Statement F is not

## Frequently Asked Questions

Q: *How is HPS passed on from parent to child?*

- HPS is an **autosomal recessive** trait, which means that both parents must be carriers of the trait for a child to inherit the syndrome.
- HPS is a **single-gene disorder**, meaning a mutation in one single gene causes HPS.
- Although HPS is a single-gene disorder, there are nine different genes that will independently cause HPS if any one of them mutates.
- Both parents must have a mutation to the same gene (one of nine), for a child to inherit HPS.
- HPS is a **lysosomal disorder**. Each of the nine genes affects the function of the **lysosomes** in the cell.
- There are slightly different **phenotypes** for each of the nine types of HPS.
- In the medical community there is a strong suspicion that additional genes related to HPS are yet to be found.

Q: *Why was pirfenidone approved in Europe and Asia but not in the United States?*

A: Studies carried out in Europe and Asia trialed pirfenidone use for idiopathic pulmonary fibrosis—pulmonary fibrosis that occurs in otherwise healthy people without a known cause. The pirfenidone study presented in the film *RARE* was for patients with HPS, people with a known cause for their pulmonary fibrosis. The study parameters were different in the two cases, and even though initial reports on the use of pirfenidone to treat HPS looked promising, the data were not conclusive enough for pirfenidone to gain FDA licensure.

Q: *Why have there been so few lung transplants in patients with HPS?*

A: There are many factors involved:

- Patients with HPS often have **bleeding disorders**, which make major surgery much riskier than for people without bleeding disorders.
- People sometimes remain on lung transplant lists for a long time, waiting for organs to become available. People with HPS can be relatively healthy for long periods of time, only to have a sudden health crisis. When in a relatively healthy period, people with HPS may not qualify to be put on a lung transplant list. After a sudden health crisis, people with HPS may not be able to receive a transplant quickly enough.
- There are no lung transplant programs in Puerto Rico. A person from Puerto Rico who wishes to be added to a lung transplant waitlist has to first move to the U.S. This can be difficult for many reasons including the language barrier, financial burden, and family commitments.
- Living with a chronic condition such as HPS can be financially challenging. Not all medical insurance covers lung transplant surgery and the costs involved are often prohibitive for a patient and his or her family.

accurate.

## EXTENSIONS

- Dr. William Gahl was featured in a TED talk entitled, “Medical Mysteries and Rare Diseases” (available at: <http://tedxcmu.com/videos/william-gahl>), in which he addresses balancing harms and benefits in treating rare diseases. (The video runs 17:05 minutes.) Invite students to watch this talk and write a news article about it.
- Using Student Extension Handout—*InterMune Share Prices and the FDA*, have students apply graphing skills and do internet research to explore how advances and setbacks in the drug development process affect stock prices for a drug company.

## GLOSSARY

**Albinism:** A condition characterized by a lack of pigmentation, resulting in very light skin coloring, white hair, and light blue or red eyes.

**Autosomal recessive trait:** A trait both parents must carry for a child to inherit the syndrome.

**Bleeding disorder:** A medical disorder that leads to poor blood clotting and continuous bleeding.

**Futility:** Uselessness or pointlessness; reason for stopping a clinical trial if interim data show that the treatment group is unlikely to see any more improvement than the control group.

**Hermansky-Pudlak Syndrome (HPS):** A rare genetic disorder characterized by albinism, bleeding problems, and fatal pulmonary fibrosis.

**Idiopathic pulmonary fibrosis:** Pulmonary fibrosis that occurs in otherwise healthy people without a known cause.

**Lysosomal disorder:** A disorder that affects the function of lysosomes in cells.

**Lysosomes:** The part of a cell responsible for breaking down waste materials and other debris.

**Phenotype:** Observable physical or biochemical characteristics resulting from both genetic makeup and environmental influences.

**Pirfenidone:** A drug developed by InterMune Inc. for the treatment of idiopathic pulmonary fibrosis.

**Pulmonary fibrosis:** Scarring or thickening of the lungs.

**Single-gene disorder:** A disorder caused by a mutation in a single gene.

## SOURCES

*Frequently Asked Questions* section:

Kirkwood, H., Granger-Monson, M., Fullerton, M., Wilfond, W. (Panel discussion following viewing of film *RARE*, Pacific Science Center, Seattle, June 4, 2012).

Image used for Chalk Talk posters has been released into the public domain.

Information about InterMune and pirfenidone prices was gathered from:

<http://seekingalpha.com/article/203187-intermune-left-gasping-by-fda-rejection-of-pirfenidone>

<http://www.medicalnewstoday.com/releases/182700.php>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3039013/>

# STUDENT HANDOUT

## Post-Film Stakeholder Quotes and Guiding Questions

Name \_\_\_\_\_ Date \_\_\_\_\_ Period \_\_\_\_\_

During this small group discussion, you will talk about a number of themes from the film. For each theme, a quote and a question are provided. Rotate the facilitator role among group members with each change in theme. During your turn as facilitator, follow these steps:

1. Facilitator reads the quote(s) and the question for each theme.
2. Students discuss the question from their **stakeholder's** perspective, using the film (and/or their notes) to back up their statements.
3. Facilitator invites students to discuss the question from their own personal perspective, if they choose to do so.
4. Facilitator makes sure everyone who wishes to speak has a chance to contribute.
5. Facilitator tries to paraphrase what others have said.
6. Repeat the steps above, moving on to the next theme and a new facilitator.

**Futility:** Uselessness or pointlessness; reason for stopping a clinical trial if interim data show that the treatment group is unlikely to see any more improvement than the control group.

**Hermansky-Pudlak Syndrome (HPS):** A rare genetic disorder characterized by albinism, bleeding problems, and fatal pulmonary fibrosis.

**Rare disease:** A disease that affects fewer than 1 in 1,500 people (in the U.S.). They are mostly genetic conditions passed on from parent to child.

**Stakeholder:** A person with an interest or concern in something.

### Theme One: Inspiration

#### Facilitated by the student representing Donna

Quote from Donna:

"...And I wanted to know where those 23 people are, and I want to know what they're doing, and I want to know who's researching this, and where is the cure...and I found nothing."

Quotes from Dr. Gahl:

"Although **HPS** affects a small number of people, we are really hoping that studying it will eventually lead to therapies for more common diseases." "Donna Appell used her persuasive powers to influence us to study HPS..."

Question:

Why study a disease that affects so few people?

### Theme Two: Harms and Benefits

#### Facilitated by the student representing Heather

Quote from Heather:

"You would never want to be in this position [having a **rare disease**], but if you have to be in it, it is gratifying to know that you can play a role in helping to find a cure, helping to find a treatment so that the next generation of people with HPS don't have to face the problems we're facing."

Question:

What are some of the benefits and drawbacks each person experienced in their involvement in the clinical trial? (What does each person stand to lose or gain?)

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## Theme Three: Conflicts of Interest

### Facilitated by the student representing Dr. Gahl

Quote from Donna:

"I've learned what good science is now, and I feel that it is also the right thing to do, but...I'm her mom, and everything I've worked for and worked towards is to try to get a cure or treatment for HPS, so to exclude her was a little difficult, but...it's the right thing to do and it's what we have to do."

Quote from Dr. Gahl:

"There's disappointment when a patient is not eligible, and there's a temptation to skirt the rules or to fudge things a tad. One has to be diligent not to do that because it ruins the studies."

Question:

In the film there is a conflict between "good science" and the personal interests of Dr. Gahl, Donna, and Heather. What is the conflict for each? Specifically, how does Dr. Gahl handle the conflict between his role as a physician and his role as an ally to Donna and her family? How does each resolve the conflict?

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## Theme Four: Futility

### Facilitated by any student

Quote from Dr. Gahl:

"That interim analysis indicated that there would never be a difference between the pirfenidone-treated and the non-treated individuals, and **futility** is a cause to stop a trial."

Question:

How was each individual affected by the news that the trial would be stopped due to futility?

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## Theme Five: Hope

### Facilitated by any student

Quote from patient speaking to Dr. Gahl after the trial is stopped:

"...He is my dream maker. You are my hope. The NIH is my hope. I am so blessed."

Question:

What do you think gives each individual in the film hope? How could this statement be both comforting and challenging from different perspectives?

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## Wrap-up

### Facilitated by any student


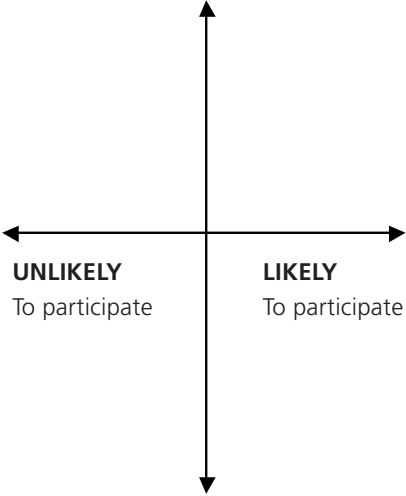
What other stakeholder views or concerns would you like to discuss with the group?



# TEACHER RESOURCE

## Silent Chalk Talk Posters

Recreate these posters on large pieces of butcher paper to allow ample room for comments and thought development. Give participants a chance to comment on the posters both **before** and **after** viewing the film *RARE*. If possible, use different colors of marker for comments made before and after viewing.

<p><b>In what way can a clinical trial offer hope? Lead to disappointment?</b></p>	 <p><b>What does this image say to you?</b></p> <p>(For larger copies of these images, see the Teacher Resource—<i>Images for Chalk Talk Posters</i>.)</p>	<p><b>What would “good science” look like in a clinical trial?</b></p>
<p><b>People who participate in research are...</b></p>	<p><b>Clinical Trials</b></p> <p>I know <b>A LOT</b> about this topic</p>  <p>I know <b>LITTLE</b> about this topic (Have participants plot their own position/knowledge point.)</p>	<p><b>Why study a rare disease that affects so few people?</b></p>

- 1. Respond to the main comment anywhere on the poster you would like.**
- 2. Respond to others by drawing an arrow from their comment to yours.**
- 3. Keep all responses respectful and school-appropriate.**
- 4. If you agree with a comment add an exclamation point (!) or star (\*).**
- 5. If you disagree with something that someone said, explain why you disagree, using appropriate language.**
- 6. Do not cross out or write over anyone else's comments.**
- 7. Pictures are completely permissible; just keep them appropriate.**
- 8. NO TALKING!**

# TEACHER RESOURCE

## Image for Chalk Talk Posters



*This image has been released into the public domain.*

### Clinical Trial Design for Pirfenidone Study Slide Set

*The Science and Ethics of Humans in Research*  
 RARE Film Guide:  
 Curriculum Supplement—Exploring Rare Disease Research

**NWABR.ORG**  
 Northwest Association for Biomedical Research

### Clinical Trial Design for Pirfenidone Study

**Study purpose:**  
 To discover whether the use of **pirfenidone** in patients with **Hermansky-Pudlak Syndrome (HPS)** decreases the loss of lung function better than a **placebo**, and to find out how safe pirfenidone is compared to a placebo.



### Inclusion Criteria

(all of these conditions must be met to participate in the study)

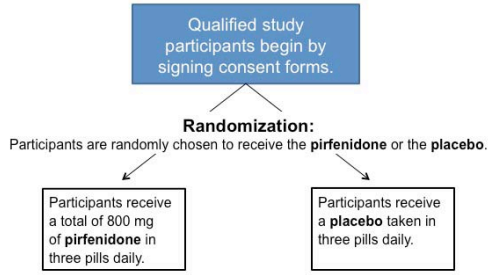
- Diagnosis of **Hermansky-Pudlak Syndrome (HPS)**.
- Male or female over the age of 18.
- Lung capacity test results within set range.
- No evidence of improvement in **pulmonary fibrosis** within the past year.
- Oxygen levels within set range during a six-minute walk test.
- Be available, willing, and able to come to the NIH Clinical Center in Maryland for tests and follow-up every four months for three years.
- Women of child-bearing potential must use two reliable forms of contraception if sexually active. Alternatively, female subjects must be postmenopausal (for at least one year). Women must have a negative pregnancy test at screening.

### Exclusion Criteria

(any of these conditions would *disqualify* someone from study participation)

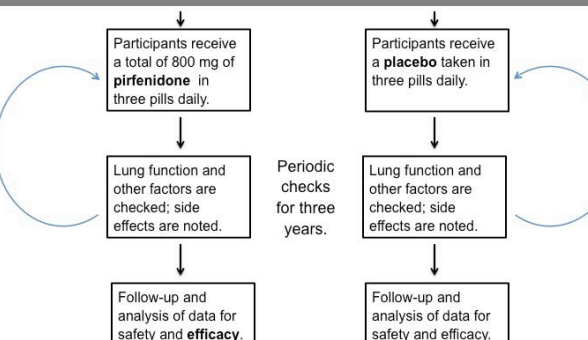
- Possibility of having **pulmonary fibrosis** for reasons other than HPS (such as through exposure to asbestos, radiation, cancer, certain types of pneumonia).
- On a lung transplantation waiting list.
- Smoking within the last six months.
- Pregnant or nursing women.
- History of alcohol abuse or recreational drug use in the past two years.
- History of human immunodeficiency virus (HIV) or chronic viral hepatitis infection.
- Chronic use of high-dose steroids.
- Prior use of **pirfenidone**.

### Clinical Trial Design for Pirfenidone Study



**Double-blind study:** To prevent bias, neither the participants nor the researchers know which treatment the participant is receiving.

### Clinical Trial Design for Pirfenidone Study



**Efficacy:** How does the drug treatment work compared to the **placebo**?

### Stakeholders in the film *RARE*

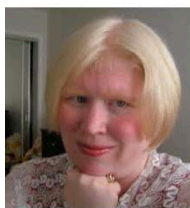


Donna Appell

Donna's daughter, Ashley, was diagnosed with HPS when she was a toddler. Donna worked to find others with the condition and founded the HPS Network in 1992. Ashley is now in her 20s and Donna has more than 700 HPS patients in her database.



### Stakeholders in the film *RARE*

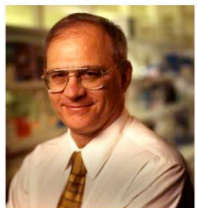


Heather Kirkwood

Heather was in her 20s before a physician suggested she might have HPS, though she had had symptoms all her life. Heather is a journalist, an advocate for people with HPS, and a participant in the clinical trial shown in the film.



### Stakeholders in the film *RARE*



Dr. William Gahl

Dr. Gahl works in the Office of Rare Disease Research at the National Institutes of Health. He is both an MD and a PhD who works as a physician and clinical researcher for rare diseases such as HPS. He is the principal investigator of the clinical trial presented in the film.



# TEACHER RESOURCE

## Key Phrases and Stopping Points

Time Point, 36-min version	Time Point, 56-min version	POV	Key Phrases	Themes and Questions
3:25	2:11	Donna	"...And I wanted to know where those 23 people are, and I want to know what they're doing, and I want to know who's researching this, and where is the cure...and I found nothing."	<b>Inspiration</b> Why study a disease that affects so few people?
8:54	8:05	Dr. Gahl	"Donna Appell used her persuasive powers to influence us to study HPS."  "Although HPS affects a small number of people, we are really hoping that studying it will eventually lead to therapies for more common diseases."	
15:58	15:36	Heather	"You would never want to be in this position [having a rare disease], but if you have to be in it, it is gratifying to know that you can play a role in helping to find a cure, helping to find a treatment so that the next generation of people with HPS don't have to face the problems we're facing."	<b>Harms and Benefits</b> What are some of the benefits and drawbacks each person experienced in their involvement in the clinical trial?
17:58	23:29	Donna	"I've learned what good science is now, and I feel that it is also the right thing to do, but... I'm her mom, and everything I've worked for and worked towards is to try to get a cure or treatment for HPS, so to exclude her was a little difficult...but it's the right thing to do and it's what we have to do."	<b>Conflicts of Interest</b> How does Dr. Gahl handle the conflict between his role as a physician and his role as an ally to Donna and her family? How do other stakeholders respond to conflicts between "good science" and personal interest?
19:06	24:36	Dr. Gahl	"There's disappointment when a patient is not eligible, and there's a temptation to skirt the rules or to fudge things a tad. One has to be diligent not to do that because it ruins the studies."	
27:24	40:33	Dr. Gahl Donna Heather	"That interim analysis indicated that there would never be a difference between the pirfenidone-treated and the non-treated individuals, and <b>futility</b> is a cause to stop a trial."	<b>Futility</b> How was each individual affected by the news that the trial would be stopped due to futility?
32:23	51:10	Dr. Gahl	Patient speaking to Dr. Gahl after the trial is stopped: "...he is my dream maker. You are my hope. The NIH is my hope. I am so blessed to have you in my life."	<b>Hope</b> How could this statement be both comforting and challenging from different perspectives? What do you think gives each individual in the film hope?

The film *RARE* illustrates both the hopes and the challenges of enrolling people with HPS into a **clinical trial** for the drug **pirfenidone**. In earlier studies, pirfenidone showed promising results in the treatment of Idiopathic Pulmonary Fibrosis, a lung condition that is a complication for some people with HPS. In the **Phase II** trial shown in the film, pirfenidone (or a **placebo**) was given to eligible trial participants with HPS who also suffer from pulmonary fibrosis.

### Study purpose:

To see if the use of pirfenidone decreases the loss of lung function better than a placebo, and to find out how safe pirfenidone is compared to a placebo.

### Study title:

**Randomized, Double-Blind, Placebo-Controlled**, *Study to Evaluate the Safety and Efficacy of Oral Pirfenidone for Pulmonary Fibrosis in subjects with Hermansky-Pudlak Syndrome*

### Inclusion/Exclusion criteria:

The study has strict criteria for participation. To participate in the trial, the subject must meet the following criteria:

#### **Inclusion criteria** (all of these conditions must be met):

- Diagnosis of HPS.
- Male or female over the age of 18.
- Lung capacity test results within set range.
- No evidence of improvement in pulmonary fibrosis within the past year.
- Oxygen levels within set range during a six-minute walking test.
- Be available, willing, and able to come to the NIH Clinical Center in Bethesda, Maryland for tests and follow-up every four months for three years.
- Women of child-bearing potential must use two reliable forms of contraception if sexually active. Alternatively, female subjects must be postmenopausal (for at least one year). Women must have a negative pregnancy test at screening.

#### **Exclusion criteria** (any of these conditions would disqualify someone from participation):

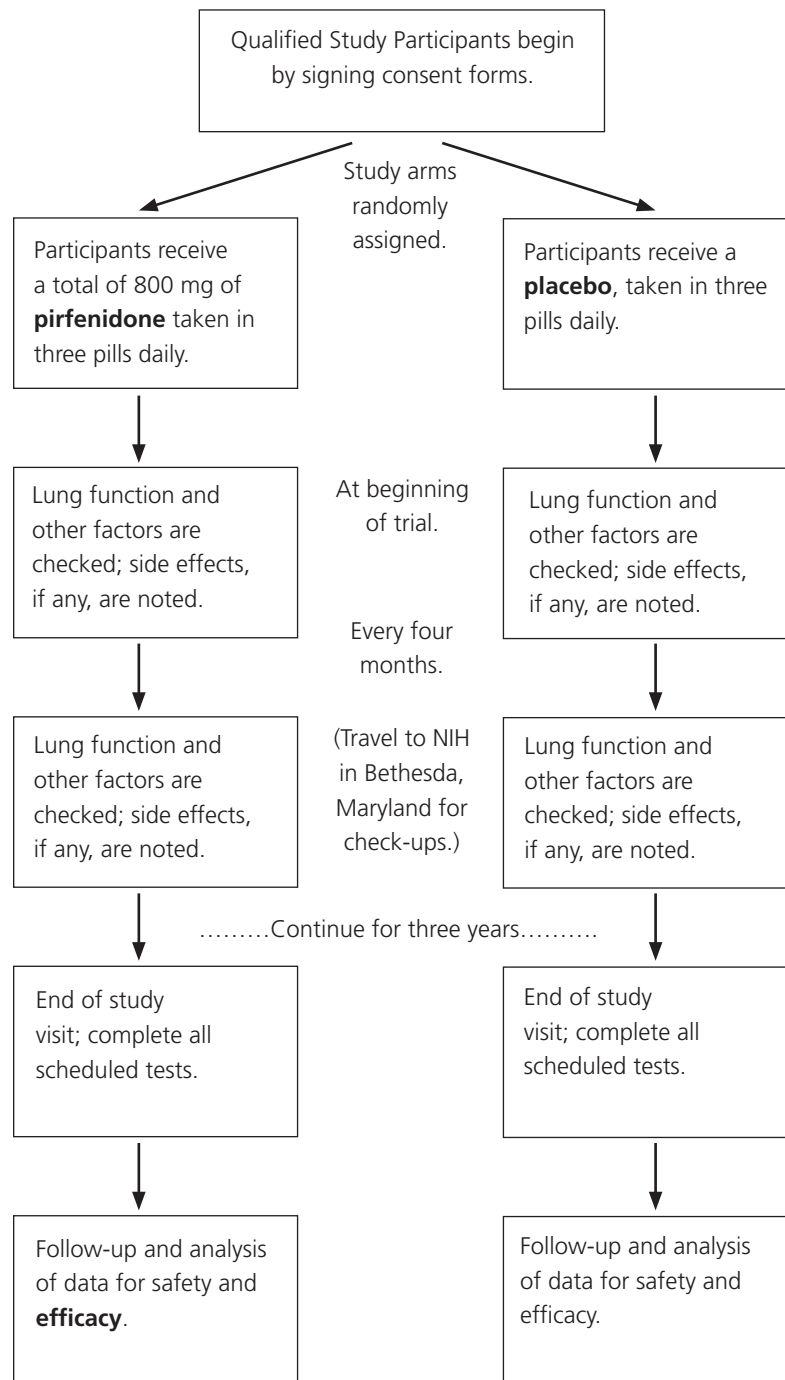
- Possibility of having pulmonary fibrosis for reasons other than HPS (such as through exposure to asbestos, radiation, cancer, or certain types of pneumonia).
- Use of steroids.
- On a lung transplantation waiting list.
- Smoking within the last six months.
- Pregnant or nursing women.
- History of alcohol abuse or recreational drug use in the past two years.
- History of human immunodeficiency virus (HIV) or chronic viral **hepatitis** infection.
- Prior use of pirfenidone.

**Randomized:** Those who qualify are randomly (by chance) put into one of the two study arms.

**Placebo-controlled:** Placebos contain no medicine or treatment, and are sometimes referred to as “sugar pills.” They serve as a control for the research study.

**Double-blind study:** To prevent bias, neither the participants nor the researchers know which treatment the participant is receiving.

**Efficacy:** Effectiveness as measured in a controlled clinical trial.



View the original study at ClinicalTrials.Gov: <http://clinicaltrials.gov/ct2/show/NCT00001596?term=pirfenidone&rank=2>.



# STUDENT EXTENSION HANDOUT

## InterMune Share Prices and the FDA

Name \_\_\_\_\_ Date \_\_\_\_\_ Period \_\_\_\_\_

**Background:** The **clinical trial** process is used to find out whether drugs and treatments are safe and effective enough to be licensed by the Food and Drug Administration (FDA) for prescription use in particular populations. Gaining FDA licensure can be a long and expensive process.

InterMune is a California biotechnology company that makes the drug **pirfenidone**, which was tested in the clinical trial shown in the film to treat **idiopathic pulmonary fibrosis (IPF)** in patients with **HPS**. InterMune purchased the patent for the drug's use in the United States and Europe from another company in 2007. Pirfenidone is considered an orphan drug, a drug developed to treat an **orphan disease**.

**Table 1**

Year	Month	Price/share, in \$*
2009	January	10
	April	16
	July	15
	October	16
2010	January	14
	April	45
	July	9
	October	13
2011	January	38
	April	48
	July	35
	October	20
2012	January	12
	April	15

\* On first day of trading in that month

### Questions:

1. At **point A** on the graph, the FDA Advisory Committee recommended that pirfenidone be licensed by the FDA. What happened to stock prices?
2. At **point B** on the graph, the FDA ruled that they were not satisfied with the data from the clinical trial on which the advisory committee based their recommendation. The FDA did *not* approve pirfenidone. What happened to stock prices?
3. Do an internet search to find out what might have happened between April 2011 and January 2012.

**Clinical trials:** Systematic research studies for health-related benefits that involve human participants.

**Hermansky-Pudlak Syndrome (HPS):** A rare genetic disorder characterized by albinism, bleeding problems, and fatal pulmonary fibrosis.

**Idiopathic pulmonary fibrosis:** Pulmonary fibrosis that occurs in otherwise healthy people without a known cause.

**Rare disease (or orphan disease):** A disease that affects fewer than 1 in 1,500 people (in the U.S.). They are mostly genetic conditions passed on from parent to child.

The data in **Table 1** represents the price of a single share of InterMune stock, rounded to the nearest dollar.

### Instructions:

1. Graph the information from the data table. Put the year and month along the x axis, and put the stock price on the y axis.
2. Mark March 2010 on your graph with an "A."
3. Mark May 2010 on your graph with a "B."
4. Mark the lowest historical price of the stock with a "C."

