ATS DAILY BULLETIN
Where today's science meets tomorrow's care™
Tuesday, May 17, 2016
San Francisco, California
May 13-May 18, 2016

ATS 2016 Draws Big Crowds

Early attendance numbers show ATS 2016 in San Francisco, California, is a popular destination. As of Monday afternoon, there were more than 17,000 registered attendees from 90 countries. Nearly 7,000 scientific abstracts, case reports, and late-breaking abstracts were presented this year. Please join us for ATS 2017, May 19-24, in Washington, D.C. The ATS is seeking input for sessions in all areas of respiratory, critical care, and sleep medicine with a clinical, basic science, and/or translational focus. All proposals must be submitted online by 5 p.m. EDT June 29, 2016. Visit **conference.thoracic.org** to learn more.

Ebola Fighter Catalyst for Change

Katie Meyler will share the story of her compelling work as one of the "Ebola Fighters," collectively recognized by TIME magazine as the 2014 Person of the Year, during the Plenary Session on Tuesday. At the onset of the largest Ebola epidemic in history, Ms. Meyler was spurred to turn her school for girls in Liberia into a disaster-response center.

In 2009, Ms. Meyler founded the More Than Me Academy, a tuition-free girls school located in a Liberian slum. She helped girls get off the streets and into school by providing scholarships, free meals and supplies, and an after-school program. The More Than Me Academy opened its doors in 2013.

A year later, when Ebola broke out, airlines canceled flights and the U.S. Peace Corps left Liberia. Ms. Meyler was fundraising in the United States, but she returned to Liberia. With the help of a donor, she transformed the school into a disaster-response center. Her team took in Ebola orphans, organized meetings, distributed food, provided home health care, and ran an ambulance service transporting the sick for medical treatment. According to More Than Me, its ambulance service reduced response times from the local service's four days to 30 minutes, which likely

see PLENARY page 4

Thomas Lhomme for More Than Me

More Than Me Academy founder, Katie Meyler, started a school and ended up fighting Ebola. Hear her story during Tuesday's Plenary Session.

TUESDAY, WEDNESDAY
KEYNOTE SERIES

COPD, GPCR Signaling, ARDS, Asthma

Tuesday's Keynote Series presentations will examine chronic obstructive pulmonary disease (COPD) and G-protein coupled receptor (GPCR) signaling. Presenters on Wednesday will cover biomarkers for precision medicine in asthma and acute respiratory distress syndrome (ARDS). The lectures will be given concurrently from 8 to 8:45 a.m.

TUESDAY

Bartolome R. Celli, MD

The Changing Natural Course of COPD

Moscone Center, Room 134 (North Building, Lower Level)

Bartolome R. Celli, MD, physician at Brigham and Women's Hospital, and professor of medicine at Harvard Medical School, Boston, Massachusetts

Brian K. Kobilka, MD

Structural Insights Into GPCR Signaling: Implications for Drug Discovery

Moscone Center, Room 135 (North Building, Lower Level)

Brian K. Kobilka, MD, Nobel laureate; Helene Irwin Fagan Chair in Cardiology, and professor of chemical and systems biology at the Stanford School of Medicine, California

The Changing Natural Course of COPD (K5) is supported by educational grants from AstraZeneca LP and GlaxoSmith-Kline.

Structural Insights Into GPCR Signaling: Implications for Drug Discovery (K6) is supported by educational grants from AstraZeneca LP, Genentech,

see KEYNOTE page 3

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through innovative research, access,

and education programs.

GILEAD

Q&A: 2016-17 President-Elect David Gozal, MD

An interview with David Gozal, MD, ATS President-Elect

Q: What are your top priorities as President this year?

A: My priorities are twofold.

Support for travel and attendance at the International Conference is on the decline. In response, we're exploring alternative conference models that will better serve neighboring North American countries. This brings ATS engagement to our neighbors' own backyards and should help to diversify revenue.

Implementing new clinical guidelines can be time-consuming and overwhelming. So, we're working to provide better support to Assemblies in creating and updating official statements and position papers. A few ideas to smooth this transition include better resources, such as technology or dedicated staff. Essentially, we would expand the scope of producing guidelines and equip operational facilitators with tools to help them better perform their jobs. If we help strengthen these roles in managing institution-wide implementation, quality improves across the board.

To achieve these goals, teamwork and shared values are integral to our work as members of the ATS Executive Committee, Board of Directors, and staff. Open communication is needed to receive the most insightful feedback on issues. Ongoing dialogue and close collaboration keep parties informed throughout a project, and it is not the work of one but the work of many that leads to a plan's development and success. Moving forward, we have decided to relinquish annual presidential initiatives beginning in 2016. The change should effectively permit the ATS's long-term strategy and enhance sustainability between leadership successions.

Q: How can the Society work to enhance patient-focused care?

A: In the last two decades, the ATS has diligently worked to put patients in the forefront. At the International Conference, this is evident through the patients involved with the Public Advisory Roundtable, from patients who participate to those who present in our Meet-the-Experts Forum. The PAR is vital to public dialogue on health care, and the program gives a voice to the patient through greater patient-provider engagement.

The ATS Patient Information Series covers a wide range of conditions on the website and in ATS Journals. These are an outstanding means of disseminating resources to the public and sister service groups.

Q: How can the ATS provide more academic capital to its members?

A: The majority of our constituency is clinicians, often with dual role appointments in higher education. Academic currency is essential for career development, and the ATS is a conduit. We welcome abstract submissions, presentations, committee participation, and journal involvement from early career professionals. Also encouraged is participation at the international level, through programs such as the Methods in Epidemiological, Clinical, and Operations Research (MECOR) program, Global Scholars, and International Poster Sessions showcasing the work of young investigators.

The next generation has a major stake in the future of the ATS. Those interested in getting involved will be acknowledged, and with greater involvement comes greater ownership.

I look forward to joining forces with our partners and working together to address the challenges of early career professionals. Recruiting the next generation of trainees into the specialty remains one of the field's looming challenges.

Q: How does your international background influence your perspective as the ATS president?

A: The ATS is a global Society representing a large number of international countries and continents. My globetrotter background has opened doors for me to interact with diverse members from our sister societies. In Spanish- or Portuguese-speaking countries, for example, I'm able to give presentations or take questions in both languages. I recently did this for three presentations at the 2016 SOLANEP (Latin American Society of Pediatric Pulmonology) International Congress in Florianopolis, Brazil. I spoke about sleep studies and personalized pediatric medicine. Knowing a foreign language and understanding another culture enriches—and creates for more effective—communication.

Q: How has the ATS changed since you joined as a fellow?

A: We have the potential to radically improve how we practice medicine, and we have new state-of-the-art opportunities to engage with members. We should view the present as a critical time to raise awareness about the misperception of what the ATS stands for—not merely as a place for scientists and researchers that is lacking in its offerings to clinicians, but as a true and all-encompassing home for the breadth of experts in pulmonary, critical care, and sleep medicine.

The ATS has come a long way.

I urge members to make it their mission to engage colleagues, whether through the International Conference or in their local chapters. Share the benefits and impact the ATS has had in your life, especially with nonmember clinicians. ■

KEYNOTE

Continued from page 1

GlaxoSmithKline, Meda Pharmaceuticals, Inc., and Teva Pharmaceuticals.

WEDNESDAY

Serpil C. Erzurum, MD

Biomarkers for Precision Medicine in Asthma

Moscone Center, Room 134 (North Building, Lower Level)

Serpil C. Erzurum, MD, chair of the Department of Pathobiology, joint staff with the Respiratory Institute, and the Alfred Lerner Memorial Chair in Innovative Biomedical Research at the Cleveland Clinic, Ohio

Brian Kavanagh, MD

ARDS: Mechanisms and Professional Societies

Moscone Center, Room 135 (North Building, Lower Level)

Brian Kavanagh, MD, chair of the Department of Anesthesia at the University of Toronto, the Dr. Geoffrey Barker Chair in Critical Care Medicine at the Hospital for Sick Children and the University of Toronto, and research director of the Department of Critical Care Medicine at the Hospital for Sick Children, Toronto, Ontario, Canada

Biomarkers for Precision Medicine in Asthma (K7) is supported by educational grants from AstraZeneca LP, Genentech, GlaxoSmithKline, Meda Pharmaceuticals, Inc., Sanofi US and Regeneron Pharmaceuticals, and Teva Pharmaceuticals. ■

Companies Shine Patient Perspective on Lung Diseases

Three exhibitors will share unique ways in which they endeavor to raise awareness about devastating lung diseases. From the storytelling and artistry of patients, to a documentary film memorializing an actor, to a patient who ran in Bay to Breakers 2016 during the conference, the companies will show how these individuals are not defined by their lung disease diagnoses.

Insmed Inc. in Booth 1741 paired patients with artists from around the world to create a disease awareness initiative, A Thousand Words About NTM (nontuberculous mycobacteria), which they will showcase in its booth. Their stories and words have inspired artists to create one-of-a-kind original artwork. These works of art have helped patients communicate what they've often struggled to put into words—the long, difficult journey to an NTM diagnosis.

Insmed is developing novel, targeted therapies to help serve the critical unmet needs of these patients. This exciting and unique project strives to raise awareness about NTM among physicians and could bring about earlier diagnosis for patients.

ndd Medical Technologies in Booth 2001 is the official pulmonary function testing sponsor working with Julie Nimoy and David Knight to promote COPD: Highly Illogical, a documentary film tribute to Leonard Nimoy, who had chronic obstructive pulmonary disease and died in 2015. The film illustrates the struggles Mr. Nimoy endured before, during, and after his lung disease diagnosis.

As a sponsor, ndd strives to assist in carrying out Mr. Nimoy's vision to spread the word on early diagnosis and management of COPD. Through this documentary, the company hopes to educate patients, caregivers, physicians, and all those touched by the disease.

For more information, visit **copdllap.com** or follow ndd on Twitter **@nddMedical** for updates.

Primary Ciliary Dyskinesia (PCD) Foundation in Booth 1030 will feature Mary Rose Kitlowski, who runs races around the country to raise awareness about PCD, lung diseases, rare diseases, and oxygen needs.

During Bay to Breakers 2016, she wore her portable oxygen concentrator. Ms. Kitlowski currently has a FEV1 of 40 percent and needs supplemental oxygen during strenuous activity.

Will Lewis, MD, Insmed president and CEO, and his company celebrate the artistry of patients from around the world with A Thousand Words About NTM.

She has a goal of participating in races in all 50 states. She has raced in eight states and plans to add five in 2016. Although she raced in California in 2015, she entered the Bay to Breakers 2016 to continue her efforts to raise awareness about lung-related issues and, in conjunction, bring attention to the ATS International Conference.

She and her sister, Rebekah Giannakos, who has PCD and had a double lung transplant in June 2014, are invited patient speakers for the PCD scientific symposium from 9 to 11 a.m. on Tuesday in the Moscone Center, Room 3007/3009 (West Building, Level 3). ■

Discoveries Offer Hope for Patients With PCD

Until recently, primary ciliary dyskinesia (PCD) has received little attention or research funding.

"As a result, delayed diagnosis is the rule, even though signs and symptoms of the disease are usually present right from birth," says Sharon Dell, MD.

An inherited disease, PCD causes impairment of mucociliary clearance. This impairment results in progressive bronchiectasis that may cause end-stage lung disease by adulthood. Dr. Dell is co-chair of a symposium that will highlight new insights into the mechanisms of ciliary assembly defects in PCD, which have come from animal model and human gene discovery studies, and clinical trials that are being conducted around the world.


Sharon Dell, MD

The symposium, "The Link Between Ciliary Assembly Defects, Neonatal Respiratory Distress, and Bronchiectasis in Adulthood: A Primer on Primary Ciliary Dyskinesia," will be presented from 9 to 11 a.m. on Tuesday in the Moscone Center, Room 3007/3009 (West Building, Level 3).

"Multicenter, collaborative research over the past decade has resulted in fascinating scientific discovery, diagnostic improvements, and the start of novel clinical trials for this rare disease. These discoveries provide the potential for a paradigm shift in health outcomes in PCD," says Dr. Dell, staff physician and senior associate scientist at the Hospital for Sick Children, and associate professor of pediatrics, Institute of Health Policy Management and Evaluation, at the University of Toronto, Ontario, Canada.

The symposium will highlight phenotype-genotype relationships in children and adults, emerging genetic testing, new diagnostic tests, airway microbiology, inflammation in PCD, and the impact of disease management strategies on long-term prognosis.

"This scientific symposium comes at an opportune time of scientific discovery," Dr. Dell says. "There is something for everyone to learn, from the neonatal to the adult clinician and from the basic scientist to the epidemiologist."

The program will begin with two young women who will share their experiences about living with PCD and overcoming many of the misunderstandings and devastating health outcomes associated with the disease. ■

PLENARY

Continued from page 1

saved the lives of more than 30,000 people.

"Our mission changed from helping these young girls go to school and making sure they have real choices when they graduate to keeping these children alive," Meyler told TIME.

The TIME editors' selection is based on "who best represents the news of the year," spotlighting leaders who showcase "both a snapshot of where the world is and a picture of where it's going."

On April 30, 2015, More Than Me ended its Ebola programs, and the World Health Organization declared Liberia free of Ebola transmission on May 9, 2015. According to More Than Me, a new case emerged in June 2015, but Liberian authorities acted quickly and the WHO declared Liberia Ebola-free again on Sept. 3, 2015.

The More Than Me Academy reopened on March 2, 2015, and Ms. Meyler is now working with Liberia's Ministry of Education to overhaul the education system.

Today, the More Than Me Academy serves more than 150 children and six Monrovian communities. Ms. Meyler also has been honored as a Forbes 400 Fellow, the 2014 Woman of Excellence by the Ms. JD Global Education Fund, a Nelson Mandela Changemaker by the Nelson Mandela Foundation, the 2015 Best Activist by the Shorty Awards, and an Oprah Ambassador. She also was the 2012 winner of the Chase American Giving Awards. She divides her time between Monrovia and New York, and is an inspirational speaker, performer, and spoken word poet.

The ATS Plenary Session will be from 11:45 a.m. to 1:15 p.m. in the Moscone Center, Room 303/305 (South Building, Esplanade Level). It also will feature the introduction of the ATS slate of officers, an *in memoriam* presentation; remarks from ATS President Atul Malhotra, MD, and ATS President-Elect David Gozal, MD; and presentation of the Outstanding Educator Award to Robert Kotloff, MD, chairman of the Department of Pulmonary Medicine at the Cleveland Clinic, Ohio. ■

ATS Plenary Session
11:45 a.m.-1:15 p.m. today
Moscone Center, Room 303/305
(South Building, Esplanade Level)

COPD National Action Plan

More than 10 million Americans have diagnosed chronic obstructive pulmonary disease and another 10 million are living with undiagnosed COPD, according to estimates from the Centers for Disease Control and Prevention. In response to this growing number and to help fight the impact of the disease, the ATS has developed recommendations for a COPD National Action Plan.

Those recommendations were detailed in a May 6 letter to the National Heart, Lung, and Blood Institute, which is leading a National Institutes of Health effort to develop the Action Plan.

In its letter, the ATS outlined four goals, with recommendations for each goal.

1. **Preventing COPD:** The ATS supports effective regulation of all tobacco products. Regulation should include state and federal excise taxes, FDA regulation of all tobacco products, smoke-free public spaces, prevention of youth access to points-of-sale, bans on candy flavoring and tobacco mechanizing, limits on tobacco advertising, and effective public education campaigns.
2. **Increasing COPD Recognition:** COPD-related questions should remain part of public health surveillance tools for collecting data to better understand the effects of the disease in the U.S. Additional objective assessments of spirometry as part of primary care procedures should be evaluated and considered, and biannual or triannual federal reports should be issued.
3. **Increasing COPD Detection:** A national workshop should be presented to explore opportunities for early COPD detection from low-dose spiral CT scans for lung cancer.
4. **Improving COPD Care:** The ATS itemized these five steps for raising the effectiveness of COPD care.
   - Expand clinical trials on the proper role of pulmonary rehabilitation in the treatment of COPD.
   - Expand education of patients and caregivers to optimize self-management of COPD and develop monitoring tools.
   - Collect better information on the patient experience in ordering, delivery, and use of supplemental oxygen services.
   - Develop quality measures for all aspects of COPD to reduce gaps in treatment.
   - Explore the links between COPD and sleep health.

The plan is expected to be released for public comment in the near future. For updates visit the advocacy pages of the ATS website.

Question of the Day

What Strategies Are You Using to Reduce COPD Readmissions?

"First of all, there is the importance of referring them to smoking cessation clinics. Treatment is focused to reduce exacerbations based on the severity—whether we give a bronchodilator or a bronchodilator with inhaled corticosteroids. We also have them maintain physical activities and have a pneumococcal vaccine."

Amr Suhail Albanna, DO
Jeddah, Saudi Arabia

"In our hospital, we meet as a group on a regular basis and identify those patients coming in frequently, and we discuss what interventions we might be able to use to reduce readmissions. This is a multidisciplinary group involving social workers, nursing staff, and medical staff. We also are using combination therapies."

Colin Wong, DrMED
Dunedin, New Zealand

"We normally begin with the use of bronchodilators, which have been proven to be effective. We start with that as a recommendation, and then, if needed, we add inhaled corticosteroids."

Aikaterini Dimakou, PhD
Athens, Greece

"We emphasize follow-up with the patients, which is important to maintain and then have an improvement of the obstruction. In our facility, we use the combination of LAMA-LABA, and I have had a very nice experience with it. It has reduced readmissions, and patients are quite happy about it."

Evan Mendoza, MD
Cebu City, Philippines

Get More from the ATS Journals

The ATS Journals collectively cover the entire spectrum of adult and pediatric pulmonary, critical care, and sleep medicine—from bench to bedside.

- Researchers appreciate the journals' emphasis on translating basic science discoveries into clinical advances
- Clinicians turn to the journals for the latest clinical guidelines and important reviews of the literature on the diagnosis and treatment of respiratory disease
- More issues feature CME, ABIM, and ABP MOC opportunities
- Renowned editors include Jadwiga A. Wedzicha, MD, the clinical chair in respiratory medicine at Imperial College London, who is now the new Blue Editor

Join the ATS today!

Member benefits include:

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http://www.thoracic.org/membership/join-the-ats.php

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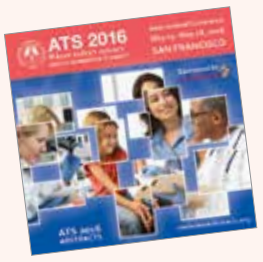

Abstracts on DVD

Pick up your FREE copy at the following locations:

Friday, Saturday, Wednesday
- Best of the ATS Booth, Moscone Center, Lobby (South Building, Upper Level)
- Membership/ATS Center Booth, Moscone Center, Lobby (North Building, Upper Level)

Sunday-Tuesday
- Booth #2303 in the Exhibit Hall

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We have you covered with ePosters. Abstract presenters have been invited to prepare an ePoster of their research. Attendees may view available ePosters by logging in to **https://cms.psav.com/library/ats_eposter_itinerary/login**.

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2016 ATS Assembly Awards

Assembly	Award	2016 Awardees
Allergy, Immunology, and Inflammation	Early Career Achievement Award	Christine M. Freeman, PhD
	Scientific Accomplishment Award	Marc Peters-Golden, MD
Behavioral Science and Health Services Research	Early Career Achievement Award	Michelle Eakin, PhD
	Lifetime Achievement Award	Frederick S. Wamboldt, MD
Clinical Problems	Early Career Achievement Award	Surya P. Bhatt, MD
	Educator Award	Lynn T. Tanoue, MD
	Sreedhar Nair Early Stage Investigator Award in COPD *Funded by a generous donation from the National Emphysema Foundation*	Carlos Martinez, MD
	Sreedhar Nair Lifetime Achievement Award in COPD *Funded by a generous donation from the National Emphysema Foundation*	James D. Crapo, MD
Critical Care	Early Career Achievement Awards	Christopher W. Seymour, MD, MSc
	Lifetime Achievement Award	Jesse B. Hall, MD
Environmental, Occupational, and Population Health	David Bates Award	Mary Rice, MD, MPH
	John Peters Award	John R. Balmes, MD
	Val Vallyathan Award *Funded by a generous donation from the National Emphysema Foundation, honoring Velayudhan "Val" Vallyathan, MD*	Junior Award—Emmanuel Paul, PhD
		Senior Award—Daniel L. Costa, DSc
Microbiology, Tuberculosis, and Pulmonary Infections	Junior Level Award—Early Career Achievement Award	Oriol Sibila, MD, PhD
	Mid Career Award	Scott Evans, MD
	Senior Level Award	Edward A. Nardell, MD
Nursing	Early Career Achievement Award	Nina Elise Bracken, ACNPC, MSN
	Marilyn Hansen Award	Iain Armstrong, RGN
Pediatrics	Pediatric Clinical Educator Award	Sharon D. M. Dell, MD
	Pediatric Founders Award	Carl F. Doershuk, MD
	Robert Mellins Award	Lucas R. Hoffman, MD, PhD
	Scientific Abstract Awards	Douglas Bush, MD
Pulmonary Circulation	Early Career Achievement Award	Vinicio De Jesus Perez, MD
	Robert Grover Prize	Marlene Rabinovitch, MD
	Leadership Award	Timothy M. Moore, MD, PhD
	Jane Morse Award	Charaka Hadinnapola, MB, MRCP
Pulmonary Rehabilitation	Early Career Achievement Award	Frits Franssen, MD, PhD
	Recognition Awards	Americas—Roger S. Goldstein, MD
		Outside the Americas—Anne E. Holland, PhD
		In Memoriam Emeritus or Senior—Karlman Wasserman, MD
Respiratory Cell and Molecular Biology	Carol Basbaum Award	Steven K. Huang, MD
	Jo Rae Wright Award	Benjamin Singer, MD
Respiratory Structure and Function	Stuart J. Hirst Award	Christopher Pascoe, PhD
	Joseph R. Rodarte Award	Andrew J. Halayko, PhD
	Ann Woolcock Memorial Award	Amir A. Zeki, MD
	Lifetime Achievement Award in Honor of Robert A. Crapo, MD	Charles G. Irvin, PhD
Sleep and Respiratory Neurobiology	Sleep Fragments Award	Mudiaga O. Sowho, MD, MPH
	James B. Skatrud New Investigator Award	Bradley Allan Edwards, PhD
Thoracic Oncology	Early Career Achievement Award	Alex Balekian, MD
	Lifetime Achievement Award	Frank C. Detterbeck, MD

Orenitram is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity

FOR PULMONARY ARTERIAL HYPERTENSION

ORENITRAM DOSING ADAPTS

Introduce prostacyclin treatment early with Orenitram, which enables you to adjust dose based on tolerability and clinical response.

The only prostacyclin analogue in a tablet:

For PAH, a **progressive disease**[1-3]

Early use in FC II and III[1]

Ability to **transition from treprostinil** parenteral therapy[1]*

Orenitram allows you to initiate treatment with 0.125 mg TID (~8 hrs apart) or 0.25 mg BID (~12 hrs apart), then titrate up or down every 3 to 4 days as needed per Full Prescribing Information (PI). In the pivotal trial, dose was titrated based on clinical response and tolerability. If not tolerated, titrate slower or decrease dose by 0.25 mg. Avoid abrupt discontinuation. Orenitram tablets should be taken whole and with food. If a dose is missed, please refer to the PI. Orenitram should not be used in patients with moderate hepatic impairment. Dose adjustments required for mild hepatic impairment.

*In a 24-week, multicenter, open-label study to establish safety and tolerability of transition, WHO Group 1 patients (FC I or II) on stable doses of IV/SC treprostinil as well as a PDE-5i and/or ERA were evaluated.

INDICATION

Orenitram is a prostacyclin vasodilator indicated for treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity.

The study that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH (75%) or PAH associated with connective tissue disease (19%). When used as the sole vasodilator, the effect of Orenitram on exercise is about 10% of the deficit, and the effect, if any, on a background of another vasodilator is probably less than this.

IMPORTANT SAFETY INFORMATION FOR ORENITRAM

CONTRAINDICATIONS

- Orenitram is contraindicated in patients with severe hepatic impairment (Child Pugh Class C)

WARNINGS AND PRECAUTIONS

- Abrupt discontinuation or sudden large reductions in dosage of Orenitram may result in worsening of PAH symptoms
- Orenitram inhibits platelet aggregation and increases the risk of bleeding
- The Orenitram tablet shell does not dissolve. In patients with diverticulosis, Orenitram tablets can lodge in a diverticulum

DRUG INTERACTIONS/SPECIFIC POPULATIONS

- Concomitant administration of Orenitram with diuretics, antihypertensive agents, or other vasodilators increases the risk of symptomatic hypotension
- Orenitram inhibits platelet aggregation; there is an increased risk of bleeding, particularly among patients receiving anticoagulants
- Co-administration of Orenitram and the CYP2C8 enzyme inhibitor gemfibrozil increases exposure to treprostinil; therefore, Orenitram dosage reduction may be necessary in these patients
- Pregnancy Category C. Animal reproductive studies with Orenitram have shown an adverse effect on the fetus. There are no adequate and well-controlled studies in humans
- It is not known whether treprostinil is excreted in human milk or absorbed systemically after ingestion. Because many drugs are excreted in human milk, choose Orenitram or breastfeeding
- Safety and effectiveness in patients under 18 years of age have not been established
- There is a marked increase in the systemic exposure to treprostinil in hepatically impaired patients

ADVERSE REACTIONS

- In the 12-week placebo-controlled monotherapy study, adverse reactions that occurred at rates at least 5% higher on Orenitram than on placebo included headache, diarrhea, nausea, flushing, pain in jaw, pain in extremity, hypokalemia, and abdominal discomfort

OREISIhcpJAN16

Please see the Brief Summary of the Full Prescribing Information for Orenitram on the following page.

For additional information about Orenitram, visit www.orenitram.com or call 1-877-UNITHER (1-877-864-8437).

References

1. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corporation; 2016. **2.** Clapp LH, Gurung R. The mechanistic basis of prostacyclin and its stable analogues in pulmonary arterial hypertension: role of membrane versus nuclear receptors. *Prostaglandins Other Lipid Mediat*. 2015;120:56-71. **3.** McLaughlin VV et al. ACCF/AHA 2009 expert consensus on pulmonary hypertension: developed in collaboration with the ACCP, ATS, and the PHA. *Circulation*. 2009;119(16):2250-2290.

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11:30 AM–12:00 PM

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BRIEF SUMMARY

The following is a brief summary of the full prescribing information for Orenitram® (treprostinil) Extended-Release Tablets. Please review the full prescribing information before prescribing Orenitram.

INDICATIONS AND USAGE

Orenitram is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity. The study that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH (75%) or PAH associated with connective tissue disease (19%). When used as the sole vasodilator, the effect of Orenitram on exercise is about 10% of the deficit, and the effect, if any, on a background of another vasodilator is probably less than this.

CONTRAINDICATIONS

Severe hepatic impairment (Child Pugh Class C).

WARNINGS AND PRECAUTIONS

Worsening PAH Symptoms upon Abrupt Withdrawal—Abrupt discontinuation or sudden large reductions in dosage of Orenitram may result in worsening of PAH symptoms.

Risk of Bleeding—Orenitram inhibits platelet aggregation and increases the risk of bleeding.

Use in Patients with Blind-end Pouches—The tablet shell does not dissolve. In patients with diverticulosis, Orenitram tablets can lodge in a diverticulum.

ADVERSE REACTIONS

Clinical Trials Experience—Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. In a 12-week placebo-controlled monotherapy study (Study 1; WHO Group 1; functional class II-III), the most commonly reported adverse reactions that occurred in patients receiving Orenitram included: headache, diarrhea, nausea and flushing. Table 1 lists the adverse reactions that occurred at a rate on Orenitram at least 5% higher than on placebo. Orenitram patients in Table 1 for Study 1 (N = 151) had access to 0.25 mg tablets at randomization. Approximately 91% of such patients experienced an adverse reaction, but only 4% discontinued therapy for an adverse reaction (compared to 3% receiving placebo). The overall discontinuation rate for any reason was 17% for active and 14% for placebo.

Orenitram was studied in a long-term, open-label extension study in which 824 patients were dosed for a mean duration of approximately 2 years. About 70% of patients continued treatment with Orenitram for at least a year. The mean dose was 4.2 mg BID at one year. The adverse reactions were similar to those observed in the placebo-controlled trials.

Table 1. Adverse Reactions with Rates at Least 5% Higher on Orenitram Monotherapy than on Placebo

	Treatment (%)	
Reaction	**Orenitram (N=151)**	**Placebo (N=77)**
Headache	63%	19%
Diarrhea	30%	16%
Nausea	30%	18%
Flushing	15%	6%
Pain in jaw	11%	4%
Pain in extremity	14%	8%
Hypokalemia	9%	3%
Abdominal discomfort	6%	0%

The safety of Orenitram was also evaluated in an open-label study transitioning patients from Remodulin. The safety profile during this study was similar to that observed in the three pivotal studies.

DRUG INTERACTIONS

Antihypertensive Agents or Other Vasodilator—Concomitant administration of Orenitram with diuretics, antihypertensive agents or other vasodilators increases the risk of symptomatic hypotension.

Anticoagulants—Treprostinil inhibits platelet aggregation; there is increased risk of bleeding, particularly among patients receiving anticoagulants.

Effect of CYP2C8 Inhibitors—Co-administration of Orenitram and the CYP2C8 enzyme inhibitor gemfibrozil in healthy adult volunteers increases exposure to treprostinil. Reduce the starting dose of Orenitram to 0.125 mg BID and use 0.125 mg BID increments every 3 to 4 days.

Effect of Other Drugs on Orenitram—Based on human pharmacokinetic studies, no dose adjustment of Orenitram is recommended when coadministered with either fluconazole, rifampin, sildenafil, bosentan, or esomeprazole.

Warfarin—A drug interaction study was carried out with Remodulin co-administered with warfarin (25 mg/day) in healthy volunteers. There was no clinically significant effect of either medication on the pharmacokinetics of treprostinil. Additionally, treprostinil did not affect the pharmacokinetics or pharmacodynamics of warfarin. The pharmacokinetics of R- and S- warfarin and the international normalized ratio (INR) in healthy subjects given a single 25 mg dose of warfarin were unaffected by continuous subcutaneous infusion of treprostinil at an infusion rate of 10 ng/kg/min.

USE IN SPECIFIC POPULATIONS

Pregnancy—*Pregnancy Category C*. Animal reproductive studies with treprostinil diolamine have shown an adverse effect on the fetus. There are no adequate and well-controlled studies in humans.

Labor and Delivery—The effect of Orenitram on labor and delivery in humans is unknown.

No treprostinil treatment related effects on labor and delivery were seen in animal studies.

Nursing Mothers—It is not known whether treprostinil is excreted in human milk or absorbed systemically after ingestion. Because many drugs are excreted in human milk, choose Orenitram or breastfeeding.

Pediatric Use—Safety and effectiveness in pediatric patients have not been established.

Geriatric Use—Clinical studies of Orenitram did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently from younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic or cardiac function, and of concomitant disease or other drug therapy.

Patients with Hepatic Impairment—Plasma clearance of treprostinil is reduced in patients with hepatic insufficiency. Patients with hepatic insufficiency may therefore be at increased risk of dose-dependent adverse reactions because of an increase in systemic exposure. Titrate slowly in patients with hepatic insufficiency, because such patients will likely be exposed to greater systemic concentrations relative to patients with normal hepatic function. In patients with mild hepatic impairment (Child Pugh Class A) start at 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days. Avoid use of Orenitram in patients with moderate hepatic impairment (Child Pugh Class B). Orenitram is contraindicated in patients with severe hepatic impairment (Child Pugh Class C).

Patients with Renal Impairment—No dose adjustments are required in patients with renal impairment. Orenitram is not removed by dialysis.

OVERDOSAGE

Signs and symptoms of overdose with Orenitram during clinical trials reflect its dose-limiting pharmacologic effects and include severe headache, nausea, vomiting, diarrhea, and hypotension. Treat supportively.

United Therapeutics Corporation, Research Triangle Park, NC 27709
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Mythbusters Challenge COPD Therapies

Recent studies are making many researchers re-evaluate long-standing ideas on the development of chronic obstructive pulmonary disease. An ATS mythbusters symposium on Wednesday will examine the emerging theory that the alteration of lung tissue regeneration, not inflammation, plays a driving role in the pathogenesis of COPD.


Renat Shaykhiev, MD, PhD

Presenters will explain how aberrant airway and alveolar regeneration contribute to the pathogenesis of airway remodeling, emphysema, and inflammation in COPD, and how this could be translated into personalized approaches to prevent, diagnose, and treat the disease.

"The goal of this symposium is to facilitate a better understanding of COPD as a complex disease by discussing cutting-edge discoveries in the field. We hope to stimulate innovative ideas based on these discoveries, which could lead to novel approaches to prevent and treat this incurable disease," says Renat Shaykhiev, MD, PhD.

Dr. Shaykhiev is one of the moderators of "ATS Mythbusters: Aberrant Tissue Regeneration Is a Primary Driver of COPD Pathogenesis," which will be presented from 9 to 11 a.m. in the Moscone Center, Room 2016/2018 (West Building, Level 2).

"A long-standing dogma in the field of COPD research has been that lung tissue derangement in this disease develops as a result of an exaggerated inflammatory response of lung cells to cigarette smoke or other environmental stressors," says Dr. Shaykhiev, assistant professor of medicine at Weill Cornell Medical College, New York, New York.

However, anti-inflammatory therapies have not been fully effective in treating patients with COPD. This suggests that other mechanisms may be the driving force of COPD pathogenesis, he says. The results of recent studies link several aspects of lung tissue regeneration to the development of COPD, with endogenous stem cells playing a key role in this process and inflammation taking a secondary role.

"This session will provide an interactive forum where researchers who contributed to the innovative concept will discuss their ideas and data with the audience and a panel of internationally recognized speakers," Dr. Shaykhiev says. "To facilitate a balanced discussion, the list of mythbusters and speakers includes researchers who study various aspects of COPD pathogenesis."

This scientific symposium continues a series of mythbuster sessions presented at previous ATS conferences. It features five presentations and a discussion with renowned researchers.

A related session on the disease is "COPD Exacerbations: Biology and Targets for Novel Treatments," presented from 1:30 to 3:30 p.m. Wednesday in the Moscone Center, Room 134 (North Building, Lower Level).

Six presentations will explain that inflammation is not the only mechanism for COPD exacerbations, the roles of cells and mechanisms in COPD exacerbations, and the role of novel treatments. ■

"COPD Exacerbations: Biology and Targets for Novel Treatments" (D83) is supported by educational grants from AstraZeneca LP and GlaxoSmithKline.

Non-CME Symposia Wrap Up on Tuesday

The ATS encourages attendees to participate in Non-CME Symposia taking place today at various locations.

6:30-9:30 p.m.
SAN FRANCISCO MARRIOTT MARQUIS: GOLDEN GATE BALLROOM A (B2 LEVEL)

Do You Know Your Asthma Patients' Phenotypes?
(open to non-U.S. attendees only)
Chaired by Professor Eric D. Bateman, an internationally renowned faculty will discuss the impact of asthma pathophysiology on approaches to management, barriers to improving control of symptomatic asthma, and the evidence for using anticholinergic bronchodilator therapy for asthma. Attendance at this symposium is for non-U.S. health care professionals only.
Speakers:
- Professor Eric D. Bateman (South Africa) [Chair]
- Professor Christian Taube (the Netherlands)
- Professor Huib Kerstjens (the Netherlands)
- Professor William Busse (United States)

Company: Boehringer Ingelheim Pharma GmbH & Co. KG

6:30-9:30 p.m.
SAN FRANCISCO MARRIOTT MARQUIS: YERBA BUENA BALLROOM 7 (LOWER B2 LEVEL)

Evolving Perspectives in Asthma Heterogeneity: The Role of Eosinophils
This non-CME dinner symposium will explore current and emerging scientific concepts in asthma heterogeneity and the role of eosinophils in uncontrolled asthma.
Speakers:
Bartolome Celli, U.S. (Chair)
Unmet Need in Uncontrolled Asthma and Barriers to Improved Outcomes (~30 mins) Mark FitzGerald (Canada)
Cellular and Molecular Endotypes and Phenotypes in Uncontrolled Asthma (~30 mins) Parameswaran Nair (Canada)
The Biology and Role of Eosinophils in Uncontrolled Asthma (~30 mins) Andrew Menzies-Gow (UK)
Understanding Disease Heterogeneity and the Importance of Biomarkers (~30 mins) Rey Panettieri (U.S.)
Company: AstraZeneca Pharmaceuticals Inc.

6:30-9:30 p.m.
SAN FRANCISCO MARRIOTT MARQUIS: YERBA BUENA BALLROOM 9 (LOWER B2 LEVEL)

Fixed Dose LAMA/LABA Inhalers in COPD: What the Trials Tell Us
Evidence increasingly supports a prominent role for fixed-dose combinations of long-acting muscarinic antagonists and long-acting ß2-agonists (LAMA/LABA) in the management of patients with COPD. This interactive symposium will present the latest efficacy and safety data of new and emerging fixed-dose LAMA/LABA combinations, including application to specific patient case scenarios.
Speaker: Chair: **Richard H. Casaburi, MD, MEng, PhD**
Company: The France Foundation (supported by a grant from Boehringer Ingelheim Pharmaceuticals Inc.)

6:30-9:30 p.m.
SAN FRANCISCO MARRIOTT MARQUIS: GOLDEN GATE BALLROOM B (B2 LEVEL)

Holding Court in PAH
Experience the drama and excitement of Holding Court in PAH, as some of the most challenging treatment issues are argued by leading experts in pulmonary hypertension. With the honorable judge Lewis Rubin, MD presiding, you the jury will deliberate the evidence, then cast your vote for a winner. Register at www.pah.tv.
Speakers: (Chair) **Lewis J. Rubin, MD, APMC**, *Professor of Medicine, Pulmonary and Critical Care Division, Director, PAH Program UC San Diego School of Medicine, San Diego, California. Faculty:* **Richard Channick, MD**, *Director, Pulmonary Hypertension and Thromboendarterectomy Program, Massachusetts General Hospital, Boston, Massachusetts;* **Martha Kingman Liberty, FNP-C, DNP**, *Nurse Practitioner, Pulmonary Services, Heart & Lung Center, UT Southwestern Medical Center, Dallas, Texas;* **Richard A. Krasuski, MD, FACC, FAHA, FESC**, *Professor of Medicine and Pediatrics, Director of the Adult Congenital Heart Disease Center, Director of Hemodynamic Research, Duke University Medical Center, Durham, North Carolina;* **Vallerie McLaughlin, MD**; **Kim A. Eagle, MD**, *Endowed Professor of Cardiovascular Medicine, Dept. of Internal Medicine/Cardiovascular Medicine, University of Michigan, Ann Arbor, Michigan;* **Ioana Preston, MD**, *Associate Professor of Medicine, Pulmonary Function Lab Director,*

Today's Non-CME Symposia offer several presentations from 6:30 to 9:30 p.m. at various area locations.

Director, Pulmonary Hypertension Center, Tufts University School of Medicine, Boston, Massachusetts; **Rajan Saggar, MD**, *Assistant Clinical Professor of Medicine, Pulmonary & Critical Care, Director of the Medical Intensive Care Unit, Heart-Lung Transplant & Pulmonary Hypertension Programs, Ronald Reagan UCLA Medical Center, Los Angeles, California;* **Sean Studer, MD, MSc**, *Chief of Medicine, NYU-Woodhull Medical Center, New York, NY;* **Victor Tapson, MD**, *Professor of Pulmonary and Critical Care Medicine, Cedars-Sinai Medical Center, Los Angeles, California*
Company: PAH.TV (supported by an unrestricted educational grant from Actelion Pharmaceuticals)

6:30-9:30 p.m.
HILTON UNION SQUARE: CONTINENTAL BALLROOM 6 (BALLROOM LEVEL)

IPF Case Discussions: What Have We Learned After 18 Months With Pirfenidone and Nintedanib?

Supported by an independent grant, this highly interactive activity will focus on how the multidisciplinary team works together to manage patients with IPF. Experts will dissect and debate cases that illustrate clinical quandaries not addressed by recent clinical studies. This interactive learning format will enhance the learners' ability to apply knowledge and expert experience to clinical practice. Participants can register for a select few spots to meet in small groups with the faculty, immediately following the symposium, to discuss their own clinical cases.
Speakers: Chair—**Paul W. Noble, MD**, *Chair, Department of Medicine, Director, Women's Guild Lung Institute, Cedars-Sinai Medical Center, Los Angeles, California;* **Alison G. Wilcox, MD, FSCCT**, *Associate Professor of Radiology and Internal Medicine, Section Chief, Cardiothoracic Imaging, Medical Director, Imaging, Keck Hospital of USC, Keck Medical Center of USC, Los Angeles, California;* **Professor Luca Richeldi, MD, PhD**, *Professor of Respiratory Medicine, Chair of Interstitial Lung Disease, University of Southampton, UK*
Company: The France Foundation (supported by grants from Boehringer Ingelheim Pharmaceuticals Inc. and Genentech Inc.)

6:30-9:30 p.m.
HILTON UNION SQUARE: CONTINENTAL BALLROOM 5 (BALLROOM LEVEL)

NTM—A Patient-Centered Approach to Evaluation and Management

Join us for a dinner program that will examine the patient's journey to diagnosis, the current treatment paradigm, and strategies for managing comorbid conditions in patients with nontuberculous mycobacterial (NTM) lung disease. The program will conclude with a question-and-answer session with the expert faculty panel.
Company: Insmed Inc.

6:30-9:30 p.m.
HILTON UNION SQUARE: CONTINENTAL BALLROOM 4 (BALLROOM LEVEL)

The Role of Eosinophils in the Management of Severe Asthma

This complimentary dinner program will provide an overview of the pathogenesis of an unmet need in severe asthma. Information regarding the role of eosinophils and the changing landscape in the management of severe asthma will be reviewed.
Speakers: **Mark S. Forshag, MD**, *MHA, U.S. Medical Affairs Lead, GSK, Research Triangle Park, North Carolina;* **Peter Howarth, MD**, *Global Medical Expert, GSK, Brentford, UK*
Company: GlaxoSmithKline

Exhibit Hall Hours

TODAY
8 a.m.-2:45 p.m.
Unopposed Hours 1:15-2:15 p.m.

ATS Weighs In on Clean Power Lawsuit

An ATS amicus brief cites multiple studies documenting that climate change is having adverse effects on human health.

A battle over climate change is brewing in U.S. courts, and the ATS is fighting for the health of our patients.

The Environmental Protection Agency has finalized regulations—known as the Clean Power Plan—to reduce greenhouse gas carbon pollution emissions from U.S. power plants. Power plants are responsible for one-third of total carbon dioxide emissions in the U.S. The EPA's Clean Power Plan requires each state to develop its own plan to make significant reductions in carbon pollution emissions for power plants. States are expected to achieve these carbon pollution emissions reductions no later than 2030.

The power, coal, and coal-producing states strongly oppose the Clean Power Plan and are suing the EPA in federal court to block implementation of the Clean Power Plan.

The ATS has taken a firm stand that climate change is a direct threat to human health and has organized a coalition of medical organizations to submit an amicus brief—or "friend of court" petition—in the case to explain to the court why climate change is such a serious health threat to our patients.

The Society's amicus brief cites multiple studies documenting that climate change is having adverse effects on human health, including:

- Climate-driven heat waves cause excess morbidity and mortality.
- Rising temperatures that can lead to increased ozone pollution, resulting in longer and more intense pollen seasons.
- Climate-forced droughts leading to forest fires, causing injury and illness and reducing air quality

In a recent ATS survey of its U.S. members, a majority of respondents concurred that climate change is occurring, it is having a direct impact on the health of their patients, these impacts are particularly harmful for children, and even greater climate-driven adverse human health impacts are anticipated. Other medical society surveys have had similar results.

The ATS is joined in the amicus brief by the American Academy of Pediatrics, American College of Occupational and Environmental Medicine, American College of Preventive Medicine, American Medical Association, American Public Health Association, National Medical Association, and National Association for the Medical Direction of Respiratory Care. ■

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* post-operative pulmonary complications

1. Restrepo, et al. Expert Review Respiratory Medicine, 2014.
2. Klein K, et al. Impact of Early Mobilization on Mechanical Ventilation and Cost in Neurological ICU. Neurocrit Care; Oct, 2015.

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Managing IPF With Personalized Treatment

Great progress has been made in the treatment of patients with idiopathic pulmonary fibrosis, but the use of molecular markers to implement precision medicine could revolutionize treatment in the near future.


Richard Marshall, MD, PhD

"We need to understand for a given patient at a given stage of disease what core biological mechanisms are driving their disease, so we can identify the best treatment and optimize the risks and benefits," says Richard Marshall, MD, PhD, one of the moderators for "The Road to Precision Medicine in IPF: Biomarkers and Clinical Predictors."

Seven presenters will explain the role of molecular markers, the potential value of lung and bronchoalveolar lavage molecular analyses in diagnosis and management, and new findings on the clinical management of patients with IPF.

The session will be presented from 1:30 to 3:30 p.m. Wednesday in the Moscone Center, Room 135 (North Building, Lower Level).

Those advances will build on the use of two new medicines—pirfenidone and nintedanib—that have been approved for treatment of patients with IPF.

"With the recent arrival of these two medicines, plus the promise of more to come, not surprisingly the respiratory community's attention is turning to personalization," says Dr. Marshall, vice president of respiratory, GlaxoSmithKline, United Kingdom.

A great amount of information has been collected about the use of molecular markers, and speakers in the interactive session will use social media and dynamic interaction to discuss the potential for clinical application.

"There is a good opportunity to identify biomarkers in blood, urine, or lung samples, with a number of very plausible candidate markers already having been identified," Dr. Marshall says. "Attendees will hear a lot more about these at the session, as well as about collaborative efforts to further identify and refine the best biomarkers to use. I think we should be optimistic that they are out there, which is good news for patients."

"The Road to Precision Medicine in IPF: Biomarkers and Clinical Predictors" (D82) is supported by an educational grant from Boehringer Ingelheim Pharmaceuticals, Inc., and Genentech.

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Stem Cells: Unveiling Their Promise for Lung Diseases

The use of stem cells to prevent and treat human diseases has led to unprecedented growth in regenerative medicine. Increasing evidence has shown that an individual's own cells have the potential for development of stem cell-based therapeutic approaches.

Tuesday's scientific symposium on "Progress in Stem Cell Biology and Disease Applications" will provide a basic scientific, clinical rationale, and current state-of-the-art in this rapidly developing area.

The presenters, who are accomplished stem cell investigators from outside the respiratory field, will bring knowledge and perspective to help guide future developments in lung regenerative medicine. The four presentations and their speakers are:

- "Normal and Neoplastic Stem Cells"—Irving Weissman, MD, the Virginia and D.K. Ludwig Professor for Clinical Investigation in Cancer Research, professor of developmental biology, professor of pathology, and professor of developmental biology at Stanford University, California
- "Imaging Cancer Heterogeneity and Therapy Resistance in Real Time"—Tannishtha Reya, PhD, professor of pharmacology and medicine at the University of California, San Diego, in La Jolla
- "Interspecific Blastocyst Complementation: A Novel Approach to Generate Functional Organs Speaker"—Tamir Rashid, MD, King's College, London, UK
- "Defining the Lung Cell By Cell"—Mark Krasnow, PhD, professor of biochemistry and executive director of the Wall Center for Pulmonary Vascular Disease at Stanford University, California

The symposium co-chairs are Daniel Weiss, MD, PhD, professor of medicine at the University of Vermont, Burlington, and Darrell N. Kotton, MD, professor of medicine and pathology and director of the Center for Regenerative Medicine at Boston University, Massachusetts.

Clinicians, basic science researchers, and other lung health care professionals looking to learn about developments in stem cell biology and their applications to respiratory diseases and critical illnesses are encouraged to attend the symposium. It will be from 9 to 11 a.m Tuesday in the Moscone Center, Room 2016/2017 (West Building, Level 2). ■

Burden of Respiratory Disease on Migrants

The crisis in the Middle East has raised awareness about the challenges encountered by migrant populations, especially their access to health care. Migrant populations around the world, including those from Mexico and Latin America entering the United States, face similar challenges.

"War, economics, and geopolitical factors have forced hundreds of thousands away from their lands and families into countries that are often unprepared to care for their needs," says Jesse Roman, MD. "The ATS and its Health Equality Subcommittee are concerned about the respiratory health of these populations. They are likely to suffer from tobacco-related disorders, asthma, pulmonary infections, sleep-disordered breathing, and critical care illnesses."


Jesse Roman, MD

Dr. Roman and three other physicians are leading "Respiratory Health in Migrant Populations," which will raise awareness about health care access and delivery in migrant populations. The symposium will be from 1:30 to 3:30 p.m. Wednesday in the Moscone Center, Room 2009/2011 (West Building, Level 2).

"The burden of respiratory disease in migrants is essentially unknown, and appropriate models for delivering health care to these populations have yet to be implemented and tested. The speakers will address the burden of respiratory disease in these populations and the problems encountered in their care," says Dr. Roman, professor and chair of medicine, professor of pharmacology and toxicology, and chief of the Division of Pulmonary, Critical Care, and Sleep Disorders Medicine at the University of Louisville, Kentucky.

The symposium will address the health inequality in Latinos crossing the border, the impact of asthma and sleep-disordered breathing, and infectious diseases in refugee populations and survivors of torture. It also will highlight the use of tele-health in pulmonary and critical care settings in Syria.

"Considering the widespread nature of this problem, we are hopeful audience members will return to their workplaces equipped with new knowledge, enabling them to identify problems and tackle them adequately," Dr. Roman says. "Importantly, we hope to raise enthusiasm among trainees interested in devoting their efforts—and perhaps their careers—to these important issues." ■

24-hour BREO—Approved for Asthma

For adult patients with asthma uncontrolled on an ICS or whose disease severity clearly warrants an ICS/LABA. BREO is NOT indicated for the relief of acute bronchospasm.

Important Safety Information

WARNING: ASTHMA-RELATED DEATH

- **Long-acting beta$_2$-adrenergic agonists (LABA), such as vilanterol, one of the active ingredients in BREO, increase the risk of asthma-related death. A placebo-controlled trial with another LABA (salmeterol) showed an increase in asthma-related deaths. This finding with salmeterol is considered a class effect of all LABA. Currently available data are inadequate to determine whether concurrent use of inhaled corticosteroids (ICS) or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA. Available data from controlled clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients.**
- **When treating patients with asthma, only prescribe BREO for patients not adequately controlled on a long-term asthma control medication, such as an ICS, or whose disease severity clearly warrants initiation of treatment with both an ICS and a LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (e.g., discontinue BREO) if possible without loss of asthma control and maintain the patient on a long-term asthma control medication, such as an ICS. Do not use BREO for patients whose asthma is adequately controlled on low- or medium-dose ICS.**

CONTRAINDICATIONS

- BREO is contraindicated for primary treatment of status asthmaticus or other acute episodes of chronic obstructive pulmonary disease (COPD) or asthma where intensive measures are required.
- BREO is contraindicated in patients with severe hypersensitivity to milk proteins or demonstrated hypersensitivity to fluticasone furoate, vilanterol, or any of the excipients.

WARNINGS AND PRECAUTIONS

- BREO should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD or asthma.
- BREO should not be used for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. Acute symptoms should be treated with an inhaled, short-acting beta$_2$-agonist.
- BREO should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medicines containing LABA, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs. Patients using BREO should not use another medicine containing a LABA (e.g., salmeterol, formoterol fumarate, arformoterol tartrate, indacaterol) for any reason.
- Oropharyngeal candidiasis has occurred in patients treated with BREO. Advise patients to rinse the mouth with water without swallowing following inhalation to help reduce the risk of oropharyngeal candidiasis.
- Patients who use corticosteroids are at risk for potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex. A more serious or even fatal course of chickenpox or measles may occur in susceptible patients. Use caution in patients with the above because of the potential for worsening of these infections.
- Particular care is needed for patients who have been transferred from systemically active corticosteroids to inhaled corticosteroids because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids. Taper patients slowly from systemic corticosteroids if transferring to BREO.
- Hypercorticism and adrenal suppression may occur with very high dosages or at the regular dosage of inhaled corticosteroids in susceptible individuals. If such changes occur, discontinue BREO slowly.

WARNINGS AND PRECAUTIONS (cont'd)

- Caution should be exercised when considering the coadministration of BREO with long-term ketoconazole and other known strong CYP3A4 inhibitors (e.g., ritonavir, clarithromycin, conivaptan, indinavir, itraconazole, lopinavir, nefazodone, nelfinavir, saquinavir, telithromycin, troleandomycin, voriconazole) because increased systemic corticosteroid and cardiovascular adverse effects may occur.
- If paradoxical bronchospasm occurs, discontinue BREO immediately and institute alternative therapy.
- Hypersensitivity reactions such as anaphylaxis, angioedema, rash, and urticaria may occur after administration of BREO. Discontinue BREO if such reactions occur.
- Vilanterol can produce clinically significant cardiovascular effects in some patients as measured by increases in pulse rate, systolic or diastolic blood pressure, and also cardiac arrhythmias, such as supraventricular tachycardia and extrasystoles. If such effects occur, BREO may need to be discontinued. BREO should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.
- Decreases in bone mineral density (BMD) have been observed with long-term administration of products containing inhaled corticosteroids. Patients with major risk factors for decreased bone mineral content, such as prolonged immobilization, family history of osteoporosis, postmenopausal status, tobacco use, advanced age, poor nutrition, or chronic use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids) should be monitored and treated with established standards of care.
- Glaucoma, increased intraocular pressure, and cataracts have been reported in patients with COPD or asthma following the long-term administration of inhaled corticosteroids. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma, and/or cataracts.
- Use with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, ketoacidosis, and in patients who are unusually responsive to sympathomimetic amines.
- Be alert to hypokalemia and hyperglycemia.
- Orally inhaled corticosteroids may cause a reduction in growth velocity when administered to children and adolescents.

ADVERSE REACTIONS

- In a 12-week trial, adverse reactions (≥2% incidence and more common than placebo) reported in subjects taking BREO 100/25 (and placebo) were: nasopharyngitis, 10% (7%); headache, 5% (4%); oropharyngeal pain, 2% (1%); oral candidiasis, 2% (0%); and dysphonia, 2% (0%). In a separate 12-week trial, adverse reactions (≥2% incidence) reported in subjects taking BREO 200/25 (or BREO 100/25) were: headache, 8% (8%); nasopharyngitis, 7% (6%); influenza, 3% (3%); upper respiratory tract infection, 2% (2%); oropharyngeal pain, 2% (2%); sinusitis, 2% (1%); bronchitis, 2% (<1%); and cough, 1% (2%).
- In addition to the adverse reactions reported in the two 12-week trials, adverse reactions (≥2% incidence) reported in subjects taking BREO 200/25 once daily in a 24-week trial included viral respiratory tract infection, pharyngitis, pyrexia, and arthralgia, and with BREO 100/25 or 200/25 in a 12-month trial included pyrexia, back pain, extrasystoles, upper abdominal pain, respiratory tract infection, allergic rhinitis, pharyngitis, rhinitis, arthralgia, supraventricular extrasystoles, ventricular extrasystoles, acute sinusitis, and pneumonia.
- In a 24- to 76-week trial of subjects with a history of 1 or more asthma exacerbations within the previous 12 months, asthma-related hospitalizations occurred in 1% of subjects treated with BREO 100/25. There were no asthma-related deaths or asthma-related intubations observed in this trial.

DRUG INTERACTIONS

- Caution should be exercised when considering the coadministration of BREO with long-term ketoconazole and other known strong CYP3A4 inhibitors (e.g., ritonavir, clarithromycin, conivaptan, indinavir, itraconazole, lopinavir, nefazodone, nelfinavir, saquinavir, telithromycin, troleandomycin, voriconazole) because increased systemic corticosteroid and cardiovascular adverse effects may occur.
- BREO should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QTc interval, or within 2 weeks of discontinuation of such agents, because the effect of adrenergic agonists, such as vilanterol, on the cardiovascular system may be potentiated by these agents.

gsk

BREO ELLIPTA was developed in collaboration with Theravance

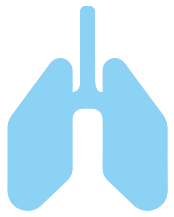
Reach With Confidence

In patients uncontrolled on an ICS alone, BREO has been proven to:

Deliver 24-hour lung function improvement

with one inhalation, once daily*

Reduce asthma exacerbations



in patients with a history of exacerbations†

Increase days without asthma symptoms

and increase days without use of rescue medication‡

Important Safety Information (cont'd)

DRUG INTERACTIONS (cont'd)

- Use beta-blockers with caution as they not only block the pulmonary effect of beta-agonists, such as vilanterol, but may also produce severe bronchospasm in patients with COPD or asthma.
- Use with caution in patients taking non–potassium-sparing diuretics, as electrocardiographic changes and/or hypokalemia associated with non–potassium-sparing diuretics may worsen with concomitant beta-agonists.

USE IN SPECIFIC POPULATIONS

- BREO is not indicated for use in children and adolescents. The safety and efficacy in pediatric patients (aged 17 years and younger) have not been established.
- Use BREO with caution in patients with moderate or severe hepatic impairment. Fluticasone furoate systemic exposure increased by up to 3-fold in subjects with hepatic impairment. Monitor for corticosteroid-related side effects.

Please see Brief Summary of Prescribing Information, including Boxed Warning, for BREO on the following pages.

Supporting Clinical Study Information

*In a randomized, double-blind (RDB) study of 1039 patients§ symptomatic on a mid- to high-dose ICS, BREO 100/25 once daily (n=312) demonstrated a 108 mL improvement from baseline in weighted mean (wm) FEV_1 (0-24 hours) at the end of the 12-week treatment period vs fluticasone furoate (FF) 100 mcg once daily (n=288) ($P<0.001$).[1] (In an RDB, placebo-controlled study of 609 patients§ symptomatic on a low- to mid-dose ICS, in a subset of patients, BREO 100/25 once daily [n=108] demonstrated a change from baseline in wm FEV_1 [0-24 hours] at the end of the 12-week treatment period vs FF 100 mcg once daily [n=106] of 116 mL [95% CI: –5, 236; $P=0.06$].[2])

†In a 24- to 76-week RDB study of 2019 patients§ with ≥1 exacerbations in the prior year, BREO 100/25 once daily (n=1009) reduced the risk of experiencing an exacerbation by 20% (Hazard Ratio=0.795, $P=0.036$) vs FF 100 mcg once daily (n=1010).[3] An exacerbation was defined as a deterioration of asthma requiring the use of systemic corticosteroids (SCS) for ≥3 days or an in-patient hospitalization or emergency department visit due to asthma that required SCS.

‡In an RDB study of 1039 patients§ symptomatic on a mid- to high-dose ICS, BREO 100/25 once daily (n=345) provided an increase from baseline in the % of rescue-free and the % of symptom-free 24-hour periods during the 12-week treatment period of 12.2% and 7.8%, respectively ($P\leq0.002$), vs FF 100 mcg once daily (n=346).[1]

§Studies included patients with asthma ≥12 years of age; BREO is only approved for use in patients ≥18 years of age.

References: 1. Bernstein DI et al. *J Asthma.* 2015. doi:10.3109/02770903.2015.1056350. **2.** Bleecker ER et al. *J Allergy Clin Immunol Pract.* 2014;2(5):553-561. **3.** Bateman ED et al. *Thorax.* 2014;69(4):312-319.

Visit BREOhcp.com for more information, including Patient Assistance Programs.

BREO® ELLIPTA®
(fluticasone furoate 100 mcg and vilanterol 25 mcg inhalation powder)

BRIEF SUMMARY

BREO® ELLIPTA® 100/25 (fluticasone furoate 100 mcg and vilanterol 25 mcg inhalation powder), for oral inhalation
BREO® ELLIPTA® 200/25 (fluticasone furoate 200 mcg and vilanterol 25 mcg inhalation powder), for oral inhalation

The following is a brief summary only and is focused on the asthma indication. See full prescribing information for complete product information.

WARNING: ASTHMA-RELATED DEATH

Long-acting beta$_2$-adrenergic agonists (LABA), such as vilanterol, one of the active ingredients in BREO, increase the risk of asthma-related death. Data from a large placebo-controlled US trial that compared the safety of another LABA (salmeterol) with placebo added to usual asthma therapy showed an increase in asthma-related deaths in subjects receiving salmeterol. This finding with salmeterol is considered a class effect of LABA. Currently available data are inadequate to determine whether concurrent use of inhaled corticosteroids (ICS) or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA. Available data from controlled clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients.

Therefore, when treating patients with asthma, physicians should only prescribe BREO for patients not adequately controlled on a long-term asthma control medication, such as an ICS, or whose disease severity clearly warrants initiation of treatment with both an ICS and a LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (e.g., discontinue BREO) if possible without loss of asthma control and maintain the patient on a long-term asthma control medication, such as an ICS. Do not use BREO for patients whose asthma is adequately controlled on low- or medium-dose ICS *[see Warnings and Precautions (5.1)]*.

1 INDICATIONS AND USAGE

1.2 Treatment of Asthma BREO is a combination ICS/LABA indicated for the once-daily treatment of asthma in patients aged 18 years and older. LABA, such as vilanterol, one of the active ingredients in BREO, increase the risk of asthma-related death. Available data from controlled clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients *[see Warnings and Precautions (5.1), Adverse Reactions (6.2), Use in Specific Populations (8.4)]*. Therefore, when treating patients with asthma, physicians should only prescribe BREO for patients not adequately controlled on a long-term asthma control medication, such as an ICS, or whose disease severity clearly warrants initiation of treatment with both an ICS and a LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (e.g., discontinue BREO) if possible without loss of asthma control and maintain the patient on a long-term asthma control medication, such as an ICS. Do not use BREO for patients whose asthma is adequately controlled on low- or medium-dose ICS.
Important Limitation of Use: BREO is NOT indicated for the relief of acute bronchospasm.

4 CONTRAINDICATIONS

The use of BREO is contraindicated in the following conditions: Primary treatment of status asthmaticus or other acute episodes of COPD or asthma where intensive measures are required *[see Warnings and Precautions (5.2)]*; Severe hypersensitivity to milk proteins or demonstrated hypersensitivity to fluticasone furoate, vilanterol, or any of the excipients *[see Warnings and Precautions (5.11), Description (11) of full prescribing information]*.

5 WARNINGS AND PRECAUTIONS

5.1 Asthma-Related Death LABA, such as vilanterol, one of the active ingredients in BREO, increase the risk of asthma-related death. Currently available data are inadequate to determine whether concurrent use of ICS or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA. Available data from controlled clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients. Therefore, when treating patients with asthma, physicians should only prescribe BREO for patients not adequately controlled on a long-term asthma control medication, such as an ICS, or whose disease severity clearly warrants initiation of treatment with both an ICS and a LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (e.g., discontinue BREO) if possible without loss of asthma control and maintain the patient on a long-term asthma control medication, such as an ICS. Do not use BREO for patients whose asthma is adequately controlled on low- or medium-dose ICS.
A 28-week, placebo-controlled, US trial that compared the safety of another LABA (salmeterol) with placebo, each added to usual asthma therapy, showed an increase in asthma-related deaths in subjects receiving salmeterol (13/13,176 in subjects treated with salmeterol vs. 3/13,179 in subjects treated with placebo; relative risk: 4.37 [95% CI: 1.25, 15.34]). The increased risk of asthma-related death is considered a class effect of LABA, including vilanterol, one of the active ingredients in BREO. No trial adequate to determine whether the rate of asthma-related death is increased in subjects treated with BREO has been conducted.
5.2 Deterioration of Disease and Acute Episodes BREO should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD or asthma. BREO has not been studied in subjects with acutely deteriorating COPD or asthma. The initiation of BREO in this setting is not appropriate. Increasing use of inhaled, short-acting beta$_2$-agonists is a marker of deteriorating asthma. In this situation, the patient requires immediate reevaluation with reassessment of the treatment regimen, giving special consideration to the possible need for replacing the current strength of BREO with a higher strength, adding additional ICS, or initiating systemic corticosteroids. Patients should not use more than 1 inhalation once daily of BREO. BREO should not be used for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. BREO has not been studied in the relief of acute symptoms and extra doses should not be used for that purpose. Acute symptoms should be treated with an inhaled, short-acting beta$_2$-agonist. When beginning treatment with BREO, patients who have been taking oral or inhaled, short-acting beta$_2$-agonists on a regular basis (e.g., 4 times a day) should be instructed to discontinue the regular use of these drugs and to use them only for symptomatic relief of acute respiratory symptoms. When prescribing BREO, the healthcare provider should also prescribe an inhaled, short-acting beta$_2$-agonist and instruct the patient on how it should be used.
5.3 Excessive Use of BREO and Use with Other Long-Acting Beta$_2$-Agonists BREO should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medicines containing LABA, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs. Patients using BREO should not use another medicine containing a LABA (e.g., salmeterol, formoterol fumarate, arformoterol tartrate, indacaterol) for any reason.
5.4 Local Effects of ICS In clinical trials, the development of localized infections of the mouth and pharynx with *Candida albicans* has occurred in subjects treated with BREO. When such an infection develops, it should be treated with appropriate local or systemic (i.e., oral) antifungal therapy while treatment with BREO continues, but at times therapy with BREO may need to be interrupted. Advise the patient to rinse his/her mouth with water without swallowing following inhalation to help reduce the risk of oropharyngeal candidiasis.
5.6 Immunosuppression Persons who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in susceptible children or adults using corticosteroids. In such children or adults who have not had these diseases or been properly immunized, particular care should be taken to avoid exposure. How the dose, route, and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If a patient is exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If a patient is exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered. ICS should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract; systemic fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex.
5.7 Transferring Patients from Systemic Corticosteroid Therapy Particular care is needed for patients who have been transferred from systemically active corticosteroids to ICS because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer from systemic corticosteroids to less systemically available ICS. After withdrawal from systemic corticosteroids, a number of months are required for recovery of hypothalamic-pituitary-adrenal (HPA) function. Patients who have been previously maintained on 20 mg or more of prednisone (or its equivalent) may be most susceptible, particularly when their systemic corticosteroids have been almost completely withdrawn. During this period of HPA suppression, patients may exhibit signs and symptoms of adrenal insufficiency when exposed to trauma, surgery, or infection (particularly gastroenteritis) or other conditions associated with severe electrolyte loss. Although BREO may control COPD or asthma symptoms during these episodes, in recommended doses it supplies less than normal physiological amounts of glucocorticoid systemically and does NOT provide the mineralocorticoid activity that is necessary for coping with these emergencies. During periods of stress, a severe COPD exacerbation, or a severe asthma attack, patients who have been withdrawn from systemic corticosteroids should be instructed to resume oral corticosteroids (in large doses) immediately and to contact their physicians for further instruction. These patients should also be instructed to carry a warning card indicating that they may need supplementary systemic corticosteroids during periods of stress, a severe COPD exacerbation, or a severe asthma attack. Patients requiring oral corticosteroids should be weaned slowly from systemic corticosteroid use after transferring to BREO. Prednisone reduction can be accomplished by reducing the daily prednisone dose by 2.5 mg on a weekly basis during therapy with BREO. Lung function (FEV_1 or peak expiratory flow), beta-agonist use, and COPD or asthma symptoms should be carefully monitored during withdrawal of oral corticosteroids. In addition, patients should be observed for signs and symptoms of adrenal insufficiency, such as fatigue, lassitude, weakness, nausea and vomiting, and hypotension. Transfer of patients from systemic corticosteroid therapy to BREO may unmask allergic conditions previously suppressed by the systemic corticosteroid therapy (e.g., rhinitis, conjunctivitis, eczema, arthritis, eosinophilic conditions). During withdrawal from oral corticosteroids, some patients may experience symptoms of systemically active corticosteroid withdrawal (e.g., joint and/or muscular pain, lassitude, depression) despite maintenance or even improvement of respiratory function.
5.8 Hypercorticism and Adrenal Suppression Inhaled fluticasone furoate is absorbed into the circulation and can be systemically active. Effects of fluticasone furoate on the HPA axis are not observed with the therapeutic doses of BREO. However, exceeding the recommended dosage or coadministration with a strong cytochrome P450 3A4 (CYP3A4) inhibitor may result in HPA dysfunction *[see Warnings and Precautions (5.9), Drug Interactions (7.1)]*. Because of the possibility of significant systemic absorption of ICS in sensitive patients, patients treated with BREO should be observed carefully for any evidence of systemic corticosteroid effects. Particular care should be taken in observing patients postoperatively or during periods of stress for evidence of inadequate adrenal response. It is possible that systemic corticosteroid effects such as hypercorticism and adrenal suppression (including adrenal crisis) may appear in a small number of patients who are sensitive to these effects. If such effects occur, BREO should be reduced slowly, consistent with accepted procedures for reducing systemic corticosteroids, and other treatments for management of COPD or asthma symptoms should be considered.
5.9 Drug Interactions with Strong Cytochrome P450 3A4 Inhibitors Caution should be exercised when considering the coadministration of BREO with long-term ketoconazole and other known strong CYP3A4 inhibitors (e.g., ritonavir, clarithromycin, conivaptan, indinavir, itraconazole, lopinavir, nefazodone, nelfinavir, saquinavir, telithromycin, troleandomycin, voriconazole) because increased systemic corticosteroid and increased cardiovascular adverse effects may occur *[see Drug Interactions (7.1), Clinical Pharmacology (12.3) of full prescribing information]*.
5.10 Paradoxical Bronchospasm As with other inhaled medicines, BREO can produce paradoxical bronchospasm, which may be life threatening. If paradoxical bronchospasm occurs following dosing with BREO, it should be treated immediately with an inhaled, short-acting bronchodilator; BREO should be discontinued immediately; and alternative therapy should be instituted.
5.11 Hypersensitivity Reactions, Including Anaphylaxis Hypersensitivity reactions such as anaphylaxis, angioedema, rash, and urticaria may occur after administration of BREO. Discontinue BREO if such reactions occur. There have been reports of anaphylactic reactions in patients with severe milk protein allergy after inhalation of other powder medications containing lactose; therefore, patients with severe milk protein allergy should not use BREO *[see Contraindications (4)]*.
5.12 Cardiovascular Effects Vilanterol, like other beta$_2$-agonists, can produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, systolic or diastolic blood pressure, and also cardiac arrhythmias, such as supraventricular tachycardia and extrasystoles. If such effects occur, BREO may need to be discontinued. In addition, beta-agonists have been reported to produce electrocardiographic changes, such as flattening of the T wave, prolongation of the QTc interval, and ST segment depression, although the clinical significance of these findings is unknown. Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs. In healthy subjects, large doses of inhaled fluticasone furoate/vilanterol (4 times the recommended dose of vilanterol, representing a 12- or 10-fold higher systemic exposure than seen in subjects with COPD or asthma, respectively) have been associated with clinically significant prolongation of the QTc interval, which has the potential for producing ventricular arrhythmias. Therefore, BREO, like other sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.
5.13 Reduction in Bone Mineral Density Decreases in bone mineral density (BMD) have been observed with long-term administration of products containing ICS. The clinical significance of small changes in BMD with regard to long-term consequences such as fracture is unknown. Patients with major risk factors for decreased bone mineral content, such as prolonged immobilization, family history of osteoporosis, postmenopausal status, tobacco use, advanced age, poor nutrition, or chronic use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids) should be monitored and treated with established standards of care.
5.14 Glaucoma and Cataracts Glaucoma, increased intraocular pressure, and cataracts have been reported in patients with COPD or asthma following the long-term administration of ICS. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma, and/or cataracts.
5.15 Coexisting Conditions BREO, like all medicines containing sympathomimetic amines, should be used with caution in patients with convulsive disorders or thyrotoxicosis and in those who are unusually responsive to sympathomimetic amines. Doses of the related beta$_2$-adrenoceptor agonist albuterol, when administered intravenously, have been reported to aggravate preexisting diabetes mellitus and ketoacidosis.
5.16 Hypokalemia and Hyperglycemia Beta-adrenergic agonist medicines may produce significant hypokalemia in some patients, possibly through intracellular shunting, which has the potential to produce adverse cardiovascular effects. The decrease in serum potassium is usually transient, not requiring supplementation. Beta-agonist medications may produce transient hyperglycemia in some patients. In clinical trials evaluating BREO in subjects with COPD or asthma, there was no evidence of a treatment effect on serum glucose or potassium.
5.17 Effect on Growth Orally inhaled corticosteroids may cause a reduction in growth velocity when administered to children and adolescents. *[See Use in Specific Populations (8.4) of full prescribing information.]*

6 ADVERSE REACTIONS

LABA, such as vilanterol, one of the active ingredients in BREO, increase the risk of asthma-related death. Currently available data are inadequate to determine whether concurrent use of ICS or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA. Available data from controlled clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients. Data from a large placebo-controlled US trial that compared the safety of another LABA (salmeterol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in subjects receiving salmeterol. *[See Warnings and Precautions (5.1).]* Systemic and local corticosteroid use may result in the following: *Candida albicans* infection *[see Warnings and Precautions (5.4)]*; Immunosuppression *[see Warnings and Precautions (5.6)]*; Hypercorticism and adrenal suppression *[see Warnings and Precautions (5.8)]*; Reduction in bone mineral density *[see Warnings and Precautions (5.13)]*. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.
6.2 Clinical Trials Experience in Asthma BREO for the treatment of asthma was studied in 18 double-blind, parallel-group, controlled trials (11 with placebo) of 4 to 76 weeks' duration, which enrolled 9,969 subjects with asthma. BREO 100/25 was studied in 2,369 subjects and BREO 200/25 was studied in 956 subjects. While subjects aged 12 to 17 years were included in these trials, BREO is not approved for use in this age-group *[see Use in Specific Populations (8.4)]*. The safety data described below are based on two 12-week efficacy trials, one 24-week efficacy trial, and two long-term trials.
12-Week Trials Trial 1 was a 12-week trial that evaluated the efficacy of BREO 100/25 in adolescent and adult subjects with asthma compared with fluticasone furoate 100 mcg and placebo. Of the 609 subjects, 58% were female and 84% were white; the mean age was 40 years.
In Trial 1, adverse reactions (≥2% incidence and more common than placebo) reported in subjects with asthma taking BREO 100/25 (n=201) (fluticasone furoate 100 mcg [n=205] or placebo [n=203]) were: nasopharyngitis,

10% (7%, 7%); headache, 5% (4%, 4%); oropharyngeal pain, 2% (2%, 1%); oral candidiasis, 2% (2%, 0%); and dysphonia, 2% (1%, 0%). Oral candidiasis includes oral candidiasis and oropharyngeal candidiasis.
Trial 2 was a 12-week trial that evaluated the efficacy of BREO 100/25, BREO 200/25, and fluticasone furoate 100 mcg in adolescent and adult subjects with asthma. This trial did not have a placebo arm. Of the 1,039 subjects, 60% were female and 88% were white; the mean age was 46 years.
In Trial 2, adverse reactions (≥2% incidence) reported in subjects with asthma taking BREO 200/25 (n=346) (BREO 100/25 [n=346] or fluticasone furoate 100 mcg [n=347]) were: headache, 8% (8%, 9%); nasopharyngitis, 7% (6%, 7%); influenza, 3% (3%, 1%); upper respiratory tract infection, 2% (2%, 3%); oropharyngeal pain, 2% (2%, 1%); sinusitis, 2% (1%, <1%); bronchitis, 2% (<1%, 2%); and cough, 1% (2%, 1%).
24-Week Trial Trial 3 was a 24-week trial that evaluated the efficacy of BREO 200/25 once daily, fluticasone furoate 200 mcg once daily, and fluticasone propionate 500 mcg twice daily in adolescent and adult subjects with asthma. Of the 586 subjects, 59% were female and 84% were white; the mean age was 46 years. This trial did not have a placebo arm. In addition to the reactions shown for Trials 1 and 2 above, adverse reactions occurring in greater than or equal to 2% of subjects treated with BREO 200/25 included viral respiratory tract infection, pharyngitis, pyrexia, and arthralgia.
12-Month Trial Long-term safety data is based on a 12-month trial that evaluated the safety of BREO 100/25 once daily (n = 201), BREO 200/25 once daily (n = 202), and fluticasone propionate 500 mcg twice daily (n = 100) in adolescent and adult subjects with asthma (Trial 4). Overall, 63% were female and 67% were white. The mean age was 39 years; adolescents (aged 12 to 17 years) made up 16% of the population. In addition to the reactions shown for Trials 1 and 2 above, adverse reactions occurring in greater than or equal to 2% of the subjects treated with BREO 100/25 or BREO 200/25 for 12 months included pyrexia, back pain, extrasystoles, upper abdominal pain, respiratory tract infection, allergic rhinitis, pharyngitis, rhinitis, arthralgia, supraventricular extrasystoles, ventricular extrasystoles, acute sinusitis, and pneumonia.
Exacerbation Trial In a 24- to 76-week trial, subjects received BREO 100/25 (n = 1,009) or fluticasone furoate 100 mcg (n = 1,010) (Trial 5). Subjects participating in this trial had a history of one or more asthma exacerbations that required treatment with oral/systemic corticosteroids or emergency department visit or in-patient hospitalization for the treatment of asthma in the year prior to trial entry. Overall, 67% were female and 73% were white; the mean age was 42 years (adolescents aged 12 to 17 years made up 14% of the population). While subjects aged 12 to 17 years were included in this trial, BREO is not approved for use in this age-group *[see Use in Specific Populations (8.4)]*. Asthma-related hospitalizations occurred in 10 subjects (1%) treated with BREO 100/25 compared with 7 subjects (0.7%) treated with fluticasone furoate 100 mcg. Among subjects aged 12 to 17 years, asthma-related hospitalizations occurred in 4 subjects (2.6%) treated with BREO 100/25 (n = 151) compared with 0 subjects treated with fluticasone furoate 100 mcg (n = 130). There were no asthma-related deaths or asthma-related intubations observed in this trial.
6.3 Postmarketing Experience In addition to adverse reactions reported from clinical trials, the following adverse reactions have been identified during postapproval use of BREO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These events have been chosen for inclusion due to either their seriousness, frequency of reporting, or causal connection to BREO or a combination of these factors.
Cardiac Disorders Palpitations, tachycardia.
Immune System Disorders Hypersensitivity reactions, including anaphylaxis, angioedema, rash, and urticaria.
Musculoskeletal and Connective Tissue Disorders Muscle spasms.
Nervous System Disorders Tremor.
Psychiatric Disorders Nervousness.

7 DRUG INTERACTIONS

7.1 Inhibitors of Cytochrome P450 3A4 Fluticasone furoate and vilanterol, the individual components of BREO, are both substrates of CYP3A4. Concomitant administration of the strong CYP3A4 inhibitor ketoconazole increases the systemic exposure to fluticasone furoate and vilanterol. Caution should be exercised when considering the coadministration of BREO with long-term ketoconazole and other known strong CYP3A4 inhibitors (e.g., ritonavir, clarithromycin, conivaptan, indinavir, itraconazole, lopinavir, nefazodone, nelfinavir, saquinavir, telithromycin, troleandomycin, voriconazole) *[see Warnings and Precautions (5.9), Clinical Pharmacology (12.3) of full prescribing information]*.
7.2 Monoamine Oxidase Inhibitors and Tricyclic Antidepressants Vilanterol, like other beta$_2$-agonists, should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QTc interval or within 2 weeks of discontinuation of such agents, because the effect of adrenergic agonists on the cardiovascular system may be potentiated by these agents. Drugs that are known to prolong the QTc interval have an increased risk of ventricular arrhythmias.
7.3 Beta-Adrenergic Receptor Blocking Agents Beta-blockers not only block the pulmonary effect of beta-agonists, such as vilanterol, a component of BREO, but may also produce severe bronchospasm in patients with COPD or asthma. Therefore, patients with COPD or asthma should not normally be treated with beta-blockers. However, under certain circumstances, there may be no acceptable alternatives to the use of beta-adrenergic blocking agents for these patients; cardioselective beta-blockers could be considered, although they should be administered with caution.
7.4 Non–Potassium-Sparing Diuretics The electrocardiographic changes and/or hypokalemia that may result from the administration of non–potassium-sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta-agonists, especially when the recommended dose of the beta-agonist is exceeded. Although the clinical significance of these effects is not known, caution is advised in the coadministration of beta-agonists with non–potassium-sparing diuretics.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Teratogenic Effects Pregnancy Category C. There are no adequate and well-controlled trials with BREO in pregnant women. Corticosteroids and beta$_2$-agonists have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Because animal reproduction studies are not always predictive of human response, BREO should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Women should be advised to contact their physicians if they become pregnant while taking BREO. *Fluticasone Furoate and Vilanterol:* There was no evidence of teratogenic interactions between fluticasone furoate and vilanterol in rats at approximately 5 and 40 times, respectively, the maximum recommended human daily inhalation dose (MRHDID) in adults (on a mcg/m^2 basis at maternal inhaled doses of fluticasone furoate and vilanterol, alone or in combination, up to approximately 95 mcg/kg/day). *Fluticasone Furoate:* There were no teratogenic effects in rats and rabbits at approximately 4 and 1 times, respectively, the MRHDID in adults (on a mcg/m^2 basis at maternal inhaled doses up to 91 and 8 mcg/kg/day in rats and rabbits, respectively). There were no effects on perinatal and postnatal development in rats at approximately 1 time the MRHDID in adults (on a mcg/m^2 basis at maternal doses up to 27 mcg/kg/day). *Vilanterol:* There were no teratogenic effects in rats and rabbits at approximately 13,000 and 160 times, respectively, the MRHDID in adults (on a mcg/m^2 basis at maternal inhaled doses up to 33,700 mcg/kg/day in rats and on an AUC basis at maternal inhaled doses up to 591 mcg/kg/day in rabbits). However, fetal skeletal variations were observed in rabbits at approximately 1,000 times the MRHDID in adults (on an AUC basis at maternal inhaled or subcutaneous doses of 5,740 or 300 mcg/kg/day, respectively). The skeletal variations included decreased or absent ossification in cervical vertebral centrum and metacarpals. There were no effects on perinatal and postnatal development in rats at approximately 3,900 times the MRHDID in adults (on a mcg/m^2 basis at maternal oral doses up to 10,000 mcg/kg/day).
Nonteratogenic Effects Hypoadrenalism may occur in infants born of mothers receiving corticosteroids during pregnancy. Such infants should be carefully monitored.
8.2 Labor and Delivery There are no adequate and well-controlled human trials that have investigated the effects of BREO during labor and delivery. Because beta-agonists may potentially interfere with uterine contractility, BREO should be used during labor only if the potential benefit justifies the potential risk.
8.3 Nursing Mothers It is not known whether fluticasone furoate or vilanterol are excreted in human breast milk. However, other corticosteroids and beta$_2$-agonists have been detected in human milk. Since there are no data from controlled trials on the use of BREO by nursing mothers, caution should be exercised when it is administered to a nursing woman.
8.4 Pediatric Use BREO is not indicated for use in children and adolescents. The safety and efficacy in pediatric patients (aged 17 years and younger) have not been established. In a 24- to 76-week exacerbation trial, subjects received BREO 100/25 (n = 1,009) or fluticasone furoate 100 mcg (n = 1,010). Subjects had a mean age of 42 years and a history of one or more asthma exacerbations that required treatment with oral/systemic corticosteroids or emergency department visit or in-patient hospitalization for the treatment of asthma in the year prior to study entry. *[See Clinical Studies (14.2) of full prescribing information.]* Adolescents aged 12 to 17 years made up 14% of the study population (n = 281), with a mean exposure of 352 days for subjects in this age-group treated with BREO 100/25 (n = 151) and 355 days for subjects in this age-group treated with fluticasone furoate 100 mcg (n = 130). In this age-group, 10% of subjects treated with BREO 100/25 reported an asthma exacerbation compared with 7% for subjects treated with fluticasone furoate 100 mcg. Among the adolescents, asthma-related hospitalizations occurred in 4 subjects (2.6%) treated with BREO 100/25 compared with 0 subjects treated with fluticasone furoate 100 mcg. There were no asthma-related deaths or asthma-related intubations observed in the adolescent age-group.
Effects on Growth Orally inhaled corticosteroids may cause a reduction in growth velocity when administered to children and adolescents. A reduction of growth velocity in children and adolescents may occur as a result of poorly controlled asthma or from use of corticosteroids, including ICS. The effects of long-term treatment of children and adolescents with ICS, including fluticasone furoate, on final adult height are not known. *[See Warnings and Precautions (5.17); Use in Special Populations (8.4) of full prescribing information.]*
8.5 Geriatric Use Based on available data, no adjustment of the dosage of BREO in geriatric patients is necessary, but greater sensitivity in some older individuals cannot be ruled out. Clinical trials of BREO for asthma included 854 subjects aged 65 years and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger subjects.
8.6 Hepatic Impairment Fluticasone furoate systemic exposure increased by up to 3-fold in subjects with hepatic impairment compared with healthy subjects. Hepatic impairment had no effect on vilanterol systemic exposure. Use BREO with caution in patients with moderate or severe hepatic impairment. Monitor patients for corticosteroid-related side effects *[see Clinical Pharmacology (12.3) of full prescribing information]*.
8.7 Renal Impairment There were no significant increases in either fluticasone furoate or vilanterol exposure in subjects with severe renal impairment (CrCl less than 30 mL/min) compared with healthy subjects. No dosage adjustment is required in patients with renal impairment *[see Clinical Pharmacology (12.3) of full prescribing information]*.

10 OVERDOSAGE

No human overdosage data has been reported for BREO. BREO contains both fluticasone furoate and vilanterol; therefore, the risks associated with overdosage for the individual components described below apply to BREO. Treatment of overdosage consists of discontinuation of BREO together with institution of appropriate symptomatic and/or supportive therapy. The judicious use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such medicine can produce bronchospasm. Cardiac monitoring is recommended in cases of overdosage.
10.1 Fluticasone Furoate Because of low systemic bioavailability (15.2%) and an absence of acute drug-related systemic findings in clinical trials, overdosage of fluticasone furoate is unlikely to require any treatment other than observation. If used at excessive doses for prolonged periods, systemic effects such as hypercorticism may occur *[see Warnings and Precautions (5.8)]*. Single- and repeat-dose trials of fluticasone furoate at doses of 50 to 4,000 mcg have been studied in human subjects. Decreases in mean serum cortisol were observed at dosages of 500 mcg or higher given once daily for 14 days.
10.2 Vilanterol The expected signs and symptoms with overdosage of vilanterol are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the signs and symptoms of beta-adrenergic stimulation (e.g., seizures, angina, hypertension or hypotension, tachycardia with rates up to 200 beats/min, arrhythmias, nervousness, headache, tremor, muscle cramps, dry mouth, palpitation, nausea, dizziness, fatigue, malaise, insomnia, hyperglycemia, hypokalemia, metabolic acidosis). As with all inhaled sympathomimetic medicines, cardiac arrest and even death may be associated with an overdose of vilanterol.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).
Asthma-Related Death **Inform patients with asthma that LABA, such as vilanterol, one of the active ingredients in BREO, increase the risk of asthma-related death and may increase the risk of asthma-related hospitalization in pediatric and adolescent patients. Also inform them that currently available data are inadequate to determine whether concurrent use of ICS or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA.**
Not for Acute Symptoms Inform patients that BREO is not meant to relieve acute symptoms of COPD or asthma and extra doses should not be used for that purpose. Advise patients to treat acute symptoms with an inhaled, short-acting beta$_2$-agonist such as albuterol. Provide patients with such medication and instruct them in how it should be used. Instruct patients to seek medical attention immediately if they experience any of the following: Decreasing effectiveness of inhaled, short-acting beta$_2$-agonists; Need for more inhalations than usual of inhaled, short-acting beta$_2$-agonists; Significant decrease in lung function as outlined by the physician. Tell patients they should not stop therapy with BREO without physician/provider guidance since symptoms may recur after discontinuation.
Do Not Use Additional Long-Acting Beta$_2$-Agonists Instruct patients not to use other LABA for COPD and asthma.
Local Effects Inform patients that localized infections with *Candida albicans* occurred in the mouth and pharynx in some patients. If oropharyngeal candidiasis develops, it should be treated with appropriate local or systemic (i.e., oral) antifungal therapy while still continuing therapy with BREO, but at times therapy with BREO may need to be temporarily interrupted under close medical supervision. Advise patients to rinse the mouth with water without swallowing after inhalation to help reduce the risk of thrush.
Immunosuppression Warn patients who are on immunosuppressant doses of corticosteroids to avoid exposure to chickenpox or measles and, if exposed, to consult their physicians without delay. Inform patients of potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex.
Hypercorticism and Adrenal Suppression Advise patients that BREO may cause systemic corticosteroid effects of hypercorticism and adrenal suppression. Additionally, inform patients that deaths due to adrenal insufficiency have occurred during and after transfer from systemic corticosteroids. Patients should taper slowly from systemic corticosteroids if transferring to BREO.
Reduction in Bone Mineral Density Advise patients who are at an increased risk for decreased BMD that the use of corticosteroids may pose an additional risk.
Ocular Effects Inform patients that long-term use of ICS may increase the risk of some eye problems (cataracts or glaucoma); consider regular eye examinations.
Risks Associated with Beta-Agonist Therapy Inform patients of adverse effects associated with beta$_2$-agonists, such as palpitations, chest pain, rapid heart rate, tremor, or nervousness.
Hypersensitivity Reactions, Including Anaphylaxis Advise patients that hypersensitivity reactions (e.g., anaphylaxis, angioedema, rash, urticaria) may occur after administration of BREO. Instruct patients to discontinue BREO if such reactions occur. There have been reports of anaphylactic reactions in patients with severe milk protein allergy after inhalation of other powder medications containing lactose; therefore, patients with severe milk protein allergy should not use BREO.

BREO was developed in collaboration with Theravance.

GlaxoSmithKline
Research Triangle Park, NC 27709

Revised 9/2015 BRE:6BRS

Industry Theaters Explore Lung Disease Treatments

Have lunch while learning about new product launches and treatment options in during Tuesday's Industry Theater and Mini Industry Theater discussions in the Exhibit Hall. Complimentary boxed lunches will be provided by the ATS while supplies last.

Learn about product launches and treatment options at Tuesday's Industry Theaters and Mini Industry Theaters in the Exhibit Hall. Boxed lunches will be provided while supplies last.

MINI INDUSTRY THEATER

11:30 a.m.-Noon

Managing COPD Exacerbations With the Experts

Managing exacerbations remains a challenge for patients with severe COPD. Join us for a dynamic case-based presentation led by an expert panel. The objective of this program is to provide health care professionals with insights into the complexities associated with COPD exacerbation management as well as strategies for reducing the risk of exacerbations in severe COPD patients.

Speakers: **Donald P. Tashkin, MD**, *Professor Emeritus of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California;* **Ronald C. Balkissoon, MD**, *MSc, Pulmonary Consultant, Denver, Colorado*

Company: AstraZeneca Pharmaceuticals Inc.

INDUSTRY THEATER 1

11:30 a.m.-12:15 p.m.

Thrombosis: DVT/PE An Exploration in Risk Reduction

This lecture will discuss treatment options for patients with deep vein thrombosis and pulmonary embolism, and how they can reduce the risk of recurrent thrombotic events.

Speaker: **Joseph K. Choo, MD, FACC**, *Staff Cardiologist, Christ Hospital Physicians, Ohio Heart and Vascular, Cincinnati, Ohio*

Company: Janssen Pharmaceuticals Inc.

INDUSTRY THEATER 2

11:30 a.m.-12:15 p.m.

ORKAMBI® (lumacaftor/ivacaftor) Treatment Initiation and Clinical Management

Speaker: **Manu Jain, MD, MSc**, *Northwestern University*

Company: Vertex Pharmaceuticals Inc.

MINI INDUSTRY THEATER

12:30-1 p.m.

COPD Is a Struggle. Let's Talk About a Maintenance Therapy Option

The objective of this presentation is to provide pertinent, balanced information to health care professionals on the efficacy and safety of nebulized long-acting bronchodilator therapy for patients with COPD. It is designed to afford health care professionals the opportunity to review, evaluate, and discuss the role of nebulized long-acting bronchodilator therapy as an option for patients with COPD, including chronic bronchitis and emphysema, in order to make informed treatment decisions for their patients.

Speaker: **Antonio Anzueto, MD**, *Professor of Medicine, University of Texas, Health Science Center at San Antonio, San Antonio, Texas*

Company: Sunovion Pharmaceuticals Inc.

INDUSTRY THEATER 1

1:15-2 p.m.

Insights in IPF: Perspectives on the Disease and Its Diagnosis

Join us for a 45-minute Insights in IPF educational program examining the evolving understanding of idiopathic pulmonary fibrosis (IPF), including the science of the disease and the complexity of diagnosis. An expert in the field of interstitial lung disease will provide insight into the challenges of managing a patient with IPF, with perspectives on how to address these challenges in the clinic.

Speaker: **Amy M. Olson MD, MSPH**; *National Jewish Health*

Company: Boehringer Ingelheim Pharmaceuticals Inc.

INDUSTRY THEATER 2

1:15-2 p.m.

Treatment Strategies for COPD Exacerbation Prevention: New Evidence

(open to non-U.S. attendees only)

During this Novartis-supported industry theater, a faculty of world-renowned experts will explore the burden of COPD exacerbations and new evidence for exacerbation prevention in high-risk patients with dual bronchodilator indacaterol/glycopyrronium. The potential implications of these data on the position of dual bronchodilators in COPD management also will be explored.

Speakers:

5 minutes: **Addressing COPD treatment goals: LABA/LAMA vs. LABA/ICS**—Claus Vogelmeier (Chair)

10 minutes: **Unmet needs in COPD management: The importance of exacerbations and their prevention**—Nicolas Roche

5 minutes: **Piecing the evidence together: Treating high-risk patients**—Claus Vogelmeier

15 minutes: **Preventing exacerbations in high-risk patients: New evidence**—Ken Chapman

5 minutes: **Implications of new evidence with LABA/LAMA for the treatment of COPD**—Claus Vogelmeier

5 minutes: **Q&A:** All

Company: Novartis Pharma AG

MINI INDUSTRY THEATER

1:30-2 p.m.

COPD Disease Management to Reduce Hospital Readmissions

Discuss a program to reduce hospital readmissions for the COPD patient.

Speaker: Dr. Sai Parthasarthy

Company: Philips Respironics Inc.

ATS Welcomes Decision on Shorter MDR-TB Regimen

On May 12, the World Health Organization released recommendations aimed to speed up detection and improve treatment outcomes for multidrug resistant tuberculosis (MDR-TB) through the use of a novel, rapid diagnostic test and a shorter, cheaper treatment regimen.

The American Thoracic Society welcomes the WHO's recently released recommendations, which shorten treatment to nine to 12 months, making it easier for patients to complete treatment. The recommended conventional MDR-TB regimen involves 18 to 24 months of daily therapy, making it challenging for patients to complete.

"The new WHO-recommended MDR-TB treatment regimen is a significant advance for many patients with MDR-TB who will no longer have to endure almost two years of treatment and harsh drug side effects," says ATS Past President Philip C. Hopewell, MD, professor of medicine and director of the Curry International Tuberculosis Center at the University of California, San Francisco. "Though the new regimen will ease treatment for some MDR-TB patients, there remains an urgent need for shorter, easier treatment for all patients with drug-susceptible and drug-resistant TB, faster point-of-care diagnostics, and effective vaccines to prevent TB in all populations."

According to the WHO, tuberculosis is a top infectious disease killer worldwide. It notes these staggering statistics:

- In 2014, 9.6 million people fell ill with TB, and 1.5 million died from the disease.
- More than 95 percent of TB deaths occur in low- and middle-income countries, and it is among the top five causes of death for women aged 15 to 44.
- In 2014, an estimated 1 million children became ill with TB and 140,000 children died of TB.
- TB is a leading killer of HIV-positive people: In 2015, one in three HIV deaths was due to TB.

The WHO's Millennium Development Goal target of halting and reversing the TB epidemic by 2015 has been met globally. According to the WHO:

- TB incidence has fallen an average of 1.5 percent per year since 2000, and is now 18 percent lower than the level of 2000.
- The TB death rate dropped 47 percent between 1990 and 2015.
- An estimated 43 million lives were saved through TB diagnosis and treatment between 2000 and 2014.
- Ending the TB epidemic by 2030 is among the health targets of the newly adopted Sustainable Development Goals.

"The battle against TB must be prioritized if we are to halt this pandemic," says Dr. Hopewell, co-chair of the committee for the WHO International Standards for Tuberculosis Care (third edition, published in 2014), and a member of the ATS Assembly on Microbiology, Tuberculosis & Pulmonary Infections.

For Dr. Hopewell, the ATS is well positioned to advocate for research that leads to the eradication of tuberculosis.

"The ATS is the organization with the most experience in dealing with TB, both as a clinical and a public health problem. We were founded by a group of physicians who were directors of TB sanatoria and hospitals back in 1905, and that progressively broadened to include all of respiratory disease," Dr. Hopewell says.

In addition to several poster presentations on TB, a symposium on Wednesday will examine "New Concepts in TB Immunity and Targets for Treatment" from 9 to 11 a.m. in the Moscone Center, Room 3016/3018, (West Building, Level 3). ■

> "The battle against TB must be prioritized if we are to halt this pandemic."
>
> *Philip C. Hopewell, MD*

ATS Daily Bulletin
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PULMONARY • CRITICAL CARE • SLEEP

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Step Up With the ATS Walking Challenge

Lisa Bacolini (left) and Joyce Alejo-Stone, both of Fibrogen, Inc., joined the ATS Walking Challenge Monday, picking up their complimentary fitness trackers at the ATS Walking Challenge information booth in the Moscone Center Lobby (South Building, Upper Level). Find out who among your ATS colleagues are "high steppers" by watching live results reported on leaderboards in the ATS Walking Challenge booth and at TEVA Respiratory in Booth 419. Or perhaps you would like to add some steps of your own. Check out some San Francisco famed sites that are within walking distance of the Moscone Center, such as Lombard Street, which takes about 3,600 steps.

Join the Conversation on Twitter: #ATS2016

Doctor Chad @chadchima "The opposite of love is not hate. It is indifference." Impressed to hear Elie Wiesel quoted in #healthcare #disparities session at #ATS2016

John Blakey @johndblakey Some great posters from @JHUGlobalHealth at #ATS2016 exploring the effect of the urban environment on #asthma in Peru

Maxwell Tran @MaxwellTran Gained 40 followers today after the #entrepreneurship session at #ATS2016. Maybe I should live tweet more often!

Oliver @CPC_Munich Incredibly well-deserved: Marlene Rabinovitch gives Amberson Lecture at #ATS2016 @atscommunity @ATS_RCMB

Jack Iwashyna @iwashyna Prognosis is never purely biological, but rather shaped by society's willingness to invest in support & environmental adaptations #ATS2016

Catherine Disch @CatherineDisch1 At ATS in San Francisco! Amazing Meeting #ATS2016

The ATS Center Shows Global Reach

Learn about all that the American Thoracic Society has to offer, including its activities around the world, at the ATS Center in Booth 937 in the Exhibit Hall at Moscone Center, Halls A-C (South Building, Lower Level). Be sure to visit from 8 a.m. to 2:45 p.m. on Tuesday.

The colorful ATS Center was redesigned to feature a large touchscreen world map that illustrates the center's theme, "ATS: Providing a World of Opportunity to Improve Global Lung Health."

Thirty four percent of the ATS's members hail from 129 countries, making it a truly global Society. An overarching goal of this reach is to improve world lung health, and the Society has developed initiatives and related activities to:

- Engage international organizations, such as the World Health Organization.
- Provide global education, research, and research training.
- Engage ATS members to participate in global initiatives.
- Pursue its broad global health policy.
- Provide technical assistance and other capacity to build support.

At the ATS Center, find out about the Society's involvement in specific global activities, such as the Forum of International Respiratory Societies; Methods in Epidemiologic, Clinical, and Operations Research (MECOR); tuberculosis control efforts; the ATS Global Scholars Program; and peer conferences.

FDA-APPROVED ACTHAR

FOR SYMPTOMATIC SARCOIDOSIS

SARCOIDOSIS HAS NUMEROUS CLINICAL MANIFESTATIONS AND RANGES IN SEVERITY[1]

- Lungs are affected in more than 90% of sarcoidosis cases[2]
- Concomitant involvement of extrapulmonary organs can be seen in up to 50% of cases[3]
- Extrapulmonary sarcoidosis adds to the morbidity and mortality of patients with pulmonary sarcoidosis[3]
  - The number of organs impacted by sarcoidosis is likely to increase over time[4]

To learn more, visit us at Mallinckrodt Booth #603 in the ATS 2016 Exhibit Hall

INDICATION

H.P. Acthar® Gel (repository corticotropin injection) is indicated for symptomatic sarcoidosis.

IMPORTANT SAFETY INFORMATION

- Acthar should never be administered intravenously.
- Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of Acthar.
- Acthar is contraindicated where congenital infections are suspected in infants.
- Acthar is contraindicated in patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, primary adrenocortical insufficiency, adrenocortical hyperfunction or sensitivity to proteins of porcine origin.
- The following may be associated with Acthar: increased susceptibility to infections, hypothalamic-pituitary-axis suppression and adrenal insufficiency, Cushing's syndrome, elevated blood pressure, salt and water retention, hypokalemia, masking of symptoms of other disorders, gastrointestinal perforation and bleeding, behavioral and mood disturbances, worsening of comorbid diseases, ophthalmic effects, immunogenicity potential, negative effects on growth and physical development, decrease in bone density and embryocidal effects. Patients may need to be monitored for signs and symptoms.
- Common adverse reactions for Acthar are similar to those of corticosteroids and include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite, and weight gain.
- Specific adverse reactions reported in IS clinical trials in infants and children under 2 years of age included: infection, hypertension, irritability, Cushingoid symptoms, constipation, diarrhea, vomiting, pyrexia, weight gain, increased appetite, decreased appetite, nasal congestion, acne, rash, and cardiac hypertrophy.

Other adverse events reported are included in the full Prescribing Information.

Please see adjacent page for Brief Summary of Acthar full Prescribing Information for additional Important Safety Information.

References: 1. Judson MA. The clinical features of sarcoidosis: a comprehensive review. *Clin Rev Allerg Immunol.* 2015;49:63-78. **2.** Baughman RP, Culver DA, Judson MA. A concise review of pulmonary sarcoidosis. *Am J Respir Crit Care Med.* 2011;183:573-581. **3.** Shigemitsu H, Patel HV, Schreiber MP. Extrapulmonary sarcoidosis. In: Judson MA, ed. *Pulmonary Sarcoidosis: A Guide for the Practicing Clinician.* Vol 17. New York, NY: Springer Science+Business Media; 2014:149-186. **4.** Judson MA, Boan AD, Lackland DT. The clinical course of sarcoidosis: presentation, diagnosis, and treatment in a large white and black cohort in the United States. *Sarcoidosis Vasc Diffuse Lung Dis.* 2012;29:119-127.

Mallinckrodt Pharmaceuticals

H.P. Acthar® GEL
(repository corticotropin injection) 80 U/mL

H.P. **Acthar**® GEL
(repository corticotropin injection) 80 U/mL

Brief Summary of Prescribing Information. For complete prescribing information (including Medication Guide), consult official package insert. H.P. Acthar Gel (repository corticotropin injection) INJECTION, GEL for INTRAMUSCULAR / SUBCUTANEOUS use. INDICATIONS AND USAGE Infantile spasms: H.P. Acthar Gel (repository corticotropin injection) is indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age. **Multiple Sclerosis:** H.P. Acthar Gel (repository corticotropin injection) is indicated for the treatment of acute exacerbations of multiple sclerosis in adults. Controlled clinical trials have shown H.P. Acthar Gel to be effective in speeding the resolution of acute exacerbations of multiple sclerosis. However, there is no evidence that it affects the ultimate outcome or natural history of the disease. **Rheumatic Disorders:** As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: Psoriatic arthritis, Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), Ankylosing spondylitis. **Collagen Diseases:** During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis). **Dermatologic Diseases:** Severe erythema multiforme, Stevens-Johnson syndrome. **Allergic States:** Serum sickness. **Ophthalmic Diseases:** Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation. **Respiratory Diseases:** Symptomatic sarcoidosis. **Edematous State:** To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus. **CONTRAINDICATIONS** H.P. Acthar Gel is contraindicated for intravenous administration. H.P. Acthar Gel is contraindicated where congenital infections are suspected in infants. Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of H.P. Acthar Gel. H.P. Acthar Gel is contraindicated in patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, primary adrenocortical insufficiency, adrenocortical hyperfunction or sensitivity to proteins of porcine origin. **WARNINGS AND PRECAUTIONS** The adverse effects of H.P. Acthar Gel are related primarily to its steroidogenic effects. Not all of the adverse events described below have been seen after treatment with H.P. Acthar Gel, but might be expected to occur. [*see Adverse Reactions*]. **Infections** H.P. Acthar Gel may increase the risks related to infections with any pathogen, including viral, bacterial fungal, protozoan or helminthic infections. Patients with latent tuberculosis or tuberculin reactivity should be observed closely, and if therapy is prolonged, chemoprophylaxis should be instituted. **Cushing's Syndrome and Adrenal Insufficiency Upon Withdrawal** Treatment with H.P. Acthar Gel can cause hypothalamic-pituitary-axis (HPA) suppression and Cushing's syndrome. These conditions should be monitored especially with chronic use. Suppression of the HPA may occur following prolonged therapy with the potential for adrenal insufficiency after withdrawal of the medication. Patients should be monitored for signs of insufficiency such as weakness, hyperpigmentation, weight loss, hypotension and abdominal pain. The symptoms of adrenal insufficiency in infants treated for infantile spasms can be difficult to identify. The symptoms are non-specific and may include anorexia, fatigue, lethargy, weakness, excessive weight loss, hypotension and abdominal pain. It is critical that parents and caregivers be made aware of the possibility of adrenal insufficiency when discontinuing H.P. Acthar Gel and should be instructed to observe for, and be able to recognize, these symptoms. [*see Information for Patients*] The recovery of the adrenal gland may take from days to months so patients should be protected from the stress (e.g. trauma or surgery) by the use of corticosteroids during the period of stress. The adrenal insufficiency may be minimized in adults and infants by tapering of the dose when discontinuing treatment. Signs or symptoms of Cushing's syndrome may occur during therapy but generally resolve after therapy is stopped. Patients should be monitored for these signs and symptoms such as deposition of adipose tissue in characteristics sites (e.g., moon face, truncal obesity), cutaneous striae, easy bruisability, decreased bone mineralization, weight gain, muscle weakness, hyperglycemia, and hypertension. **Elevated Blood Pressure, Salt and Water Retention and Hypokalemia** H.P. Acthar Gel can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium and calcium. Dietary salt restriction and potassium supplementation may be necessary. Caution should be used in the treatment of patients with hypertension, congestive heart failure, or renal insufficiency. **Vaccination** Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of H.P. Acthar Gel. Killed or inactivated vaccines may be administered; however, the response to such vaccines can not be predicted. Other immunization procedures should be undertaken with caution in patients who are receiving H.P. Acthar Gel, especially when high doses are administered, because of the possible hazards of neurological complications and lack of antibody response. **Masking Symptoms of Other Diseases** H.P. Acthar Gel often acts by masking symptoms of other diseases/disorders without altering the course of the other disease/disorder. Patients should be monitored carefully during and for a period following discontinuation of therapy for signs of infection, abnormal cardiac function, hypertension, hyperglycemia, change in body weight and fecal blood loss. **Gastrointestinal Perforation and Bleeding** H.P. Acthar Gel can cause GI bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain gastrointestinal disorders. Signs of gastrointestinal perforation, such as peritoneal irritation, may be masked by the therapy. Use caution where there is the possibility of impending perforation, abscess or other pyogenic infections, diverticulitis, fresh intestinal anastomoses, and active or latent peptic ulcer. **Behavioral and Mood Disturbances** Use of H.P. Acthar Gel may be associated with central nervous system effects ranging from euphoria, insomnia, irritability (especially in infants), mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated. **Comorbid Diseases** Patients with a comorbid disease may have that disease worsened. Caution should be used when prescribing H.P. Acthar Gel in patients with diabetes and myasthenia gravis. **Ophthalmic Effects** Prolonged use of H.P. Acthar Gel may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi and viruses. **Immunogenicity Potential** H.P. Acthar Gel is immunogenic. Limited available data suggest that a patient may develop antibodies to H.P. Acthar Gel after chronic administration and loss of endogenous ACTH and H.P. Acthar Gel activity. Prolonged administration of H.P. Acthar Gel may increase the risk of hypersensitivity reactions. Sensitivity to porcine protein should be considered before starting therapy and during the course of treatment should symptoms arise. **Use in Patients with Hypothyroidism or Liver Cirrhosis** There is an enhanced effect in patients with hypothyroidism and in those with cirrhosis of the liver. **Negative Effects on Growth and Physical Development** Long-term use of H.P. Acthar Gel may have negative effects on growth and physical development in children. Changes in appetite are seen with H.P. Acthar Gel therapy, with the effects becoming more frequent as the dose or treatment period increases. These effects are reversible once H.P. Acthar Gel therapy is stopped. Growth and physical development of pediatric patients on prolonged therapy should be carefully monitored. **Decrease in Bone Density** Decrease in bone formation and an increase in bone resorption both through an effect on calcium regulation (i.e. decreasing absorption and increasing excretion) and inhibition of osteoblast function may occur. These, together with a decrease in the protein matrix of the bone (secondary to an increase in protein catabolism) and reduced sex hormone production, may lead to inhibition of bone growth in children and adolescents and to the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating therapy, and bone density should be monitored in patients on long term therapy. **Use in Pregnancy** H.P. Acthar Gel has been shown to have an embryocidal effect. Apprise women of potential harm to the fetus. [*see Use in Specific Populations*] **ADVERSE REACTIONS** Please refer to *Adverse Reactions in Infants and Children Under 2 Years of Age* for consideration when treating patients with Infantile Spasms. The adverse reactions presented are primarily provided for consideration in use in adults and in children over 2 years of age, but these adverse reactions should also be considered when treating infants and children under 2 years of age. H.P. Acthar Gel causes the release of endogenous cortisol from the adrenal gland. Therefore all the adverse effects known to occur with elevated cortisol may occur with H.P. Acthar Gel administration as well. Common adverse reactions include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain. **Clinical Studies Experience** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug, and may not reflect the rates observed in practice. **Adverse Reactions in Infants and Children Under 2 Years of Age** While the types of adverse reactions seen in infants and children under age 2 treated for infantile spasms are similar to those seen in older patients, their frequency and severity may be different due to the very young age of the infant, the underlying disorder, the duration of therapy and the dosage regimen. Below is a summary of adverse reactions specifically tabulated from source data derived from retrospective chart reviews and clinical trials in children under 2 years of age treated for infantile spasms. The number of patients in controlled trials at the recommended dose was too few to provide meaningful incidence rates or to permit a meaningful comparison to the control groups. **Incidence (%) of Treatment Emergent Adverse Events Occurring in ≥ 2% of H.P. Acthar Gel (repository corticotropin injection) Infants and Children under 2 years of Age with the recommended 75 U/m² bid dose (n=122) vs the 150 U/m² qd dose (n=37)—System Organ Class:** *Cardiac disorders:* cardiac hypertrophy (3, 0); *Endocrine disorders:* Cushingoid (3, 22); *Gastrointestinal disorders:* constipation (0, 5), diarrhea (3, 14), vomiting (3, 5); *General disorders and administration site conditions:* irritability (7, 19), pyrexia (5, 8); *Infections and infestations:* infection[1] (20, 46); *Investigations:* weight gain (1, 3); *Metabolism and nutrition disorders:* increased appetite (0, 5), decreased appetite (3, 3); *Nervous system disorders:* convulsion[2] (12, 3); *Respiratory, thoracic and mediastinal disorders:* nasal congestion (1, 5); *Skin and subcutaneous tissue disorders*: acne (0, 14), rash (0, 8); *Vascular disorders:* hypertension (11, 19). [1]Specific infections that occurred at ≥2% were candidiasis, otitis media, pneumonia and upper respiratory tract infections. [2]In the treatment of Infantile Spasms, other types of seizures/convulsions may occur because some patients with infantile spasms progress to other forms of seizures (for example, Lennox-Gastaut Syndrome). Additionally the spasms sometimes mask other seizures and once the spasms resolve after treatment, the other seizures may become visible. These adverse reactions may also be seen in adults and children over 2 years of age when treated for other purposes and with different doses and regimens. **Postmarketing Experience** The following adverse reactions associated with the use of H.P. Acthar Gel have been identified from postmarketing experience with H.P. Acthar Gel. Only adverse events that are not listed above as adverse events reported from retrospective chart reviews and non-sponsor conducted clinical trials and those not discussed elsewhere in labeling, are listed in this section. Because the adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency or establish a causal relationship to use with H.P. Acthar Gel. Events are categorized by system organ class. Unless otherwise noted these adverse events have been reported in infants, children and adults. **Allergic Reactions** Allergic responses have presented as dizziness, nausea and shock (adults only). **Cardiovascular** Necrotizing angitis (adults only) and congestive heart failure. **Dermatologic** Skin thinning (adults only), facial erythema and increased sweating (adults only). **Endocrine** Decreased carbohydrate tolerance (infants only) and hirsutism. **Gastrointestinal** Pancreatitis (adults only), abdominal distention and ulcerative esophagitis. **Metabolic** Hypokalemic alkalosis (infants only). **Musculoskeletal** Muscle weakness and vertebral compression fractures (infants only). **Neurological** Headache (adults only), vertigo (adults only), subdural hematoma, intracranial hemorrhage (adults only), and reversible brain shrinkage (usually secondary to hypertension) (infants only). **Possible Additional Steroidogenic Effects** Based on steroidogenic effects of H.P. Acthar Gel certain adverse events may be expected due to the pharmacological effects of corticosteroids. The adverse events that may occur but have not been reported for H.P. Acthar Gel are: **Dermatologic** Impaired wound healing, abscess, petechiae and ecchymoses, and suppression of skin test reactions. **Endocrine** Menstrual irregularities. **Metabolic** Negative nitrogen balance due to protein catabolism. **Musculoskeletal** Loss of muscle mass and aseptic necrosis of femoral and humeral heads. **Neurological** Increased intracranial pressure with papilledema, (pseudo-tumor cerebri) usually after treatment, and subdural effusion. **Ophthalmic** Exophthalmos. **DRUG INTERACTIONS** Formal drug-drug interaction studies have not been performed. H.P. Acthar Gel may accentuate the electrolyte loss associated with diuretic therapy. **USE IN SPECIFIC POPULATIONS Pregnancy** Pregnancy Class C: H.P. Acthar Gel has been shown to have an embryocidal effect. There are no adequate and well-controlled studies in pregnant women. H.P. Acthar Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing Mothers** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from H.P. Acthar Gel, when treating a nursing mother, a decision should be made whether to discontinue nursing or to discontinue the drug, considering the risk and benefit to the mother. **Pediatric Use** H.P. Acthar Gel is indicated as monotherapy for the treatment of infantile spasms in infants and children less than 2 years of age. Both serious and other adverse reactions in this population are discussed in Warnings and Adverse Reactions in Infants and Children Under 2 Years of Age. The efficacy of H.P. Acthar Gel for the treatment of infantile spasms in infants and children less than 2 years of age was evaluated in a randomized, single blinded (video EEG interpreter blinded) clinical trial and an additional active control supportive trial. A responding patient was defined as having both complete cessation of spasms and elimination of hypsarrhythmia. Safety in the pediatric population for infantile spasms was evaluated by retrospective chart reviews and data from non-sponsor conducted clinical trials [*see Adverse Reactions*]. While the types of adverse reactions seen in infants and children under 2 years of age treated for infantile spasms are similar to those seen in older patients, their frequency and severity may be different due to the very young age of the infant, the underlying disorder, the duration of therapy and the dosage regimen. Effects on growth are of particular concern [*see Warnings and Precautions*]. Serious adverse reactions observed in adults may also occur in children [*see Warnings and Precautions*]. **OVERDOSAGE** While chronic exposure to H.P. Acthar Gel at high doses can be associated with a variety of potential serious adverse effects, it is not expected that a single high dose, or even several large doses, has the potential for serious adverse effects compared to a standard dose. There have been no reports of death or acute overdose symptoms from H.P. Acthar Gel in clinical studies or in the published literature. The intramuscular route of administration makes it unlikely that an inadvertent acute overdose will occur. The typical daily dose of H.P. Acthar Gel to treat an infant that has a BSA of 0.4 m^2 would be 60 U/day. Using the 1-cc syringe supplied with H.P. Acthar Gel, the maximum amount that can be injected is 80 U/injection, which is a well-tolerated single dose. **HOW SUPPLIED / STORAGE AND HANDLING** H.P. Acthar Gel (repository corticotropin injection) is supplied as 5 mL multi-dose vial (63004-8710-1) containing 80 USP Units per mL. H.P. Acthar Gel (repository corticotropin injection) should be warmed to room temperature before using. Do not over pressurize the vial prior to withdrawing the product. Store H.P. Acthar Gel (repository corticotropin injection) under refrigeration between 2°-8°C (36°-46°F). Product is stable for the period indicated on the label when stored under the conditions described. **PATIENT COUNSELING INFORMATION** Caretakers of patients with infantile spasms should be informed of the availability of a Medication Guide, and they should be instructed to read the Medication Guide prior to administering H.P. Acthar Gel. Patients should be instructed to take H.P. Acthar Gel only as prescribed. They should not stop treatment suddenly unless instructed by their physician to do so. Patients, their caregivers and families should be advised as to the importance of the need for careful monitoring while on and during titration from H.P. Acthar Gel treatment and the importance of not missing any scheduled doctor's appointments. Patients, their caregivers and families should be advised that if the patient develops an infection or fever they should contact their physician. They should be educated that a fever may not necessarily be present during infection. The patient should also try to limit contact with other people with infections to minimize the risk of infection while taking H.P. Acthar Gel. [*see Warnings and Precautions and Adverse Reactions*]. Patients, their caregivers and families should be advised that if the patient experiences an increase in blood pressure they should contact their physician. [*see Warnings and Precautions and Adverse Reactions*]. Patients, their caregivers and families should be advised that if the patient or the caregiver notices blood or a change in color of the patient's stool they should contact their physician. [*see Warnings and Precautions*]. Caregivers and families of infants and children treated with H.P. Acthar Gel should be informed that the patient may show signs of irritability and sleep disturbances. These effects are reversible once H.P. Acthar Gel therapy is stopped. [*see Warnings and Precautions and Adverse Reactions*]. Patients, their caregivers and families should be advised that changes in appetite, most often leading to weight gain, are seen with H.P. Acthar Gel therapy, becoming more frequent as the dose or treatment period increases. These effects are reversible once H.P. Acthar Gel therapy is stopped. [*see Warnings and Precautions and Adverse Reactions*]. Patients, their caregivers and families should be advised that the patient may be monitored for signs of adrenal insufficiency such as weakness, fatigue, lethargy, anorexia, weight loss, hypotension, abdominal pain or hyperpigmentation (adults only) after treatment has stopped. Since the recovery of the adrenal gland varies from days to months, patients may need to be protected from the stress of trauma or surgery by the use of corticosteroids during the period of stress. [*see Warnings and Precautions*]. Patients should be advised not to be vaccinated with live or live attenuated vaccines during treatment with H.P. Acthar Gel. Additionally, other immunization procedures in patients or in family members who will be in contact with the patient should be undertaken with caution while the patient is taking H.P. Acthar Gel. [*see Warnings and Precautions*]. Patients, their caregivers and families should be advised that prolonged use of H.P. Acthar Gel in children may result in Cushing's syndrome and associated adverse reactions, may inhibit skeletal growth, and may cause osteoporosis and decreased bone density. If prolonged use is necessary, H.P. Acthar Gel should be given intermittently along with careful observation. [*see Warnings and Precautions, and Adverse Reactions*]. Patients, their caregivers and families should be informed that H.P. Acthar Gel may mask symptoms of other diseases/disorders without altering the course of the other disease/disorder. The patient will need to be monitored carefully during and for a period following discontinuation of therapy for signs of infection, abnormal cardiac function, hypertension, hyperglycemia, change in body weight, and fecal blood loss. [*see Warnings and Precautions*]. In the treatment of Infantile Spasms, other types of seizures may occur because some patients with infantile spasms progress to other forms of seizures (for example, Lennox-Gastaut Syndrome). Additionally the spasms sometimes mask other seizures and once the spasms resolve after treatment with H.P. Acthar Gel, the other seizures may become visible. Parents and caregivers should inform their physician of any new onset of seizures so that appropriate management can then be instituted. [*see Adverse Reactions*].

H.P. Acthar® Gel (repository corticotropin injection)

Manufactured for:
Mallinckrodt ARD, Inc.

Hazelwood, MO 63042 USA

Rev 01/2015

Mallinckrodt Pharmaceuticals™

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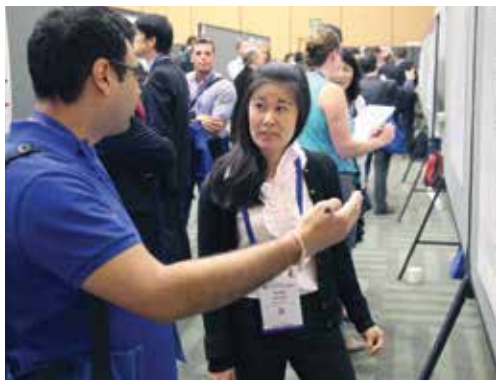

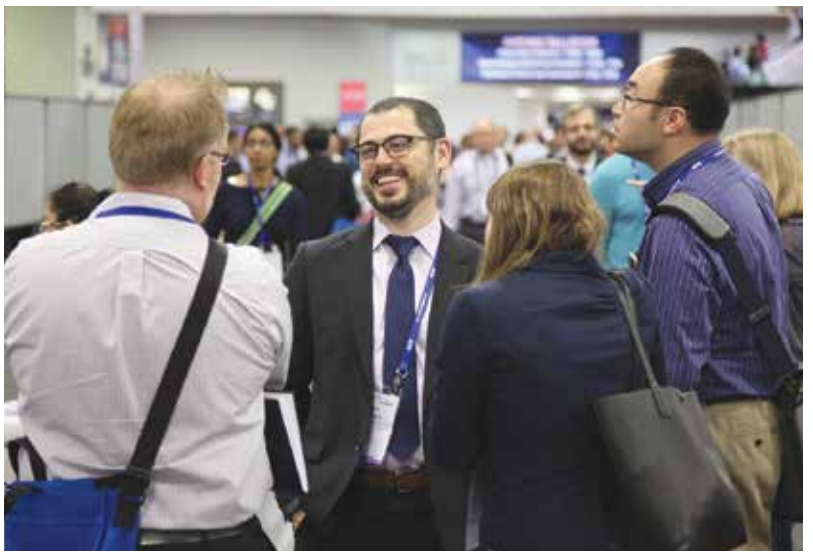

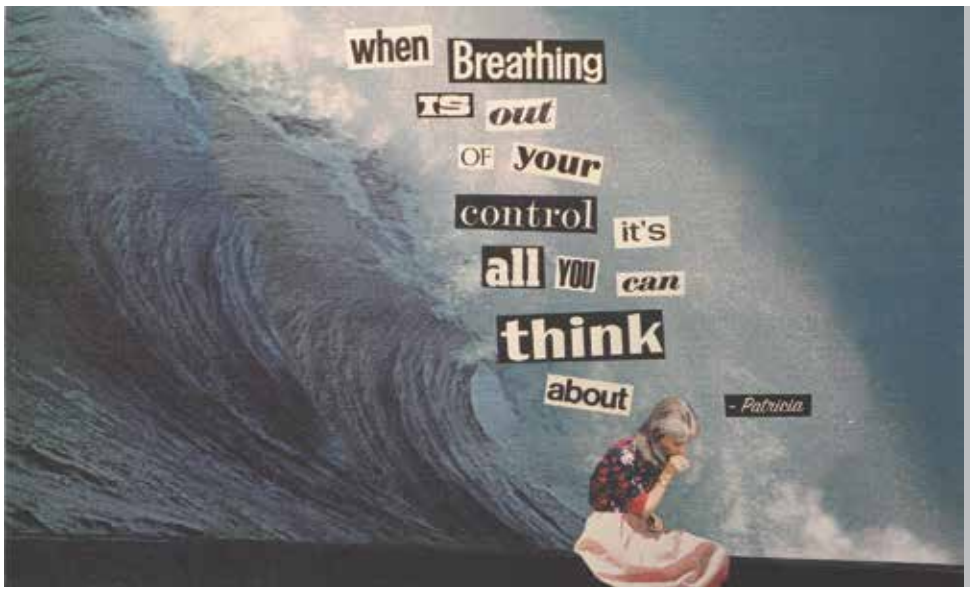

Forums Celebrate Diversity and Inclusivity

Two popular forums gave attendees the opportunity to recognize and support diversity and women in the fields of pulmonary, critical care, and sleep medicine.

Sonia C. Flores, PhD, (top left) professor of medicine, Division of Pulmonary Sciences, University of Colorado Anschutz Medical Campus, Aurora, spoke about the challenges she faced as a minority in medicine during Sunday's Diversity Forum.

Irina Petrache, MD, (top center, left) professor of medicine and chief of pulmonary, critical care, and sleep medicine at National Jewish Health, Denver, Colorado, accepts the 2016 Elizabeth A. Rich, MD, Award, from Yolanda Mageto, MD, MPH, ATS Membership Committee chair, during the Women's Forum on Monday.

Catherine R. Lucey, MD, (top right) the Faustino and Martha Molina Bernadett Presidential Chair for Medical Education, professor of medicine, and vice dean for education at the University of California, San Francisco, School of Medicine, spoke about the leadership skills needed by today's health care leaders during the Women's Forum.

Recipients of Minority Trainee Development Scholarships (bottom), selected for the quality of science in their submitted abstracts, were recognized at the Diversity Forum. ■

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