ATS DAILY BULLETIN

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Sunday
May 20, 2018
San Diego, CA • May 18-23, 2018

Clinicians Can Treat Health Care Crisis

Clinician leaders can and must deal with the crisis besetting health care in the United States and around the globe.

"It is high time that we exert our leadership for the sake of the people we serve," said Darrell G. Kirch, MD, president and CEO of the Association of American Medical Colleges. "Our patients depend on us, and future generations of patients depend on us."

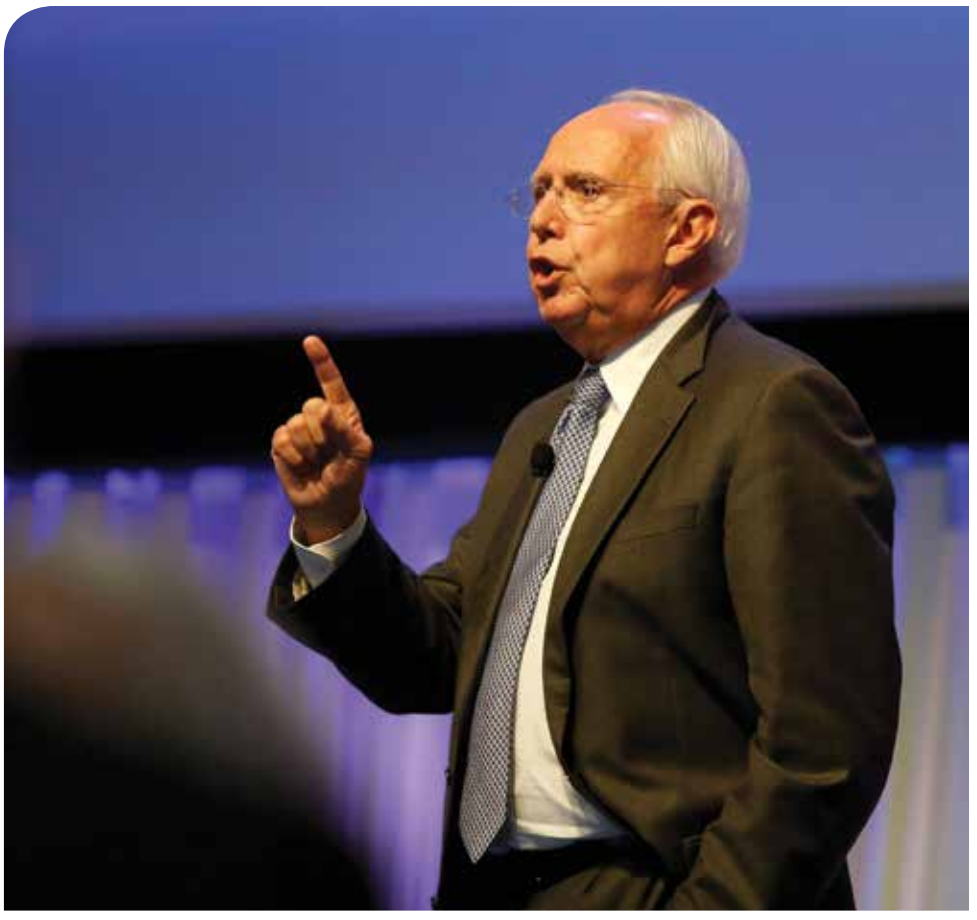
Dr. Kirch delivered the keynote address during the opening session on Saturday. He laid out six key challenges facing health care around the world. Clinicians are best equipped to meet all six.

The first challenge is the disruption of health care by successive mergers, acquisitions, and breakups. Consolidating medical practices, hospitals, and systems into ever-larger business units gives the anatomic appearance of integration but fails to achieve physiologic integration.

"We do a much better job of rescuing people than we do in keeping them well," he said. "And we are spending more than we can afford. Clinicians have ceded leadership to others, and health care has lost the balance between business rigor and clinical sensitivity."

The second challenge: living in a post-truth era where personal belief, opinion, and emotion mean more than evidence.

see OPENING page 46



Darrell G. Kirch, MD: "We do a much better job of rescuing people than we do in keeping them well."

Early Career Professionals Get Ahead

While many ATS 2018 attendees have been gearing up for the conference, some have already been hard at work already. They came early to participate in programs for early career professionals—the Student Scholars Program, the Resident Boot Camp, and the ATS Fellows Track Symposium.

The **Student Scholars Program** offers 75 motivated medical, graduate, and nursing students the opportunity to attend the ATS International Conference for free.

"The conference is a great way to meet people and find a student mentor," said Simone Norris, a graduate student at New York Medical College. "I hope to learn how to best analyze research, how to network with other professionals, and how to form collaborations for my own research."

For **Resident Boot Camp,** more than 140 faculty provided large-group lectures, small breakout sessions, and skills-based workshops to 160 incoming fellows, giving them hands-on training and skills they can use on day one of their fellowship.

The **ATS Fellows Track Symposium (FTS)** allowed 225 fellows to attend 30 lectures and two skills-based sessions, following both an adult and a pediatric track and covering sepsis, COPD, lung cancer, asthma, and interventional pulmonology.

FTS attendee Peter Hountras, MD, a third-year fellow at Northwestern University, says participants can listen to top people in their fields talk about a large range of topics. "It can be helpful for those taking their boards in the fall, and it is a great opportunity for a refresher before you set out in your career." ■

The ATS Fellows Track Symposium is supported by educational grants from Actelion Pharmaceuticals US, Inc., AstraZeneca LP, Boehringer Ingelheim Pharmaceuticals, Inc., Genentech Inc., and Vertex Pharmaceuticals. In-kind support is provided by FUJIFILM SonoSite, Inc., and nnd Medical Technologies.

DON'T MISS THESE EVENTS

How to Get the Most Out of the ATS International Conference
11 a.m.-12 p.m., Sails Pavilion (Upper Level)

Shark Tank Lung Nodules session
11:30 a.m.-12:40 p.m., Clinicians Center

Restoring Joy in Health Care
10:30 a.m.-3:30 p.m., Exhibit Hall, Booth 904
(play with puppies from 11 a.m.-2 p.m.)

KEYNOTE SERIES

Research and Slow Medicine

The ATS Keynote Series highlights major advances, recent discoveries, significant accomplishments, transformative findings, and important best practices in pulmonary, critical care, and sleep medicine. These state-of-the-art lectures are presented in two sessions at 8:15-9 a.m. each morning during the conference, when no other programming is scheduled.

Today's speakers will examine the progression of pulmonary research and improving post-ICU recovery.

James P. Kiley, PhD

NHLBI and the Evolution of Pulmonary Research (K1)
Room 6B (Upper Level), San Diego Convention Center
James P. Kiley, PhD, director of the Division of Lung Diseases, National Heart, Lung, and Blood Institute, National Institutes of Health, will discuss

see KEYNOTE SERIES page 46

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ATS Foundation Honors Donohue for Commitment to Research

James F. Donohue, MD, has spent a lifetime putting patients first. His commitment to them, in combination with his dedication to finding better treatment options for them, has earned him the highest honor bestowed by the ATS Foundation. On Saturday, the Foundation presented Dr. Donohue with the Breathing for Life Award at its 10th Annual Research Program Benefit at the Manchester Grand Hyatt San Diego.

The Foundation's Breathing for Life Award recognizes philanthropy, scientific achievement, and commitment to mentorship.

Dr. Donohue is division director emeritus of pulmonary diseases and critical care medicine at the University of North Carolina, Chapel Hill.

He played a major role in building the pulmonary diseases and critical care division at UNC Chapel Hill. He was the second physician to join the division in 1976 and served as division chief from 2002 to 2011. Today, the division has 32 faculty members and 11 fellows.

Known as a master clinician and clinical scientist, Dr. Donohue led trials of the most commonly used inhaled therapies for COPD and asthma.

Dr. Donohue chaired the ATS Foundation from 2010 to 2016. During that time, annual contributions to the Research Program nearly tripled to $1 million, and the number of research grants awarded doubled.

Commenting on his decision to accept the offer to chair the ATS Foundation, Dr. Donohue said, "I knew the generosity of the pulmonary community was going to be outstanding—and it really was. We all deeply believe in the need for research and a new generation of investigators."

In the past decade, the Research Program has awarded $17.6 million in grants to 235 investigators who have gone on to secure $268 million in federal funding.

Those dollars are critical because research is critical, said Dean Schraufnagel, MD, chair of the ATS Foundation.

"Whether you're just starting out in your career, mentoring young researchers, or treating patients who benefit from research, we all know this to be true: *research changes lives*," Dr. Schraufnagel said, just before presenting Dr. Donohue with the award.

BREATHING FOR LIFE AWARD RECIPIENTS

David Center, MD (2017)
Sally Wenzel, MD (2016)
Marvin Schwarz, MD (2015)
William Busse, MD (2014)
Gerard Turino, MD (2013)
Talmadge King, Jr., MD (2012)
Louis Libby, MD (2011)
Sen. Mike Crapo (R-Idaho) (2010)
ATS PAR (2009)

James F. Donohue, MD, (left) accepts the Breathing for Life Award from ATS Foundation Chair Dean Schraufnagel.

The ATS Foundation is now accepting applications for the 2018-2019 Research Program grant cycle. Letters of intent are due by June 12, 2018.

The ATS Foundation thanks Genentech for support of the 10th Annual ATS Foundation Research Program Benefit at the Sapphire Level; AstraZeneca LP and Boehringer Ingelheim Pharmaceuticals, Inc. at the Gold Level; FREEMAN, Gilead Sciences, Inc., Insmed Incorporated, Sunovion Pharmaceuticals Inc., Theravance Biopharma, and Mallinckrodt Pharmaceuticals at the Silver Level; and Ascend Integrated Media, Grifols, National Board for Respiratory Care, Novartis Pharma AG, Vertex Pharmaceuticals Inc., Circassia Pharmaceuticals, Inc., and GlaxoSmithKline at the Bronze Level.

For the most up-to-date list of generous donations from individuals, medical institutions, and corporate supporters of the ATS Foundation, visit **foundation.thoracic.org/benefit**. ■

Welcome!

By Jess Mandel, MD
International Conference Committee Chair

Welcome to ATS 2018, the intellectual crossroads of pulmonary, critical care, and sleep medicine!

The first ATS conference was held 114 years ago, and over the years, the conference has earned a reputation for presenting the best science and the latest clinical advances in respiratory medicine. This year's sessions and speakers will build upon that tradition.

From thought-provoking keynote addresses and major symposia to year-in-review courses and case conferences, ATS 2018 has been programmed to help each attendee stay at the forefront of his or her profession—whether you are a physician or a nurse, a basic or translational researcher, a public health expert, medical educator, or full-time clinician.


Jess Mandel, MD

The conference's more than 500 sessions will be led by some of the foremost experts in pulmonary, critical care, and sleep medicine from around the world. Sometimes, you will find that these speakers' expertise transcends respiratory medicine, while offering critical insights into it. Other times, you will be listening to a "lion(ess)" of respiratory medicine with multiple landmark studies to his or her name. Or you may just meet, as many attendees have, an early career investigator whose research helps advance your own longstanding interest in the same area.

Wherever you go this week at ATS 2018, you'll be presented with learning opportunities that only a "live" educational program can offer. You'll be able to ask questions of presenters, discuss what you've learned with friends and colleagues, and build a network of professional contacts you can call upon when you're faced with a challenging case or research question.

You'll also benefit from a vibrant Exhibit Hall, where you can learn about cutting-edge diagnostics and therapies, often through new visual modalities such as virtual reality.

Over the years, one of the things I've come to admire most about the ATS International Conference is the unpretentious and approachable tone set by attendees and presenters. Although you will learn a lot of important things at ATS 2018 just by listening, I urge you to take full advantage of this open, collaborative culture by joining some of the thousands of conversations about the future of pulmonary, critical care, and sleep medicine that take place during the conference.

I have left every ATS International Conference feeling excited and rejuvenated by all aspects of the meeting, including those side conversations and what they may mean for patients. I hope you experience the same feelings from your week here.

Enjoy the conference! ■

ATS 2018 Kicks Off

Attendees share information, learn, network, and take selfies, while finishing touches are put on exhibits.

Respiratory Innovation Summit Fills Development Gap


ATS President Marc Moss says innovation is a critical component for clinicians.

Innovation fosters innovation. That simple connection inspired the first Respiratory Innovation Summit, which launched Saturday during the ATS 2018 International Conference. ATS President Marc Moss, MD, set the tone for the day-long event.

"It took us all of a nanosecond to realize we had to squeeze the Respiratory Innovation Summit into an already packed schedule here in San Diego," Dr. Moss said. "Clinicians and clinical researchers and academicians and basic researchers are not taught to think in an entrepreneurial way. That is a huge gap in the development pipeline from idea to research to development to product launch."

The summit was designed to bring together the newest and the best ideas from clinicians, academia, industry, venture capital, and regulators. ATS membership covers those areas and more.

"ATS members are not just researchers or clinicians," Dr. Moss said. "They have seats on corporate advisory boards, they are CEOs and medical directors, and they play other key roles in the respiratory community."

The Research Innovation Summit provided an insider's look at the nuts and bolts of innovation. It takes more than a novel concept to bring an innovation to market. It takes grit, hard work, and plenty of help and advice to move from scribbles on a white board to a successful FDA marketing approval and commercial launch.

The summit focused on four product areas: biopharma, medical technology, drug delivery and diagnostics, and digital technology, plus a window into the regulatory world, innovation at the NIH, and venture capital.

The ATS annual meeting program already features multiple sessions devoted to innovation, Dr. Moss noted.

The BEAR Cage is a live, Shark Tank-style presentation on Monday from 1 to 3 p.m. Sponsored by the Drug/Device Discovery and Development Committee, the BEAR Cage gives three early career professionals the opportunity to pitch their innovative research proposals to a panel of translational science experts. The winner takes home a $5,000 cash prize and the kind of high profile recognition that can make or break new ideas.

The twisting, sometimes obscure path from off-the-wall concept to novel therapeutic agent is the focus of a Wednesday keynote. Theodore F. Reiss, MD, MBE, corporate vice president and head of I&I Clinical R&D at Celgene, will explore the inner workings of medical innovation in "On Pharma: The Complexity of Innovation" from 8:15 to 9 a.m.

"As an organization and as a community, we focus on scientific values," Dr. Moss said. "Together, we can advance our common agenda in respiratory research and development." ■

Summit Product Presenters

Biopharma: Ark Biosciences, GlycoMira Diagnostics, OrPro Therapeutics, Pieris Pharmaceuticals, Renovion, Savara, and Synspira.

Drug Delivery & Diagnostics: Avisa Pharma, FLUIDDA, Mercator, ProterixBio, and Pulmatrix.

Medical Device: CSA Medical, HCmed Innovations, Lungpacer, Nuvaira, and Sommetrics.

Digital Tech: Cohero Health, Health Care Originals, HealthUp, Tueo Health, and VIDA.

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What could be worse than having NTM?
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Nontuberculous mycobacterial (NTM) lung disease is a chronic, debilitating condition that can significantly increase patient **morbidity and mortality**[1-5]

- Approximately **2/3 of NTM patients** have moderate to severe NTM by the time they are diagnosed[6,7]
- Host susceptibility factors that **increase risk** for NTM include bronchiectasis, COPD, asthma, and other conditions or specific genetic disorders that cause structural lung damage and impaired clearance[8-10]
    - Patients with susceptibility factors, such as these underlying lung conditions, who present with pulmonary (eg, chronic cough) and nonspecific systemic symptoms (eg, malaise or fever) **should be assessed for NTM**[9,11]

Visit **NTMFacts.com** for more information.

References: 1. Griffith DE, Aksamit T, Brown-Elliott BA, et al; for the ATS Mycobacterial Diseases Subcommittee. *Am J Respir Crit Care Med.* 2007;175(4):367-416. **2.** Winthrop KL, McNelley E, Kendall B, et al. *Am J Respir Crit Care Med.* 2010;182(7):977-982. **3.** Park HY, Jeong B-H, Chon HR, Jeon K, Daley CL, Koh W-J. *Chest.* 2016;150(6):1222-1232. **4.** Adjemian J, Olivier KN, Seitz AE, Holland SM, Prevots DR. *Am J Respir Crit Care Med.* 2012;185(8):881-886. **5.** Fleshner M, Olivier KN, Shaw PA, et al. *Int J Tuberc Lung Dis.* 2016;20(5):582-587. **6.** Wagner D, van Ingen J, Adjemian J, et al. Poster presented at: European Respiratory Society (ERS) Annual Congress; September 6-10, 2014; Munich, Germany. **7.** Kotilainen H, Valtonen V, Tukiainen P, Poussa T, Eskola J, Järvinen A. *Eur J Clin Microbiol Infect Dis.* 2015;34(9):1909-1918. **8.** Andréjak C, Nielsen R, Thomsen VØ, Duhaut P, Sørensen HT, Thomsen RW. *Thorax.* 2013;68(3):256-262. **9.** Fritscher LG, Marras TK, Bradi AC, Fritscher CC, Balter MS, Chapman KR. *Chest.* 2011;139(1):23-27. **10.** Szymanski EP, Leung JM, Fowler CJ, et al. *Am J Respir Crit Care Med.* 2015;192(5):618-628. **11.** Young JD, Balagopal A, Reddy NS, Schlesinger LS. *J Respir Dis.* 2007;28(1):7-18.

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PAR Helps Patients Live Well

Everyone wants to live their best life. But for those who have a disease or condition that affects their lungs, that can be difficult to do. That's why six health care professionals gathered on Saturday to address patients and their families at the Public Advisory Roundtable (PAR) Meet-the-Experts session. Discussing the topic of "Living Well and Lung Health," the experts gave informative talks on integrative medicine, oxygen therapy, pulmonary rehabilitation, and the roles of sleep, mental health, and intimacy in lung health.

The session was designed to "support individuals with lung, sleep, and critical care issues by providing education that would lead to empowerment to living one's best life, and to finding balance and perseverance," said PAR Chair Kerri Connolly. "We put together a lineup of lung disease experts to share their expertise to help patients have a better quality of life."

Patients in the audience and their families, friends, and caregivers were eager to learn about ways they can improve their lives or the lives of their loved ones. Gina Dietzer, who has stage IV lung cancer, says she came to the session to learn more about her disease and how to live well with it.

"I can still have a good quality of life," she says. "It's all about how you deal with your disease and respond to it."

After the panel, attendees were treated to lunch and the opportunity to meet lung disease experts in breakout sessions. There, patients were able to ask questions and meet others who share their disease or condition.

"The people I've met have been wonderful role models for me," said Jenny Brengleman, also a lung cancer patient. "They give me hope."

Ms. Connolly said the program is successful if patients walk away inspired and energized by the conversations and peer-to-peer connections made during the event.

"We hope that by the end, we create building blocks of knowledge that become pathways to patients' discovery of a better understanding of their disease." ■

> "It's all about how you deal with your disease and respond to it."
>
> **Gina Dietzer, patient**

JAMA/NEJM Editors and Authors Report on Papers

Join the discussion as editors and authors present papers that were recently published in the Journal of the American Medical Association and the New England Journal of Medicine.

These interactive sessions provide a forum for attendees to have a question-and-answer period with the authors and editors, who select published papers to discuss at the conference based on their significance to the fields of critical care medicine (Session A84) and pulmonary medicine (Session A2).

These discussions are intended to provide insight into the papers, the selection process, and how research applies directly to the fields.

Gary W. K. Wong, MD, will co-chair the morning session. Dr. Wong is a professor in the Department of Pediatrics at the Chinese University of Hong Kong and an associate editor for NEJM. George T. O'Connor, MD, will also co-chair this session. Dr. O'Connor is professor of medicine at Boston University School of Medicine and an associate editor for JAMA.

Howard Bauchner, MD, JAMA editor in chief, will co-chair the afternoon session. Dr. Bauchner became the 16th editor of JAMA in July 2011. He is vice chair of pediatrics at the Boston University School of Medicine. Patricia A. Kritek, MD, will also co-chair this session. Dr. Kritek is editor of NEJM Journal Watch. She is a practicing pulmonary and critical care physician and professor of medicine in the Division of Pulmonary and Critical Care Medicine at the University of Washington, Seattle. ■

JAMA and NEJM

Discussion on the Edge: Reports of Recently Published Pulmonary Research (A2)

9:15 a.m.-11:15 a.m.

Sunday

Room 29 A-D (Upper Level), San Diego Convention Center

NEJM and JAMA

Discussion on the Edge: Reports of Recently Published Critical Care Research (A84)

2:15 p.m.-4:15 p.m.

Sunday

Room 29 A-D (Upper Level), San Diego Convention Center

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Two MECC-Organized Symposia at the ATS 2018 International Conference. All ATS 2018 International Conference attendees are invited to attend these Non-CME educational programs sponsored by The France Foundation and supported by grants from Boehringer Ingelheim Pharmaceuticals, Inc. (IPF), Genentech (IPF), and Insmed, Incorporated (NTM).

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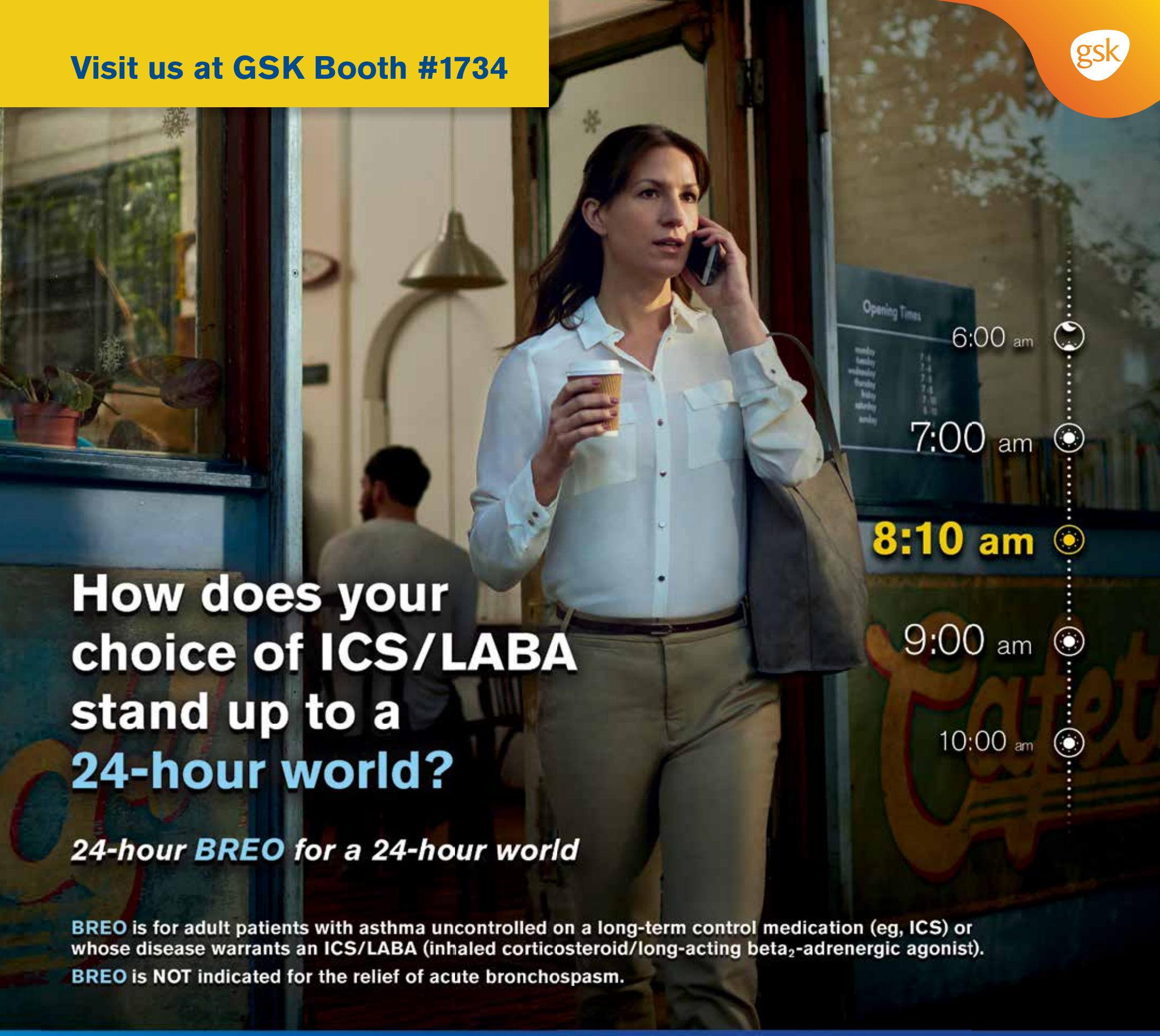


How does your choice of ICS/LABA stand up to a 24-hour world?

24-hour BREO for a 24-hour world

BREO is for adult patients with asthma uncontrolled on a long-term control medication (eg, ICS) or whose disease warrants an ICS/LABA (inhaled corticosteroid/long-acting beta$_2$-adrenergic agonist).

BREO is NOT indicated for the relief of acute bronchospasm.

Important Safety Information

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

- LABA monotherapy for asthma increases the risk of asthma-related death, and in pediatric and adolescent patients, available data also suggest an increased risk of asthma-related hospitalization. These findings are considered a class effect of LABA monotherapy. When LABA are used in fixed-dose combination with ICS, data from large clinical trials do not show a significant increase in the risk of serious asthma-related events (hospitalizations, intubations, death) compared with ICS alone.

WARNINGS AND PRECAUTIONS (cont'd)

- BREO should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD or asthma.
- BREO is not a rescue medication and should not be used for the relief of acute bronchospasm or symptoms. Acute symptoms should be treated with an inhaled, short-acting beta$_2$-agonist.
- BREO should not be used more often or at higher doses than recommended, or with another LABA (eg, salmeterol, formoterol fumarate, arformoterol tartrate, indacaterol) for any reason, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs, like LABA.
- Oropharyngeal candidiasis has occurred in patients treated with BREO. Advise patients to rinse the mouth with water without swallowing after inhalation.

Please see additional Important Safety Information for BREO on the following pages.
Please see Brief Summary of Prescribing Information for BREO on the pages following this advertisement.

BREO ELLIPTA was developed in collaboration with INNOVIVA

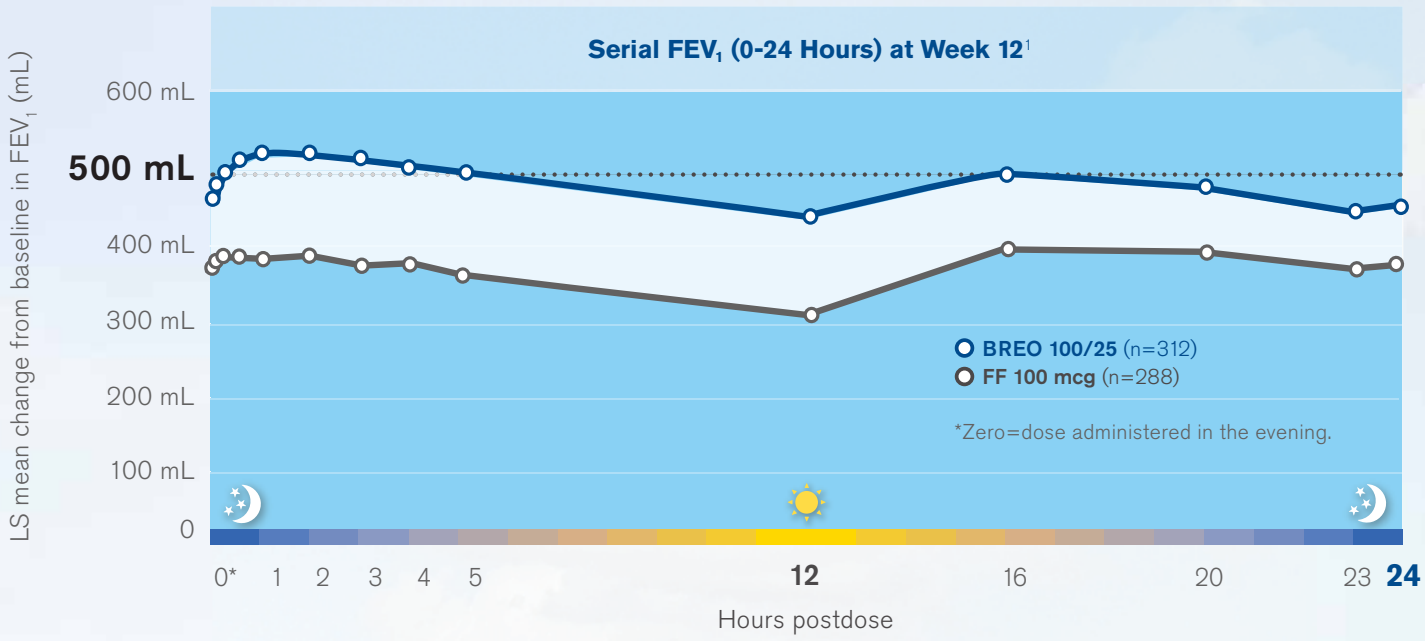
BREO ELLIPTA
(fluticasone furoate 100, 200 mcg and vilanterol 25 mcg inhalation powder)

BREO—The ***only*** ICS/LABA that provides **24-hour efficacy** with **just one daily inhalation**… *for better breathing all day and night*

In a 12-week study in patients who were symptomatic on a mid- to high-dose ICS

Primary endpoint: weighted mean (wm) FEV_1 (0-24 hours)—BREO 100/25 (n=312) provided a statistically significant 108-mL (30%) improvement in least squares (LS) mean change from baseline in wm FEV_1 (0-24 hours) compared with fluticasone furoate (FF) 100 mcg (n=288) ($P<0.001$) at Week 12.[1]

Proven to deliver continuous lung function improvement for a full 24 hours[1]



Study description[1]

Design: 12-week, randomized, double-blind study that evaluated the safety and efficacy of BREO 100/25, BREO 200/25, and FF 100 mcg (each administered once daily in the evening). Patients who reported symptoms and/or rescue $beta_2$-agonist use during a 4-week run-in period on mid- to high-dose ICS (≥250 mcg fluticasone propionate [FP] twice daily or equivalent) were randomized.

Patients: 1039 patients with asthma aged 12 years and older† (mean age: 46 years). At baseline, patients had a mean percent predicted FEV_1 of 62%.

†BREO is approved for use in patients ≥18 years of age.

Endpoint: Primary=wm FEV_1 (0-24 hours).

FEV_1=forced expiratory volume in 1 second.

In a placebo-controlled 12-week study[2]**:**

- **wm FEV_1:** In a subset of patients, BREO 100/25 (n=108) demonstrated a numerically greater improvement in change from baseline in wm FEV_1 (0-24 hours) compared with FF 100 mcg (n=106) of 116 mL (95% CI: −5, 236; $P=0.06$) and a statistically significant 302-mL improvement ($P<0.001$) compared with placebo (n=95) at Week 12

Study description: 12-week, randomized, double-blind, placebo-controlled study of 609 patients aged 12 years and older† (mean age: 40 years) with asthma, symptomatic on low- to mid-dose ICS (FP 100 mcg to 250 mcg twice daily or equivalent) during a 4-week run-in period (mean baseline percent predicted FEV_1 of 70%) randomized to BREO 100/25, FF 100 mcg, or placebo (each administered once daily in the evening). The co-primary endpoints were wm FEV_1 (0-24 hours) (in a subset of patients) and trough FEV_1 at Week 12.

†BREO is approved for use in patients ≥18 years of age.

Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Use caution in patients who use corticosteroids as they 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.
- Particular care is needed for patients transferred from systemic corticosteroids to inhaled corticosteroids because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer. 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.
- Caution should be exercised when considering the coadministration of BREO with long-term ketoconazole and other known strong CYP3A4 inhibitors (eg, 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.

Please see additional Important Safety Information for BREO on all pages. Please see Brief Summary of Prescribing Information for BREO on the pages following this advertisement.

WARNINGS AND PRECAUTIONS (cont'd)

- 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 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 (eg, 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. 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 reduce growth velocity in children and adolescents.

BREO—The ***only*** ICS/LABA proven to **reduce exacerbations** with **just one daily inhalation**

Proven to reduce the RISK and RATE of exacerbations[3]

In a 24- to 76-week study of patients with a history of asthma exacerbations

TIME TO FIRST ASTHMA EXACERBATION

20% REDUCTION IN RISK OF EXACERBATIONS

WITH BREO 100/25 (n=1009) vs FF 100 mcg (n=1010) HAZARD RATIO=0.795; *P*=0.036

ANNUAL RATE OF ASTHMA EXACERBATIONS

25% REDUCTION IN RATE OF EXACERBATIONS

PER PATIENT PER YEAR WITH BREO 100/25 (n=1009) vs FF 100 mcg (n=1010) BREO 0.14 vs FF 0.19; *P*=0.014

Study description[3]

Design: 24- to 76-week, randomized, double-blind, event-driven trial that evaluated the long-term safety and efficacy of BREO 100/25 compared with FF 100 mcg (each administered once daily in the evening). Patients with a history of 1 or more asthma exacerbations in the prior year that required treatment with oral/systemic corticosteroids or emergency department (ED) visit or inpatient hospitalization, and who were being treated with a low- to high-dose ICS or low- to mid-dose ICS/LABA entered a 2-week run-in period during which LABA treatment was stopped. Patients who reported symptoms and/or rescue $beta_2$-agonist use during the 2-week run-in period were randomized to treatment, which varied in duration from 24 to 76 weeks, as the study was stopped when 330 events had occurred. An event was defined as a patient experiencing an asthma exacerbation.

Asthma exacerbation criteria: A deterioration of asthma requiring the use of systemic corticosteroids for at least 3 days or an inpatient hospitalization or ED visit due to asthma that required systemic corticosteroids.

Patients: 2019 patients with asthma aged 12 years and older† (mean age: 42 years). At baseline, patients had a mean percent predicted FEV_1 of 72%.

†BREO is approved for use in patients ≥18 years of age.

Endpoints: Primary=time to first asthma exacerbation; Secondary=rate of asthma exacerbations (per patient per year).

Important Safety Information (cont'd)

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%).
- Additional adverse reactions (≥2% incidence) reported in subjects taking BREO 200/25 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 ≥1 asthma exacerbations in the past year, asthma-related hospitalizations occurred in 1% of subjects taking BREO 100/25. No asthma-related deaths or intubations were observed.

DRUG INTERACTIONS

- Caution should be exercised when considering the coadministration of BREO with long-term ketoconazole and other known strong CYP3A4 inhibitors. See prior Warning and Precaution regarding CYP3A4 inhibitors.

DRUG INTERACTIONS (cont'd)

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

USE IN SPECIFIC POPULATIONS

- BREO is not indicated for children and adolescents; the safety and efficacy in patients aged ≤17 years 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.

References: 1. Bernstein DI, Bateman ED, Woodcock A, et al. Fluticasone furoate (FF)/vilanterol (100/25 mcg or 200/25 mcg) or FF (100 mcg) in persistent asthma. *J Asthma*. 2015;52(10):1073-1083. **2.** Bleecker ER, Lötvall J, O'Byrne PM, et al. Fluticasone furoate-vilanterol 100-25 mcg compared with fluticasone furoate 100 mcg in asthma: a randomized trial. *J Allergy Clin Immunol Pract*. 2014;2(5):553-561. **3.** Bateman ED, O'Byrne PM, Busse WW, et al. Once-daily fluticasone furoate (FF)/vilanterol reduces risk of severe exacerbations in asthma versus FF alone. *Thorax*. 2014;69(4):312-319.

BREO ELLIPTA (fluticasone furoate and vilanterol inhalation powder)

Experience the difference with BREO...

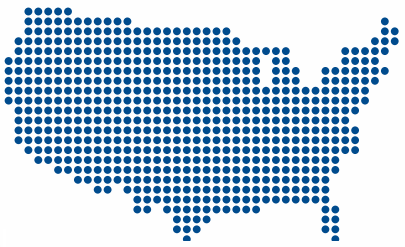
100% of eligible commercially insured patients pay no more than $10 a month*†:

A coupon for eligible patients to pay no more than $10 for each prescription for up to 12 months of BREO (30-day supplies). Not for Medicare enrollees, participants in other government programs, or patients aged 65 years or older.

Ask your Sales Representative about savings offers for BREO

*Offer is good for up to 12 uses. Patients in government programs, including Medicare, are not eligible for savings offers. Please see the savings offer for complete rules and eligibility.

†Eligible commercially insured patients will pay $10 per 30-day supply of BREO. Eligible patients without insurance to cover the cost of their prescription will receive up to $100 in savings on each 30-day supply of BREO. Patients will be responsible for any remaining out-of-pocket cost. Please visit GSKforyou.com for more details.



Individual access may vary by geography and plan benefit design.

BREO HAS BETTER FORMULARY COVERAGE NATIONALLY THAN SYMBICORT

Source: Managed Markets Insight & Technology, LLC, database as of January 2018.

6 MILLION

More Unrestricted Commercial Lives Than Symbicort

1.8 MILLION

More Unrestricted Medicare Part D Lives Than Symbicort

"Unrestricted coverage" means reimbursement from a health plan without accompanying step edits or prior authorizations.

BREO has the best unrestricted Medicare Part D formulary coverage in its class

"Best unrestricted formulary coverage" defined by percent of Medicare Part D lives with unrestricted formulary coverage for BREO 96% vs ADVAIR 86%, AirDuo 7%, Dulera 25%, and Symbicort 92%. Total covered lives on Medicare Part D plans.

What you need to know about this formulary information:

Formulary status may vary and is subject to change. Formulary comparisons do not imply comparable indications, safety, or efficacy. This is not a guarantee of partial or full coverage or payment. Consumers may be responsible for varying out-of-pocket costs based on an individual's plan and its benefit design. Each plan administrator determines actual benefits and out-of-pocket costs per its plan's policies. Verify coverage with plan sponsor or Centers for Medicare & Medicaid Services. Medicare Part D patients may obtain coverage for products not otherwise covered via the medical necessity process.

Nationally, BREO Unrestricted Commercial Coverage 162 Million; Symbicort Unrestricted Commercial Coverage 156 Million. Medicare Part D BREO Unrestricted Lives covered 39 Million; Symbicort 37 Million.

Visit us at GSK Booth #1734

BREO ELLIPTA was developed in collaboration with INNOVIVA

www.BREOHCP.com

Please see Important Safety Information for BREO on previous pages.
Please see Brief Summary of Prescribing Information for BREO on the following pages.

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BREO ELLIPTA
(fluticasone furoate and vilanterol inhalation powder)

BREO ELLIPTA
(fluticasone furoate and vilanterol inhalation powder)

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

INDICATIONS AND USAGE

1.2 Treatment of Asthma: BREO is indicated for the once-daily treatment of asthma in patients aged 18 years and older. BREO should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta$_2$-adrenergic agonist (LABA). 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 chronic obstructive pulmonary disease (COPD) or asthma where intensive measures are required *[see Warnings and Precautions (5.2)]*, and 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 Serious Asthma-Related Events – Hospitalizations, Intubations, Death: Use of LABA as monotherapy (without ICS) for asthma is associated with an increased risk of asthma-related death *[see Salmeterol Multicenter Asthma Research Trial (SMART)]*. Available data from controlled clinical trials also suggest that use of LABA as monotherapy increases the risk of asthma-related hospitalization in pediatric and adolescent patients. These findings are considered a class effect of LABA monotherapy. When LABA are used in fixed-dose combination with ICS, data from large clinical trials do not show a significant increase in the risk of serious asthma-related events (hospitalizations, intubations, death) compared with ICS alone *(see Serious Asthma-Related Events with Inhaled Corticosteroid/Long-acting Beta$_2$-adrenergic Agonists)*. Serious Asthma-Related Events with Inhaled Corticosteroid/Long-acting Beta$_2$-adrenergic Agonists: Four (4) large, 26-week, randomized, double-blind, active-controlled clinical safety trials were conducted to evaluate the risk of serious asthma-related events when LABA were used in fixed-dose combination with ICS compared with ICS alone in subjects with asthma. Three (3) trials included adult and adolescent subjects aged 12 years and older: 1 trial compared budesonide/formoterol with budesonide, 1 trial compared fluticasone propionate/salmeterol inhalation powder with fluticasone propionate inhalation powder, and 1 trial compared mometasone furoate/formoterol with mometasone furoate. The fourth trial included pediatric subjects aged 4 to 11 years and compared fluticasone propionate/salmeterol inhalation powder with fluticasone propionate inhalation powder. The primary safety endpoint for all 4 trials was serious asthma-related events (hospitalizations, intubations, death). A blinded adjudication committee determined whether events were asthma related. The 3 adult and adolescent trials were designed to rule out a risk margin of 2.0, and the pediatric trial was designed to rule out a risk margin of 2.7. Each individual trial met its pre-specified objective and demonstrated non-inferiority of ICS/LABA to ICS alone. A meta-analysis of the 3 adult and adolescent trials did not show a significant increase in risk of a serious asthma-related event with ICS/LABA fixed-dose combination compared with ICS alone. These trials were not designed to rule out all risk for serious asthma-related events with ICS/LABA compared with ICS. In a meta-analysis of serious asthma-related events in subjects with asthma aged 12 years and older taking an ICS/LABA (n=17,537) or ICS (n=17,552), events included: serious asthma-related event (number of subjects with event that occurred within 6 months after the first use of study drug or 7 days after the last date of study drug, whichever date was later; subjects can have one or more events, but only the first event was counted for analysis; a single, blinded, independent adjudication committee determined whether events were asthma related), 116, 105 (hazard ratio [95% CI], estimated using a Cox proportional hazards model for time to first event with baseline hazards stratified by each of the 3 trials: 1.10 [0.85, 1.44]); asthma-related death, 2, 0; asthma-related intubation (endotracheal), 1, 2; asthma-related hospitalization (≥24-hour stay), 115, 105. Subjects on ICS/LABA or ICS were randomized and had taken at least 1 dose of study drug. Planned treatment was used for analysis. The pediatric safety trial included 6,208 pediatric subjects aged 4 to 11 years who received ICS/LABA (fluticasone propionate/salmeterol inhalation powder) or ICS (fluticasone propionate inhalation powder). In this trial, 27/3,107 (0.9%) subjects randomized to ICS/LABA and 21/3,101 (0.7%) subjects randomized to ICS experienced a serious asthma-related event. There were no asthma-related deaths or intubations. ICS/LABA did not show a significantly increased risk of a serious asthma-related event compared with ICS based on the pre-specified risk margin (2.7), with an estimated hazard ratio of time to first event of 1.29 (95% CI: 0.73, 2.27). Salmeterol Multicenter Asthma Research Trial (SMART): A 28-week, placebo-controlled, U.S. trial that compared the safety of 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 versus 3/13,179 in subjects treated with placebo; relative risk: 4.37 [95% CI: 1.25, 15.34]). Use of background ICS was not required in SMART. The increased risk of asthma-related death is considered a class effect of LABA monotherapy.

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 Inhaled Corticosteroids: 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

Use of LABA may result in the following: serious asthma-related events – hospitalizations, intubations, death *[see Warnings and Precautions (5.1)]* and cardiovascular effects *[see Warnings and Precautions (5.12)]*. 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)]*, and 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 2 long-term trials. 12-Week Trials: Trial 1 was a 12-week trial that evaluated the efficacy of BREO 100/25 in adult and adolescent 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) in subjects with asthma taking BREO 100/25 (n=201), fluticasone furoate 100 mcg (n=205), or placebo (n=203), respectively, were: nasopharyngitis, 10%, 7%, 7%; oral candidiasis (includes oral candidiasis and oropharyngeal candidiasis), 2%, 2%, 0%; headache, 5%, 4%, 4%; oropharyngeal pain, 2%, 2%, 1%; dysphonia, 2%, 1%, 0%. Trial 2 was a 12-week trial that evaluated the efficacy of BREO 100/25, BREO 200/25, and fluticasone furoate 100 mcg in adult and adolescent 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) in subjects with asthma taking BREO 200/25 (n=346), BREO 100/25 (n=346), or fluticasone furoate 100 mcg (n=347), respectively, were: headache, 8%, 8%, 9%; nasopharyngitis, 7%, 6%, 7%; influenza, 3%, 3%, 1%; upper respiratory tract infection, 2%, 2%, 3%; sinusitis, 2%, 1%, <1%; bronchitis, 2%, <1%, 2%; oropharyngeal pain, 2%, 2%, 1%; 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 adult and adolescent 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 noted for Trials 1 and 2, adverse reactions occurring in ≥2% of subjects treated with BREO 200/25 included viral respiratory tract infection, pharyngitis, pyrexia, and arthralgia. 12-Month Trial: Long-term safety data are 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 adult and adolescent 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 noted for Trials 1 and 2, adverse reactions occurring in ≥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 1 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. Respiratory, Thoracic, and Mediastinal Disorders: paradoxical bronchospasm.

(continued on next page)

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: Risk Summary: There are insufficient data on the use of BREO, fluticasone furoate, or vilanterol in pregnant women. There are clinical considerations with use of BREO in pregnant women *(see Clinical Considerations)*. In an animal reproduction study, fluticasone furoate and vilanterol administered by inhalation alone or in combination to pregnant rats during the period of organogenesis produced no fetal structural abnormalities. The highest fluticasone furoate and vilanterol doses in this study were approximately 5 and 40 times the maximum recommended human daily inhalation doses (MRHDID) of 200 and 25 mcg in adults, respectively. *(See Data.)* The estimated risk of major birth defects and miscarriage for the indicated populations is unknown. In the U.S. general population, the estimated risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Clinical Considerations: *Disease-Associated Maternal and/or Embryofetal Risk:* In women with poorly or moderately controlled asthma, there is an increased risk of several perinatal outcomes such as pre-eclampsia in the mother and prematurity, low birth weight, and small for gestational age in the neonate. Pregnant women should be closely monitored and medication adjusted as necessary to maintain optimal control of asthma. *Labor and Delivery:* There are no human studies evaluating the effects of BREO during labor and delivery. Because of the potential for beta-agonist interference with uterine contractility, use of BREO during labor should be restricted to those patients in whom the benefits clearly outweigh the risks. Data: *Animal Data: Fluticasone Furoate and Vilanterol:* In an embryofetal developmental study, pregnant rats received fluticasone furoate and vilanterol during the period of organogenesis at doses up to approximately 5 and 40 times the MRHDID, respectively, alone or in combination (on a mcg/m^2 basis at inhalation doses up to approximately 95 mcg/kg/day). No evidence of structural abnormalities was observed. *Fluticasone Furoate:* In 2 separate embryofetal developmental studies, pregnant rats and rabbits received fluticasone furoate during the period of organogenesis at doses up to approximately 4 and 1 times the MRHDID, respectively (on a mcg/m^2 basis at maternal inhalation doses up to 91 and 8 mcg/kg/day). No evidence of structural abnormalities in fetuses was observed in either species. In a perinatal and postnatal developmental study in rats, dams received fluticasone furoate during late gestation and lactation periods at doses up to approximately 1 time the MRHDID (on a mcg/m^2 basis at maternal inhalation doses up to 27 mcg/kg/day). No evidence of effects on offspring development was observed. *Vilanterol:* In 2 separate embryofetal developmental studies, pregnant rats and rabbits received vilanterol during the period of organogenesis at doses up to approximately 13,000 and 1,000 times, respectively, the MRHDID (on a mcg/m^2 basis at maternal inhalation doses up to 33,700 mcg/kg/day in rats and on an AUC basis at maternal inhaled doses up to 5,740 mcg/kg/day in rabbits). No evidence of structural abnormalities was observed at any dose in rats or in rabbits up to approximately 160 times the MRHDID (on an AUC basis at maternal doses up to 591 mcg/kg/day). However, fetal skeletal variations were observed in rabbits at approximately 1,000 times the MRHDID (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. In a perinatal and postnatal developmental study in rats, dams received vilanterol during late gestation and the lactation periods at doses up to approximately 3,900 times the MRHDID (on a mcg/m^2 basis at maternal oral doses up to 10,000 mcg/kg/day). No evidence of effects in offspring development was observed.

8.2 Lactation: Risk Summary: There is no information available on the presence of fluticasone furoate or vilanterol in human milk, the effects on the breastfed child, or the effects on milk production. Low concentrations of other inhaled corticosteroids have been detected in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BREO and any potential adverse effects on the breastfed child from fluticasone furoate or vilanterol or from the underlying maternal condition.

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 1 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 COPD included 4,820 subjects aged 65 and older and 1,118 subjects aged 75 and older. 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 <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

See FDA-Approved Patient Labeling

Serious Asthma-Related Events: Inform patients with asthma that LABA when used alone increases the risk of asthma-related hospitalization or asthma-related death. Available data show that when ICS and LABA are used together, such as with BREO, there is not a significant increase in the risk of these events. 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, treat it 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.

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Sunday Awards Session Honors Four Recipients

Four renowned physicians and researchers will be honored during Sunday's Awards Session, featuring the Amberson Lecture and the presentation of the Trudeau Medal and two Distinguished Achievement Awards.

Scott T. Weiss, MD, MS

AMBERSON LECTURE

This year's Amberson Lecture will be delivered by Scott T. Weiss, MD, MS, who will present "Network Methods to Prevent Asthma." Dr. Weiss is a professor of medicine at Harvard Medical School. He also serves as director of Partners HealthCare Personalized Medicine and associate director of the Channing Division of Network Medicine.

In his lecture, Dr. Weiss plans to talk about network science, a relatively new branch of science that provides a framework to organize and analyze the multiple types of Omics data being generated in the wake of the Human Genome Project. Some of these data types include genome sequence, transcriptomic sequence, miRNA sequence, metabolomics, and proteomics.

Dr. Weiss will give some examples of how these data can be combined to find the molecular basis of disease, including the use of networks to find the molecular and genetic similarity between asthma and COPD, to understand how maternal asthma is related to preeclampsia, and to explore the origins of asthma by looking at vitamin D and how it influences genetic risk of asthma through its influence on the sphingolipid pathway.

Dr. Weiss says the goal of the lecture is to emphasize that combining multiomics data with a deep understanding of disease natural history and strong study designs will advance science and ultimately develop cures for disease.

"Network approaches are one of the most important developments for analysis of big or multiomics data," he says. "I think that is the cutting edge of science and where research needs to go. I want to show the ATS membership the utility of these approaches in potentially curing disease. These new methods of scientific discovery are important and can impact scientists, physicians, and patients, hopefully inspiring all of us to apply these approaches to future scientific problems."

Jeffrey A. Whitsett, MD

EDWARD LIVINGSTON TRUDEAU MEDAL

The recipient of this year's Edward Livingston Trudeau Medal is Jeffrey A. Whitsett, MD. Dr. Whitsett is co-director of the Perinatal Institute and chief of the Division of Neonatology, Perinatal, and Pulmonary Biology at Cincinnati Children's Hospital. His work involving surfactant production in preterm infants spans decades and has contributed significantly to saving the lives of countless newborns. (See related Q&A on page 17.)

DISTINGUISHED ACHIEVEMENT AWARDS

Qutayba Hamid, MBChB, PhD, and Monica Kraft, MD, will receive this year's Distinguished Achievement Awards.

Dr. Hamid is a professor of medicine, vice chancellor, and dean of medicine at the University of Sharjah in United Arab Emirates. He is also a professor of medicine at McGill University in Montreal, Canada. He was until recently the director of Meakins Christie labs, the James McGill Professor of Medicine and Pathology, and the MUHC Strauss Chair in Respiratory Medicine at McGill University Health Centre.

Qutayba Hamid, MBChB, PhD

Dr. Hamid's research focuses on better understanding the mechanisms of asthma and obstructive airway disease, especially the role of cytokines. In earlier years, he led the application of molecular biology, particularly *in situ* hybridization of lung tissue to define airway pathobiology, and pioneered the hypothesis that T2 cytokines, particularly IL-5, play a major role in allergic asthma. This led to the development of biological treatment for asthma. More recently, he has explored the role of IL-17 in patients with difficult-to-treat asthma and the mechanism of steroid resistance.

Dr. Kraft has served as the Robert and Irene Flinn Endowed Chair of Medicine at the University of Arizona Health Sciences Center since 2015. Prior to that, she was the director of the Asthma, Allergy, and Airway Center, division chief for pulmonary, allergy, and critical care medicine, vice chair for research, and Charles C. Johnson Distinguished Professor of Medicine in the Duke University Department of Medicine.

Awards Session (G2)
4:30-5:45 p.m.
Sunday
Hall H (Ground Level), San Diego Convention Center

Monica Kraft, MD

Dr. Kraft has made multiple discoveries of pathophysiologic mechanisms of inflammation and innate immunity that are directly involved in human asthma and are directly associated with clinical characteristics and outcomes of the disease. Her major accomplishments are the translation of cellular events in asthma, including the presence of distal lung inflammation, specific host-pathogen interactions, and innate immune dysfunction to relevant changes in clinical outcomes. She has discovered a link between surfactant protein A and asthma and is developing a therapeutic alternative for asthma based on the discovery. ■

Proteins Could be Key to Rare Lung Disorders

Pediatric rare lung diseases, including disorders such as childhood interstitial and diffuse lung diseases primary ciliary dyskinesia, and lung involvement in systemic juvenile inflammatory arthritis, are associated with high morbidity and are often life-threatening.

Amy L. Firth, PhD

These disorders are poorly understood, under-recognized, and have limited evidence-based therapeutic options. Despite significant advances, PRLD research is impeded by a lack of model systems and knowledge of molecular targets, largely due to a poor understanding of the disease pathogenesis.

Sunday's session "Accelerating Scientific Advancement of Rare Pediatric Lung Diseases" will focus on recent progress toward addressing scientific gaps and barriers in PRLD research. The latest model systems, tools, and technologies accelerating research in this field will be discussed, as well as recent translational advances for these diseases.

According to session moderator Amy L. Firth, PhD, assistant professor of medicine at the University of Southern California, two of the significant advances discussed during the session will cover the ciliary proteome and mutations in pediatric interstitial lung disease.

"Lawrence Ostrowski, PhD, will be presenting on the ciliary proteome and PCD," she says. "His talk will discuss quantitative analysis of the ciliary proteome and how identification of several previously unknown proteins as major constituents of human airway cilia may lead to advances for our understanding of PCD."

Cilia are essential to many cellular processes, and although many major axonemal components have been identified and studied, how they interact to form a functional axoneme is not completely understood.

"Dr. Ostrowski's research has focused on understanding the protein composition of human airway cilia and has identified over 400 proteins present in cilia," Dr. Firth says. "Many of these are previously uncharacterized proteins, some with high abundance in cilia."

Proteomic analysis may be used to identify candidate genes for the disease-causing mutations through identification and characterization of proteins that are missing in cilia from patients with PCD. The Ostrowski lab has focused on characterizing some of these, including highly abundant ERICH3, C1orf87, and CCDC181.

Accelerating Scientific Advancement of Rare Pediatric Lung Diseases (A9)
9:15-11:15 a.m.
Sunday
Room 7 A-B (Upper Level), San Diego Convention Center

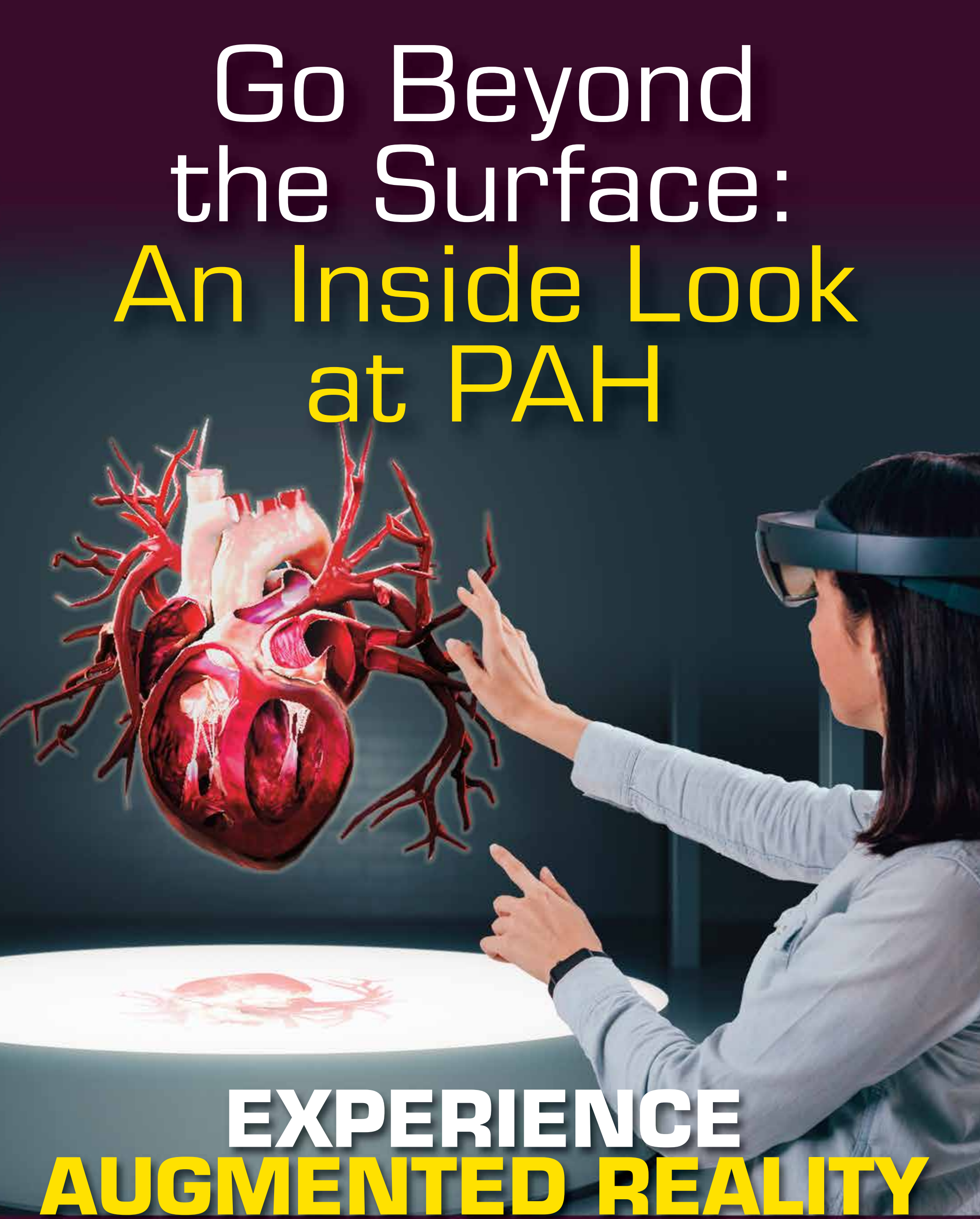
"These studies will significantly advance our understanding of motile cilia and increase our understanding of PCD defects," Dr. Firth says.

Following Dr. Ostrowksi's talk, Matthias Griese, MD, will present on adenosine triphosphate (ATP)-binding cassette subfamily A member 3 (ABCA3) mutations in pediatric interstitial lung disease. He will discuss his most recent work in this area, focusing on the evaluation of therapeutic options for patients with ABCA3 mutations.

ABCA3 is a phospholipid transporter in lung lamellar bodies essential for the assembly of pulmonary surfactant. Mutations in the ABCA3 gene cause respiratory distress syndrome in neonates and interstitial lung disease in children and adults.

"In early 2018, Dr. Griese published work demonstrating that mutant ABCA3 proteins could be rescued by bithiazole correctors C13 and C17," Dr. Firth says. "The identification of such lead molecules represents a huge step toward pharmacotherapy of ABCA3 misfolding-induced lung disease." ■

Go Beyond the Surface: An Inside Look at PAH



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Q&A Trudeau Medalist's Work Helps Save Newborns

Jeffrey A. Whitsett, MD, recipient of this year's Edward Livingston Trudeau Medal, spoke with the ATS Daily Bulletin about his research on surfactant production and function in preterm infants, the work he's doing now, his clinical contributions, and more.

Q Tell us about your research involving surfactant production and preterm infants.

A: Neonatal Intensive Care Units (NICUs) were established in the 1960s as advances in clinical care and fundamental insights into biochemistry and physiology began to enable better survival of newborn infants. My career path as a pediatrician became clear to me while training at Columbia University College of Physicians and Surgeons, as we began to care for smaller preterm infants and other critically ill children. It was clear that respiration—both the physiology and biochemistry—remained a formidable hurdle limiting their survival.

Fundamental insights regarding the surfactant system from Mary Ellen Avery, Jeremiah Mead, John Clements (all previous Trudeau awardees), and Goran Enhorning, to name a few, provided the insights supporting the development of surfactant replacement therapy.

Starting my research laboratory during my neonatology fellowship at Cincinnati Children's Hospital Medical Center—circa 1976—it seemed that we did not understand why surfactant lipids spread rapidly and tolerated "dynamic" compression and "de-compression" (churning) during the breathing cycle. Although biochemical studies of surfactant extracts that were surface "active" concluded that there were no proteins in the lipids—circa 1980—we nevertheless searched for proteins that might confer the remarkable functions of pulmonary surfactant.

Q What kind of impact has that research had for premature infants?

A: Now, nearly 40 years later, the field has a much clearer understanding of the structure, function, and regulation of surfactant lipids and proteins. Identifying SP-B and SP-C in the surfactant extracts, we worked closely with Abbott Laboratories to optimize the manufacturing and testing of surfactant replacements and were involved in the FDA approval process of surfactant for the treatment of infants with RDS. We now have an in-depth understanding of SP-A, B, C, and D, the complexity of alveolar surfactant homeostasis, the functions of alveolar type 2 cells, and alveolar macrophages.

We worked at an early time in the "molecular biology" revolution: cloning, deleting, and mutating genes in vivo, discovering gene and protein structures, and uncovering the gene networks that mediate lung structure and function. Children with mutations in genes critical for surfactant homeostasis and lung formation were identified. Advances in applying continuous positive airway pressure and mechanical modes of ventilation, antenatal steroids, infant nutrition, and surfactant replacement transformed the care of preterm infants worldwide. Progress was made possible by fundamental scientific and clinical advances contributed by so many.

Q What are you working on now?

A: I continue to be enthralled by the exponential pace of technology and discovery in science. Scientific advances were fueled by the human genome, cell-molecular biology, and now the application of bioinformatics and computer science to the world of "Omics."

My laboratory continues to be intrigued by the surfactant system, by the role of respiratory epithelium in health and disease, the molecular circuitry forming and repairing the lung, and the interrelationships among epithelial biology, inflammation, innate host defense, and the pathogenesis of chronic lung disease.

What are the molecular and cellular processes underlying chronic lung disorders in children and adults for which we lack understanding and therefore lack effective treatments? What are the cells that form the lung? How do they find themselves in correct numbers and in appropriate places to maintain lung structure and function? Will understanding the molecular circuitry that creates lung architecture and its responses to environmental challenges provide the insights needed to prevent and treat pulmonary disease? There are many roads to travel and more questions to answer.

Q What clinical contributions have you made in your region?

A: I have been privileged to care for newborn infants and, throughout my career, perhaps there has been no greater joy than to see critically ill children recover, head for home, and start their lives. As clinical expertise in the care of newborns grew in the late 20th century, it was increasingly clear that all newborn infants would benefit from the expert care that advances in neonatology and pediatrics had made possible. While neonatal intensive care was then primarily a practice in universities and tertiary centers, we thought that collaborating with all delivery hospitals in our region might improve clinical outcomes.

We established a clinical network with all local hospitals in our region, now consisting of five tertiary-quaternary care hospitals and an additional nine delivery centers, covering nearly 30,000 infant births each year. Working with incredibly capable hospital staffs, nurses, neonatologists, pediatricians, and obstetricians enabled better outcomes for infants and families in our region.

Q Why is it important to you to participate in mentoring?

A: At a certain age, perpetuity becomes ever more important. The future of science and medicine rests on our trainees, their trainees, and the institutions that support them. The greatest joy in my scientific career rests on my daily interactions with co-workers, students, fellows, and faculty. The flow of ideas, the curiosity, and capability of so many talented people is not unlike an orchestra in harmony.

Mentoring is not "how to" but a dialectic by which insights are gained and shared as we together develop confidence in scientific processes and our shared ability to ask and answer the many unanswered questions before us.

Q What does it mean to you to receive the Trudeau Medal?

A: I am pleased and honored, mostly for the reverence with which I hold our profession as scientists and clinicians, for the process of science and learning, and especially for my lifelong opportunity to work with so many remarkable colleagues, families, and their children. The Trudeau Medal links clinical care and scientific discovery with the very breaths we share and depend upon throughout our lives. ■

Exhibit Hall Hours

SUNDAY, MAY 20
10:30 a.m.–3:30 p.m.
Unopposed Hours: 1:15–2:15 p.m.

MONDAY, MAY 21
10:30 a.m.–3:30 p.m.
Unopposed Hours: 1:15–2:15 p.m.

TUESDAY, MAY 22
10:30 a.m.–3:30 p.m.
Unopposed Hours: 1:15–2:15 p.m.

Speakers Are the Key to Transparency

International Conference speakers are required to ensure that ATS audiences are aware of any professional or personal relationships they have with companies that are relevant to their presentation content.

The support that pharmaceutical and medical device companies provide for the research, education, and patient care conducted by ATS members and other International Conference speakers is instrumental to finding cures and maintaining quality of life. The ATS and industry take great care to ensure that relevant commercial support received by speakers or relevant personal investments is disclosed and made known to ATS 2018 attendees.

To comply with requirements of the Accreditation Council for Continuing Medical Education, speakers in sessions designated for CME were required to complete extensive questionnaires for review of conflicts of interest ahead of the International Conference. Speakers also re-enter the names of relevant company affiliations when they submit their presentation slides online, so that a disclosure screen automatically appears just before their talk. In addition, a written summary of disclosures is also posted on the International Conference website and available through the ATS 2018 app.

More information on ATS 2018 requirements for speakers is available at **conference.thoracic.org/speakers/session-speaker-instructions.php** ■

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Debunking Medical Myths

Exciting advances in iPS cell differentiation and *ex vivo* lung tissue bioengineering are gaining new attention as potential therapies for lung disease and transplantation. Stripping away the myths from the facts surrounding these recent advances is the goal of Sunday's session, "Mythbusters: Bioengineering Approaches Will Revolutionize Respiratory Medicine in the Next 10 Years."

Specifically, session leaders Melanie Königshoff, MD, PhD, professor of medicine at the University of Colorado, and Darcy Wagner, PhD, a Wallenberg Molecular Medicine Fellow and assistant professor at Sweden's Lund University, will explore the debate of whether exogenous cells are necessary to induce regeneration or if iPS cells, in the absence of a transplantable matrix, will be sufficient for exogenous approaches to regeneration. A group of leading experts in this field will discuss whether acellular human scaffolds are necessary for *ex vivo* regeneration of lung tissue for transplantation or if xenogeneic scaffolds can be used.

ATS Mythbusters: Bioengineering Approaches Will Revolutionize Respiratory Medicine in the Next 10 Years (A86)

2:15-4:15 p.m.

Sunday

Pacific Ballroom 18-19 (North Tower, First Floor), Marriott Marquis San Diego Marina

"Advances in iPS cell differentiation and *ex vivo* lung tissue bioengineering are important for researchers working in both fields, since one of the visions is that these technologies can be merged to generate functional lung tissue for transplantation," Dr. Königshoff says. "If the patient's own cells can be used, it may minimize the long list of complications that often are encountered following clinical transplantation. Additionally, if the promise of bioengineered organs can be achieved, it can address the huge shortage of organs for lung transplantation," Dr. Wagner adds.

Darcy Wagner, PhD

Melanie Königshoff, MD, PhD

In addressing myths in the debate, Dr. Wagner says there has been clinical success in regeneration of other organs and tissues, despite the absence of exogenous cells in the transplanted matrix. However, for the lung, because it has a more complex architecture and is heavily vascularized, researchers believe cells will be necessary for a tissue engineering approach. Conversely, other recent research suggests that if the proper cells are used and cell signaling pathways are tightly controlled with growth factors and small molecules, these cells can contain the necessary information to regenerate structures that resemble the native architecture. It is not yet known if replication of developmental programs using iPS cells will be able to achieve complete organ generation.

According to Dr. Königshoff, another potential application of both fields of research, and in particular iPS cells, is to model diseases in a dish. This provides a platform for drug testing and for personalized medicine approaches on cells derived from individual patients. In many diseases, such as cystic fibrosis, there are several known mutations. Therefore, testing different drugs on differentiated iPS cells may help predict patient responses.

"This research has huge implications for drug targeting," says Dr. Wagner. "If you only treat the cells and do not treat the underlying matrix, the disease will likely persist since the cells will continue to receive pathologic cues."

For attendees, the session will not only explore the myths in recent advances of both approaches, it will spark further dialogue about how these two fields can interact more.

"There already have been several studies that combined these approaches, but more are needed to really understand how regeneration using adult, endogenous stem and progenitor, or iPS cells can be achieved," Dr. Königshoff says. "Clinicians and basic scientists will certainly come away with new ideas and new questions about the many gaps that still exist between these two fields." ■

New Therapies Target Mitochondria

There's a new bad kid on the block driving lung disease, including pulmonary hypertension and inflammatory diseases: dysfunctional mitochondria. Mitochondrial dysfunction as a driver of oxidative injury is not new, but technological advances are helping researchers and clinicians understand just how intimately involved mitochondria can be in disease pathophysiology—and to identify new therapies that target mitochondria.

Setting the Stage: Mitochondrial Dysfunction as a Driver of Chronic Disease (A5)

9:15-11:15 a.m.

Sunday

Pacific Ballroom 21 (North Tower, First Floor), Marriot Marquis San Diego Marina

"The primary function of mitochondria is to provide energy so the cell continues to live and perform its appointed function," says Serpil Erzurum, MD, chair of the Lerner Research Institute and Alfred Lerner Memorial Chair in Innovative Biomedical Research at the Cleveland Clinic. "Mitochondria are wonderfully adaptive to environmental and nutritional factors to continue providing energy, but under some circumstances, those changes can be maladaptive and risk factors for disease."

Dr. Erzurum will co-chair the first basic science symposium of ATS this year, Setting the Stage: Mitochondrial Dysfunction as a Driver of Chronic Disease. She will share the podium with Jane C. Deng, MS, MD, associate professor of pulmonary/critical care at the University of Michigan.

Mitochondria have been recognized as essential players in human health and disease since they were identified as the primary cellular energy source used by aerobic organisms nearly a century ago. The Krebs Cycle oxidizes nutritional components to release chemical energy in the form of adenosine triphosphate. The same cycle produces precursors of amino acids and other biologically active compounds that play key roles in multiple biochemical pathways.

Serpil Erzurum, MD

Metabolism has long been known to have effects on gene expression, Dr. Erzurum says. In fact, one of the first well-understood metabolic genetic control mechanisms was the lac operon that allows prokaryotes to metabolize lactose in the absence of the preferred carbon source, glucose.

It wasn't until the 1980s that the wider regulatory functions of the mitochondria began to emerge. Mitochondrial activity doesn't just regulate energy production, it regulates cellular function and activity in response to environmental factors, such as nutrition and exposures such as tobacco smoke.

"Changes in nutrient oxidation by mitochondria can activate T-cells to differentiate along pathways to helper or regulatory cell phenotypes, which set the stage for persistence or resolution of inflammation," Dr. Erzurum says. "How mitochondria process nutrition into energy affects immune function throughout the body. Some studies suggest that nutritional supplements or pharmacologic interventions can block or divert metabolic pathways to the mitochondria and decrease inflammation or promote resolution of injury."

Lung dysfunction in COPD? Mitochondrial dysfunction from smoking can lead to immune dysregulation that alters lung function. Oxidative stress in the airways can lead to mitochondrial dysfunction and lung disease, which might be alleviated or reversed using mesenchymal stem cells. A growing list of immune-mediated disease physiology is being tracked upstream to mitochondrial dysfunction. Many of those newly recognized pathways suggest novel therapies that target the mitochondria.

"This symposium is a refresher on mitochondria and how bioenergetics dictate health and predispose to maladaptive outcomes," Dr. Erzurum says. "Life requires energy, and the mitochondria deliver that energy and drive gene expression and cell functions. Understanding mitochondrial metabolism provides new insights to mechanisms underlying resilience and disease." ■

New ATS Executive Director

ATS has a new executive director. Karen Collishaw, MPP, a highly experienced medical association leader, joined the ATS at the end of April after a national search. She succeeds Stephen C. Crane, PhD, MPH, who has served as ATS executive director since 2007 and is retiring.

"We believe that Karen is the ideal person to continue to advance the mission and vision of the ATS," says ATS President Marc Moss, MD. "We're glad she joined the ATS family, and we are looking forward to working with her."

Ms. Collishaw said that she is excited that one of her first responsibilities as the Society's new executive director is to attend the ATS International Conference. "I know how central this conference is to the respiratory community and how clinicians and researchers from all over the world look forward to sharing information and discussing ways to advance pulmonary, critical care, and sleep medicine," she says. "The conference is really at the heart of the ATS's efforts to help the world breathe."

Before joining the ATS, Ms. Collishaw assisted the American Society for Microbiology strategically plan its policy and advocacy activities. Prior to this interim position, she was the president and CEO of the Community Health Accreditation Partner.

Before leading CHAP, Ms. Collishaw served in executive leadership positions with two professional medical societies—the American Academy of Dermatology and the American College of Cardiology. At AAD, she established the first strategic plan for quality and patient safety.

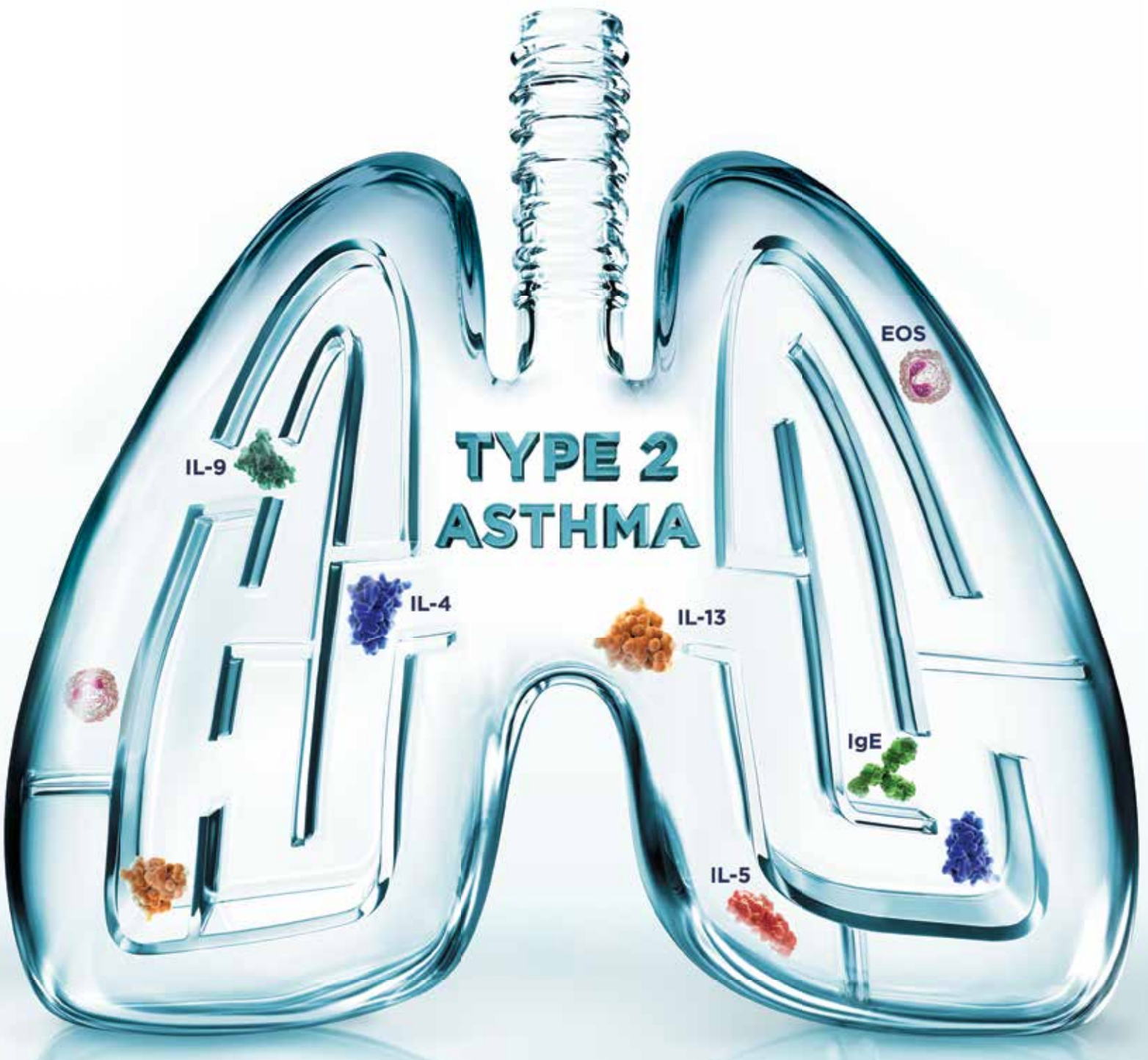
At ACC, Ms. Collishaw was responsible for significant growth in the college's policy and advocacy efforts. She also managed the ACC's annual meeting. During her tenure at ACC, the organization was recognized as one of nine highly performing associations in the book Seven Measures of Success, What Remarkable Associations Do That Others Don't.

Ms. Collishaw earned her Master of Public Policy degree from Georgetown University and a Bachelor of Arts in Government from Cornell University. She is a certified association executive and past president of the American Association of Medical Society Executives.

Both Ms. Collishaw and Dr. Crane are at ATS 2018. ■

IN YOUR PATIENTS WITH ASTHMA

LOOK BEYOND EOSINOPHIL AND IgE LEVELS TO GET A CLEARER PICTURE OF TYPE 2 INFLAMMATION



Type 2 asthma encompasses a range of biomarkers driven by Type 2 inflammation.

LEARN MORE AT BOOTH #2921
or visit UnderstandingType2Asthma.com

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Non-CME Symposia Boost Learning Potential

Don't miss the Non-CME Symposia, an important part of the ATS 2018 International Conference. The ATS encourages all full-conference participants to attend these programs. Please see the Tuesday issue of the ATS 2018 Daily Bulletin for a list of Tuesday Non-CME Symposia.

SUNDAY

6:30-9:30 p.m.

Manchester Grand Hyatt San Diego, Harbor Ballroom G-I (Second Level, Harbor Tower)

Redefining the Approach to Asthma and COPD: A New Perspective on Mechanisms of Disease

You are cordially invited to an AstraZeneca sponsored non-CME dinner program on emerging mechanisms of disease in asthma and COPD. This faculty-led symposium will examine asthma and COPD from the phenotype/endotype perspective to demonstrate the importance of relating observable characteristics to mechanisms of disease.

Speakers: **Bartolome R. Celli, MD**, *professor of medicine, Harvard Medical School;* **Nicola Hanania, MD, MS**, *associate professor of pulmonary and critical care, Baylor College of Medicine, Houston, Texas;* **Jill Ohar, MD**, *professor, Wake Forest Baptist School of Medicine, Winston-Salem, North Carolina;* **Sanjay Sethi, MD**, *professor, University of Buffalo*

Company: AstraZeneca

6:30-9:30 p.m.

Manchester Grand Hyatt San Diego, Grand Hall D (Lobby Level)

Real-World Impact in IPF: How to Make System Level Changes

IPF experts will share real-world examples of successful initiatives that have impacted clinical care of patients with IPF. Education isn't confined to this session—interested learners will be offered a series of virtual mentorships with faculty to discuss potential efforts with their own institutions.

Speakers: **Evans R. Fernández Pérez, MD, MS**, *associate professor, National Jewish Health;* **Amy L. Olson, MD, MSPH**, *assistant professor, National Jewish Health;* **Meena Kalluri, MD**, *associate professor, University of Alberta*

Company: This non-CME educational program is sponsored by The France Foundation, and supported by independent educational grants from Boehringer Ingelheim Pharmaceuticals, Inc., and Genentech.

6:30-9:30 p.m.

Manchester Grand Hyatt San Diego, Grand Hall A (Lobby Level)

New Therapies, New Opportunities, and New Challenges in Managing NTM

Wrap up your ATS experience with a pre-activity social event. Relax and challenge your colleagues in a nontuberculous mycobacterial trivia contest, and enjoy cocktail hour before we begin. Then join Drs. David Griffith, Kevin Winthrop, and Ted Marras as they describe patients at high risk for NTM lung infection and apply the latest emerging therapies to clinical cases.

Speakers: **David Griffith, MD**, *professor of medicine, University of Texas Health Science Center;* **Ted Marras, MD**, *associate professor, University of Toronto;* **Kevin Winthrop, MD, MPH**, *associate professor, Oregon Health & Science University*

Company: This non-CME educational program is sponsored by The France Foundation, and supported by an independent educational grant from Insmed, Incorporated.

6:30-9:30 p.m.

Manchester Grand Hyatt San Diego, Seaport Ballroom G-H (Second Level, Seaport Tower)

Optiflow™ Nasal High Flow Evidence and Equipoise

Delegates will learn and hear from three internationally respected researchers who will deliver clinically focused yet practical presentations on Nasal High Flow therapy with F&P Optiflow™and F&P AIRVO™.

Speakers: **Jean-Pierre Frat, MD, DR**, *Centre Hospitalier Universitaire de Poitiers;* **Nicholas S. Hill, MD**, *professor, Tufts Medical Center, Boston;* **Giacomo Grasshelli, MD**, *professor, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan*

Company: Fisher & Paykel Healthcare

6:30-9:30 p.m.

Marriott Marquis San Diego Marina, Marina Ballroom F-G (South Tower, Third Floor)

How Are We Diagnosing and Managing Our Patients With IPF? An Expert-Guided Discussion

Join us for a collaborative discussion with a multidisciplinary team of renowned interstitial lung disease experts to investigate the key barriers and benefits to timely diagnosis and management of patients with IPF.

Speakers: **Steven D. Nathan, MD**, *Inova Fairfax Hospital;* **Shyam Subramanian, MD**, *Sutter Gould Medical Foundation;* **Alison G. Wilcox, MD**, *University of Southern California*

Company: Genentech, A Member of the Roche Group

6:30-9:30 p.m.

Marriott Marquis San Diego Marina, Marina Ballroom D-E (South Tower, Third Floor)

Emerging European PAH Registry Data: Risk Assessment With the Urgency to Treat

The progressive nature of PAH, and the poor prognosis it carries for most patients, provides clinical rationale for an aggressive approach to disease management. Experts in PAH treatment will discuss current risk assessment strategies and their implementation in clinical practice to support a goal-oriented approach in the treatment of PAH.

Speakers: **Ronald Oudiz, MD**, *director, LA Biomedical Institute at Harbor-UCLA Medical Center;* **Harrison "Hap" Farber, MD**, *director, Boston Medical Center;* **Ioana Preston, MD**, *director, Tufts Medical Center;* **Susie McDevitt, RN, MSN, ACNP**, *University of Michigan Health System*

Company: United Therapeutic

6:30-9:30 p.m.

Hilton San Diego Bayfront, Indigo Ballroom D/H (Indigo Level, Level 2)

Idiopathic Pulmonary Fibrosis: From Presentation to Patient Experience

This educational symposium will feature a patient mentor who will share his or her journey of living with IPF. Our distinguished faculty, who actively diagnose and treat patients with IPF, will provide clinical context for the patient story using a case-based slide format to present background information on IPF and relevant information regarding the diagnostic process.

Speakers: **Paul W. Noble, MD**, *Cedars-Sinai Medical Center;* **Jeffrey James Swigris, DO, MS**, *National Jewish Health*

Company: Boehringer Ingelheim Pharmaceuticals, Inc.

6:30-9:30 p.m.

Hilton San Diego Bayfront, Sapphire Ballroom I/J/M/N (Sapphire Level, Level 4)

Recent Evidence in the Treatment of COPD: an Interactive Symposium

(*Open to international attendees only*)

Recently, new evidence has emerged that may provide greater clarity about which therapies are best suited to achieve GOLD's treatment goals and ensure that each patient obtains the right treatment. This scientific symposium will focus on a review of recent evidence, how it guides appropriate treatment, where evidence gaps still exist, and what future research is needed.

Speakers: **Paul Jones, PhD**, *Global Respiratory Franchise, GlaxoSmithKline, London, U.K.;* **Gerard Criner, MD**, *Temple University Hospital, Philadelphia, Pennsylvania;* **Fernando Martinez, MD, MS**, *Weill Cornell Medicine, New York, New York;* **Dave Singh, MD**, *University Of Manchester, Manchester, U.K.;* **Neil Barnes, MB, BS**, *Global Respiratory Franchise, GlaxoSmithKline, London, U.K.*

Company: GSK

6:30-9:30 p.m.

Hilton San Diego Bayfront, Indigo Ballroom A/E (Indigo Level, Level 2)

Consider the Risk: A Case-Based Look at Risk Assessment in PAH Management

Management strategies of pulmonary arterial hypertension continue to evolve. This interactive, case-based symposium will feature a panel of experts who will discuss the importance of risk assessment in PAH. Dinner will be provided. Dinner will not be provided to physicians and other health care professionals licensed in Vermont or other states where gifts and meals are prohibited.

Speakers: **Vallerie McLaughlin, MD**, *University of Michigan;* **Nick H. Kim, MD**, *University of California, San Diego; Lana Melendres-Groves, MD, University of New Mexico School of Medicine*

Company: Actelion Pharmaceuticals U.S., Inc., a Janssen Pharmaceutical Company of Johnson & Johnson

6:30-9:30 p.m.

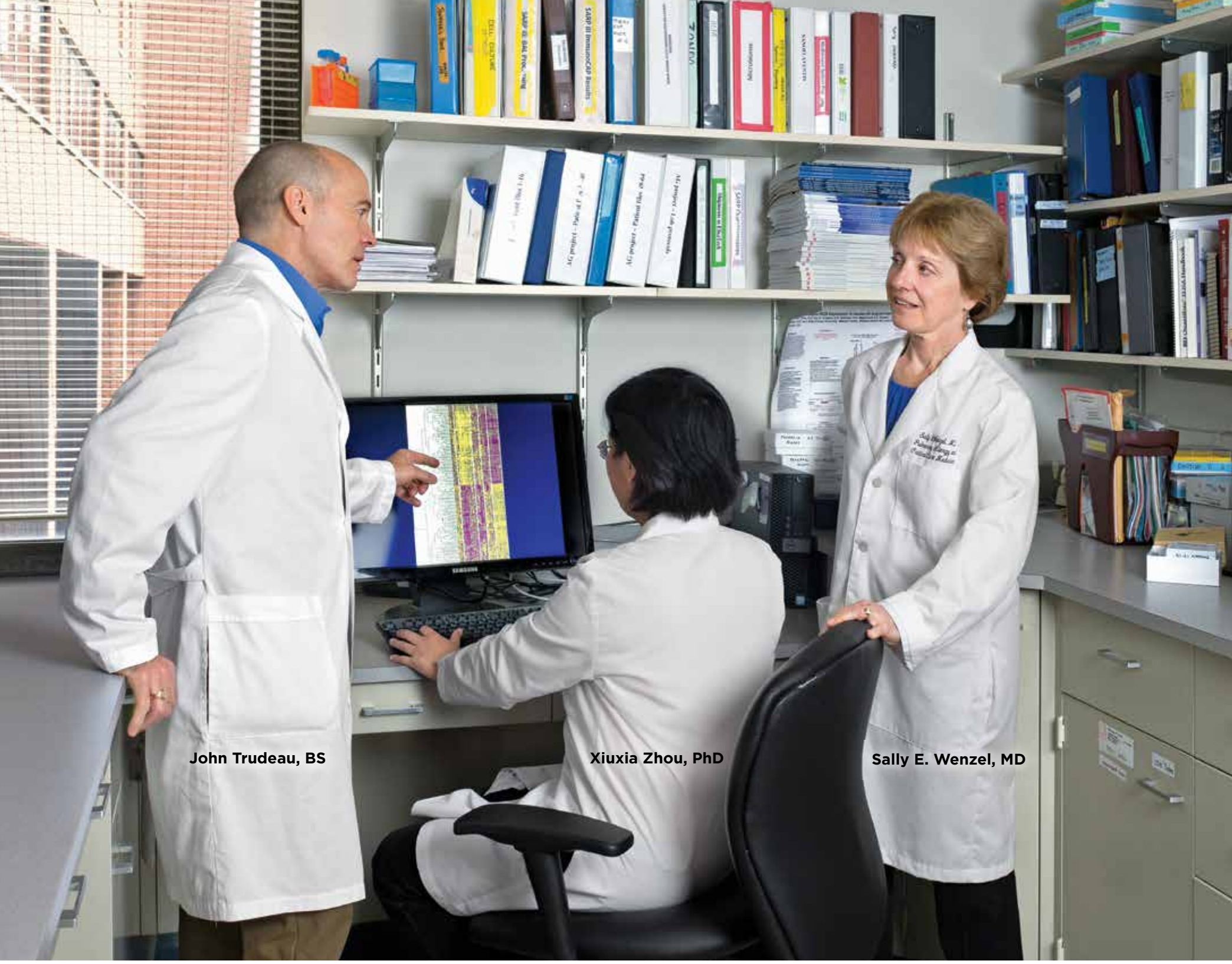
Hilton San Diego Bayfront, Sapphire Ballroom A/B/E/F (Sapphire Level, Level 4)

Clinical Issues in Severe Asthma: Debates and Discussions About Personalizing Patient Management

Please join us for an engaging and illuminating Clinical Issues™ symposium focused on evolving management strategies for severe cases of asthma. A faculty panel comprising three well-known experts in asthma research will review key diagnostic criteria; biomarkers and comorbidities that help elucidate severe phenotypes and shape therapeutic choices; and the mechanistic and clinical profiles associated with current and emerging biologic asthma therapies.

Speakers: **Reynold A. Panettieri Jr., MD**, *University of Pennsylvania;* **Michael E. Wechsler, MD, MMSc**, *National Jewish Health;* **Sally E. Wenzel, MD**, *Pulmonary, Allergy and Critical Care Medicine*

Company: Supported by an independent educational grant from Sanofi Genzyme and Regeneron Pharmaceuticals. ■



Treating severe asthma with greater precision.

BEST HOSPITALS U.S.News & WORLD REPORT HONOR ROLL 2017-18

At the University of Pittsburgh Asthma Institute at UPMC, we understand that severe asthma is not a single disease or disease process. In the clinic, we tailor our treatment approach to each patient's specific asthma phenotype, with the goal of improving outcomes. That's why we continue to conduct basic and translational research to further identify pathways of inflammation that are not traditionally associated with asthma, but appear to contribute to more severe symptoms. Using available and emerging biomarkers to help guide our therapies, we categorize patients into subgroups that allow us to deliver personalized, precision medicine based on both a molecular and clinical perspective. To learn more about how we are treating patients with greater precision than ever before, visit **UPMCPhysicianResources.com/Pulmonology**.

UPMC LIFE CHANGING MEDICINE

Affiliated with the University of Pittsburgh School of Medicine, UPMC Presbyterian Shadyside is ranked among America's Best Hospitals by *U.S. News & World Report*.

Assemblies and Sections Host Member Events

Getting the most out of the ATS 2018 International Conference means getting involved. One way to do that is to participate in your assembly and/or section activities.

The Society's assemblies and sections will hold their annual membership meetings Sunday and Monday at various San Diego locations. All ATS 2018 attendees are encouraged to attend these meetings. (See the schedule below for specific times and locations of assembly membership meetings, receptions, section meetings, and assembly dinners.)

ASSEMBLY MEMBERSHIP MEETINGS

The Assembly Membership Meetings provide updates on assembly activities from each assembly's leadership. These meetings give members the opportunity to provide input on future direction and get involved in assembly and networking activities. Voting results for the assembly's future leaders also will be announced.

These meetings will all be held at various locations from 4:30 to 7 p.m. Monday, May 21, with the exception of the Assembly on Behavioral Science and Health Services Research and the Assembly on Pediatrics, which will meet Sunday, May 20.

SUNDAY

5-7 p.m.

Pediatrics
Chair: Stephanie Davis, MD
Manchester Grand Hyatt San Diego, Harbor Ballroom A-C (Second Level, Harbor Tower)

6:30-8:30 p.m.

Behavioral Science and Health Services Research
Chair: Christopher H. Goss, MD, MSc
Manchester Grand Hyatt San Diego, Seaport Ballroom F (Second Level, Seaport Tower)

MONDAY

4:30-7 p.m.

Allergy, Immunology, and Inflammation
Chair: Bethany Moore, PhD
Manchester Grand Hyatt San Diego, Harbor Ballroom G-I (Second Level, Harbor Tower)

Clinical Problems
Chair: Sanjay Sethi, MD
Manchester Grand Hyatt San Diego, Grand Hall B (Lobby Level)

Critical Care
Chair: John P. Kress, MD
Manchester Grand Hyatt San Diego, Grand Hall A (Lobby Level)

Environmental, Occupational, and Population Health
Chair: Howard Kipen, MD, MPH
Manchester Grand Hyatt San Diego, Coronado Ballroom D-E (Fourth Level)

Nursing
Chair: Eileen G. Collins, PhD
Manchester Grand Hyatt San Diego, Coronado Ballroom A-B (Fourth Level)

Pulmonary Circulation
Chair: Karen Fagan, MD
Manchester Grand Hyatt San Diego, Grand Hall C (Lobby Level)

Pulmonary Infections and Tuberculosis
Chair: Kevin P. Fennelly, MD, MPH
Manchester Grand Hyatt San Diego, Seaport Ballroom E (Second Level, Seaport Tower)

Pulmonary Rehabilitation
Chair: Richard Casaburi, MD, PhD
Manchester Grand Hyatt San Diego, Seaport Ballroom A-B (Second Level, Seaport Tower)

Respiratory Cell and Molecular Biology
Chair: Irina Petrache, MD
Manchester Grand Hyatt San Diego, Harbor Ballroom A-C (Second Level, Harbor Tower)

Respiratory Structure and Function
Chair: Blanca Camoretti-Mercado, PhD
Manchester Grand Hyatt San Diego, Grand Hall D (Lobby Level)

Sleep and Respiratory Neurobiology
Chair: Sanjay Patel, MD
Manchester Grand Hyatt San Diego, Seaport Ballroom G-H (Second Level, Seaport Tower)

Thoracic Oncology
Chair: M. Patricia Rivera, MD
Manchester Grand Hyatt San Diego, Seaport Ballroom D (Second Level, Seaport Tower)

SECTION MEETINGS

SUNDAY

6-8 p.m.

Section on Genetics and Genomics
Co-Chairs: Blanca E. Himes, PhD, and Michael H. Cho, MD, MPH
Manchester Grand Hyatt San Diego, Seaport Ballroom C (Second Level, Seaport Tower)

TUESDAY

4:30-6:30 p.m.

Section on Medical Education
Co-Chairs: Jennifer McCallister, MD, and Henry E. Fessler, MD
Manchester Grand Hyatt San Diego, Seaport Ballroom A (Second Level, Seaport Tower)

Section on Terrorism and Inhalation Disasters
Co-Chairs: Carl White, MD, and Sven Eric Jordt, PhD
Manchester Grand Hyatt San Diego, Seaport Ballroom B (Second Level, Seaport Tower)

ASSEMBLY DINNER

SUNDAY

7-10 p.m.

Pediatrics
Manchester Grand Hyatt San Diego, Seaport Ballroom A-B (Second Level, Harbor Town)

ASSEMBLY RECEPTIONS

MONDAY

7-10 p.m.

Allergy, Immunology and Inflammation, and Respiratory Cell and Molecular Biology
Manchester Grand Hyatt San Diego, Harbor Ballroom D-F (Second Level, Harbor Tower)

Sleep and Respiratory Neurobiology
Manchester Grand Hyatt San Diego, Seaport Ballroom F (Second Level, Seaport Tower) ■

Stay Connected at ATS 2018

Enhance your International Conference experience by keeping connected through social media. Each day, the ATS promotes the conference on a variety of social media platforms. Get social and you could even win a prize!

The official hashtag is **#ATS2018**.

"I Tweet #ATS2018" ribbons are available in the Sails Pavilion in the San Diego Convention Center.

Selfie spots are located in the Exhibit Hall, Booth #239, and the ATS Center.

Get in on this year's Instagram contest. Here are the rules:

- Follow **@atscommunity** on Instagram.
- Post a photo from **#ATS2018** and tell us what you like best about our conference.
- Use **#ATS2018** in your post.

Three winners will be chosen randomly each day, and will be notified via Instagram DM.

Snapchat with the ATS during the conference. Simply scan this code to follow ATS (or search @atscommunity). Followers can check the "Our Story" page for behind-the-scenes pictures, giveaways, and conference videos.

The ATS is going live on Facebook during ATS 2018!

- **Sunday, May 20, 9:30 a.m.** Conference preview
- **Sunday, May 20, 12 p.m.** Restoring Joy in Medicine Center
- **Monday, May 21, 11 a.m. to 12 p.m.** What is health services research, and how do I become a health services researcher?
- **Tuesday, May 22, 3:30 to 4:30 p.m.** Strategies for successfully applying for and obtaining grant funding ■

Product Showcase

JOIN US FOR AN INDUSTRY-ORGANIZED SYMPOSIUM

Sponsored by Boehringer Ingelheim Pharmaceuticals, Inc.

Sunday, May 20, 2018

6:30 PM Dinner/Symposium

Hilton San Diego Bayfront
Indigo Ballroom D/H
San Diego, CA

ADMISSION IS COMPLIMENTARY AND WILL BE ON A FIRST-COME, FIRST-SERVED BASIS. DINNER WILL BE PROVIDED.

An Industry-Organized Symposium at the ATS 2018 International Conference. All ATS 2018 International Conference attendees are invited to this non-CME/CNE educational program sponsored by Boehringer Ingelheim Pharmaceuticals, Inc.

Attendance is limited to healthcare professionals only.
Aspects of this program may be reportable under the physician payments Sunshine Act.

CME, continuing medical education; CNE, continuing nursing education.

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AN EVENT IN SAN DIEGO YOU DON'T WANT TO MISS...

Emerging European PAH Registry Data

Risk Assessment With the Urgency to Treat

Sunday, May 20, 2018 | Dinner and Program: 6:30 - 9:30 p.m.

Marriott Marquis San Diego Marina | Ballroom D-E

An industry-organized symposium at the ATS 2018 International Conference

- A non-CME educational program sponsored by United Therapeutics
- Open to all ATS 2018 International Conference attendees

The progressive nature of PAH, and the poor prognosis it carries for most patients, provides a clinical rationale for an aggressive approach to disease management. Recent real-world data from 3 European PAH registries support the prognostic utility of risk stratification outlined in the 2015 ESC/ERS treatment guidelines. These results emphasize that disease stabilization may not be sufficient for all patients. Experts in PAH treatment will discuss current risk-assessment strategies and their implementation in clinical practice to support a goal-oriented approach in the treatment of PAH.

Faculty

Ronald Oudiz, MD (Chair)

Harrison (Hap) Farber, MD

Ioana Preston, MD

Susie McDevitt, NP

United Therapeutics CORPORATION

Reducing Environmental Exposures in the Disadvantaged

A staggering percentage of the world's population is exposed to unsafe air. Unfortunately, the burden of this generally falls hardest on the poorest communities, which suffer a higher prevalence of lung disease and associated health effects.

Personal exposure modification provides a means to target susceptible populations and reduce pollutant exposure. This Sunday session will investigate emerging methods of exposure mitigation and how to apply appropriate techniques to reduce environmental exposures in unique patient populations.

Reducing Disparities in Environmental Lung Disease:

Emerging Methods in Exposure Mitigation (A91)

2:15-4:15 p.m.

Sunday, May 20

Room 30 A-B (Upper Level)

San Diego Convention Center

The ATS Bulletin asked panel co-chairs Juan Celedón, MD, DrPH, from the University of Pittsburgh School of Medicine, and Emily Brigham, MD, MHS, from Johns Hopkins University School of Medicine, about findings related to certain populations and improvements that can be employed to mitigate lung disease.

Q In North America, what are the most common household environmental concerns?

A: Allergens, which can worsen lung diseases such as asthma, are an important exposure in the indoor environment. Such allergens include those present in dust mite, cockroach, mouse, mold, and pets. Levels of particulate matter, traditionally thought of as an outdoor pollutant, can be elevated in the indoor environment and are not regulated by the EPA. Tobacco smoke often contributes heavily to particulate matter in the indoor environment.

Q Which populations will you focus on for this panel?

A: Racial or ethnic minorities, children, and economically disadvantaged individuals are disproportionately affected by respiratory diseases. We have deliberately focused the panel on these populations, as well as others who may be affected.

Q What are the occupational exposure disparities of greatest concern?

A: Industries and job titles that carry the greatest risk of exposure to respiratory toxins remain staffed disproportionately by minorities and economically disadvantaged individuals. This includes miners, foundry and textile mill workers, and factory employees. The latency period that is often present between exposure and disease means that, even with improvement in working conditions and changes in workforce, disparities will persist for some time.

Q Is the U.S. looking to regulate/deregulate common household and occupational concerns?

A: Currently, there are no U.S. regulations regarding household air pollution. While environmental regulations are in place for occupational safety, it remains unclear whether U.S. administration deregulation plans will affect these precautions.

Q Do home air purifiers address the concerns in a meaningful way?

A: Home air purifiers have been proven to reduce levels of indoor particulate matter. An air purifier intervention has been associated with commensurate improvements in symptoms among children with asthma, and a study is underway looking at the effects of an air purifier intervention in COPD.

Q You have invited a patient to participate on the panel. What will her role be?

A: Our patient speaker will present her powerful story in advocating for her son's respiratory health. Her experience involved unsafe rental housing conditions linked to her son's asthma, recognition of his disease by herself and his health care provider, activation of resources available for legal advocacy, and ultimate resolution of the case with rehousing. She will provide insight into the effect of environmental health on the lives of those affected and their caregivers. She will share her personal experience with use of available legal resources to achieve a necessary step in her son's treatment: change of environment. ■

Lunch and Learn at Industry Theaters, Mini Theater

Grab a complimentary lunch and continue learning during Industry Theaters and Mini Theaters on Sunday, Monday, and Tuesday in the Exhibit Hall. Listen as supporting companies bring you the latest clinical updates related to pulmonary, critical care, or sleep medicine. Lunches are provided by ATS (while supplies last).

The theater locations are:
Industry Theater 1: **Booth 3317**
Industry Theater 2: **Booth 345**
Mini Theater: **Booth 1549**

SUNDAY

Industry Theater 1

11:30 a.m.- 2:15 p.m.

FASENRA™ (benralizumab) Subcutaneous Injection 30 mg: A Targeted Approach

You are cordially invited to attend a program to learn more about emerging mechanisms of disease and a treatment option for appropriate patients. By focusing on the underlying mechanism of disease, treatment can be tailored to the needs of individual patients. Join a national expert to explore the role of a targeted treatment option, its clinical efficacy and safety data, mechanism of action, and tips for appropriate patient identification.

Speaker: **Mario Castro, MD, MPH**, *Washington University School of Medicine*
Company: AstraZeneca

1:15-2 p.m.

The Evolving Science of Asthma

Speaker: **William J. Calhoun, MD**, *University of Texas Medical Branch*
Company: Genentech and Novartis

Industry Theater 2

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

Fundamentals of IPF: Navigating the Patient Journey

(Open to U.S. attendees only)
Join our expert physicians as they discuss how to tackle key challenges facing patients with idiopathic pulmonary fibrosis —including how to ensure a prompt diagnosis and initiate a comprehensive management plan.
Speakers: **Marilyn K. Glassberg, MD**, *University of Miami;* **Jonathan H. Chung, MD**, *University of Chicago*
Company: Genentech, A Member of the Roche Group

1:15-2:00 p.m.

COPD and Treatment With Triple Therapy

This program will answer key questions about managing patients with COPD with triple therapy. It will explore challenges facing clinicians when managing COPD and review clinical safety and efficacy data.
Company: GSK

Mini Theater

11:30 a.m.-2 p.m.

A Proven Long-Acting Muscarinic Antagonist for the Management of COPD

Speaker: **Randall Brown, MD, MPH, AE-C**, *pulmonologist and director, asthma and COPD programs, University of Michigan*
Company: Sunovion Pharmaceuticals Inc.

12:30-1:00 p.m.

New Evidence in COPD: Is There Consensus for Clinical Practice Recommendations?

(Open to international attendees only)
A faculty of experts will discuss the new evidence informing the role of LABA/LAMA and LABA/LAMA/ICS therapy in COPD management. The importance of personalized COPD management will be discussed, including clinical considerations and consensus regarding use of ICS, and evidence-based approaches to ICS withdrawal.
Speakers: **David Price, MA**, *professor, University of Aberdeen, U.K.;* **Ken Chapman, MD**, *professor, University of Toronto and Asthma and Airway Centre, University Health Network, Toronto Western Hospital, Toronto, Canada;* **Dave Singh, MD**, *professor, University of Manchester and University Hospital of South Manchester, U.K.*
Company: Novartis Pharma AG

1:30 p.m.-2 p.m.

COPD Treatments, Exacerbations, and Relationship to Peripheral Blood Eosinophil Levels

COPD has diverse presentations, and the identification of patients who are most likely to respond to a given treatment should contribute to personalized care. Two considerations for selection of COPD treatments are symptoms and history of exacerbations. An additional consideration could include elevated peripheral blood eosinophil levels. Join a pulmonary expert to hear about COPD treatments, exacerbations, and how the levels of eosinophils, assessed as a continuous variable, could impact exacerbation rates.
Speaker: **Dr. Mona Bafadhel**, *associate professor and NIHR postdoctoral fellow, respiratory medicine, University of Oxford*
Company: AstraZeneca ■

From Spanish Flu to Ebola

What happens when viruses go rogue?

Viruses evolve principally to survive and propagate. Killing the host is not part of that survival plan. When viruses go rogue, bad things happen. In talking about rogue viruses, Joshua Lederberg, the microbial geneticist and Nobel Laureate, said, "The single biggest threat to man's continued dominance on the planet is the virus."

It is this threat that brings experts together in the session From Spanish Flu of 1918 to Today: What Can We Learn from Viruses?

From Spanish Flu of 1918 to Today: What Can We Learn from Viruses? (A12)

9:15-11:15 a.m.

Sunday

Grand Ballroom 8-9 (North Tower, Lobby Level), Marriott Marquis San Diego Marina

"In the context of the 100th anniversary of the Spanish influenza pandemic of 1918—which ultimately killed more people than the First World War—we believe that a symposium that highlights from a historical, scientific, and clinical perspective what we have learned about evolving viruses would be timely and of interest to clinicians," says session moderator Seamas Donnelly, MD, professor of medicine at Trinity College Dublin in Ireland.

Seamas Donnelly, MD

The session will begin with Michael Worobey, PhD, from the University of Arizona, who will provide a historical and scientific overview on what we can learn from the Spanish flu of 1918. Following this, Dr. Donnelly and Nicholas W. Lukacs, PhD, from the University of Michigan, will each speak on how viruses contribute to an aggressive clinical phenotype in pulmonary fibrosis and asthma, respectively.

Frances E. H. Lee, MD, from Emory University, will summarize recent work in defining how viruses evolve to bypass our human immune defenses. Rounding off the session is an update on the highly topical Ebola virus and the research endeavors of Sharon Schendel, PhD, and colleagues at the Scripps Research Institute in La Jolla, California, in defining future curative therapies for viral hemorrhagic fever. ■

Tuberculosis Still Threatens Public Health Worldwide

For decades, health officials have set their sites on eradicating tuberculosis. Although the number of active TB cases has decreased in the United States and other developed countries, it remains widespread around the world. In fact, TB has regained the inglorious distinction of being the infectious disease that kills more people than any other, according to Kevin Fennelly, MD, MPH, chair of the ATS Assembly on Pulmonary Infections and TB.

Kevin Fennelly, MD, MPH

Neha Shah, MD, MPH

Neha Shah, MD, MPH, and her colleagues in the Division of TB Elimination at the Centers for Disease Control and Prevention, are presenting a two-hour public health poster forum that will focus on innovative techniques that are helping to meet the challenges of TB control, prevention, and elimination in the United States.

"This year, there is a large focus on latent TB infection or dormant infection. If we are able to catch TB early, we can prevent people from getting sick, and from transmitting it to their family and community," says Dr. Shah. "These posters focus on using new blood tests, using novel ways, such as electronic video formats to provide medication oversight, and understanding how much work we have to do in order to get to TB elimination."

CDC Tuberculosis Poster Session

7-9 p.m.

Sunday

Grand Ballroom 11-13, Marriott Marquis San Diego Marina

There are many misconceptions about TB that have given the disease a foothold worldwide. One of the biggest misunderstandings the public has about TB is that the BCG vaccination protects you from TB as an adult. It doesn't, says Dr. Shah.

"The biggest misunderstanding for providers is that only TB clinics can provide prevention therapy," she says. "All providers need to be aware of who is at risk for TB and then test and treat individuals to prevent infectious TB and protect transmission to family and friends."

Many Americans also mistakenly believe that TB is no longer a public health problem, says Dr. Fennelly. "Even many of our research colleagues tend to think that TB is 'over' for patients if there is either a microbiological cure or death," he says. "TB is actually a major contributor to pulmonary disability around the world." ■

Guru Bars Offer Learning in 30 Minutes or Less

Guru Bars are quick-burst learning sessions that allow you to collaborate with leaders on a variety of topics. Every session offers a 10-minute outline of a problem statement, mitigating factors, the host's perspective/solution, and a challenge or question posted to participants, who discuss it for the remaining 5 to 10 minutes.

Each Guru Bar seats 25 participants to create a dynamic, yet intimate, group with lots of interaction. Guru Bars are organized by categories of interest:

Guru Bars 1 and 2: Education/Awareness/Prevention or Diagnosis

Guru Bars 3 and 4: Treatment of Adherence/Compliance

Guru Bars run every 30 minutes from 11 a.m. to 2 p.m., Sunday through Tuesday, in the Exhibit Hall (Hall F, Ground Level).

SUNDAY
GURU BAR 1
Education/Awareness/Prevention or Diagnosis

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

Insights on Type 2 Inflammation: The Connection to Airway Pathology

The primary objective of this brief presentation is to increase health care provider understanding of Type 2 inflammation and how it contributes to airway pathology in asthma. Evidence supporting roles for Type 2 cytokines in epithelial and airway smooth muscle pathology, including remodeling, fibrosis, mucus production, and airway hyper-responsiveness, will be discussed.

Company: Sanofi Genzyme & Regeneron

12:30-1 p.m.

Introducing Rad Rounds—UIP to IPF: A Digital Application to Identify Usual Interstitial Pneumonia on HRCT

(*Limited to health care professionals*)

In this digitally enhanced Guru Bar, an expert pulmonologist and radiologist will introduce the recently launched Rad Rounds—UIP to IPF app. Working in tandem, these distinguished faculty will review the radiology content contained in the app, including the diagnostic algorithm, to improve recognition of usual interstitial pneumonia, a radiologic pattern associated with idiopathic pulmonary fibrosis. Authentic examples of UIP, as well as other hallmarks will be shown.

Speakers: **Marilyn K. Glassberg, MD**, *director, Rare and Interstitial Lung Disease Program, University of Miami Miller School of Medicine;* **Robert Suh, MD**, *vice chair of radiology education, Ronald Reagan UCLA Medical Center*

Company: Boehringer Ingelheim Pharmaceuticals, Inc.

1:30-2 p.m.

Challenges of Early Stage Lung Cancer Treatment and Recurrence

Clinicians face numerous challenges in the management of patients with early stage lung cancer. One of the most difficult aspects is determining the risk of recurrence for early stage patients that are treated surgically. Current treatment options have limited effectiveness and diagnostic tools often provide very limited recurrence risk information. During this interactive, case-based Guru Bar, you will hear from experts in the field regarding the need for new biomarkers to better assess the risk of recurrence and their future role in clinical practice.

Speaker: **Jeff Thompson, MD**, *Instructor of Clinical Medicine, Hospital of the University of Pennsylvania*

Company: OncoCyte Corporation

GURU BAR 2
Education/Awareness/Prevention or Diagnosis

12-12:30 p.m.

Sarcoidosis

(*open to U.S. attendees only*)

Company: Mallinckrodt Pharmaceuticals

1-1:30 p.m.

The Future of Lung Cancer and the Monarch Platform

Introduction of the Monarch Platform

Speaker: **Thomas Gildea, MD**, *Interventional Pulmonary & Critical Care Medicine, Cleveland Clinic*

Company: Auris

GURU BAR 3
Treatment or Adherence/Compliance

1:30-2 p.m.

A New Treatment Option in Distributive Shock

(*open to U.S. attendees only*)

In distributive shock adequate fluid therapy and appropriate doses of vasopressors often do not result in achievement or maintenance of target mean arterial pressure. Join us as we discuss distributive shock, including the current stepwise approach to managing patients, and an overview of the renin angiotensin aldosterone system as another potential target to help manage hypotension.

Speaker: **H. Bryant Nguyen, MD, MS**, *John G. Peterson Professor of Medicine, Emergency Medicine and Basic Sciences; division head, pulmonary, critical care, hyperbaric, and sleep medicine; vice chair, research, Loma Linda University Medical Center*

Company: La Jolla Pharmaceutical Company

GURU BAR 4
Treatment or Adherence/Compliance

1-1:30 p.m.

A New Treatment Option in Distributive Shock

(*open to U.S. attendees only*)

In distributive shock adequate fluid therapy and appropriate doses of vasopressors often do not result in achievement or maintenance of target mean arterial pressure. Join us as we discuss distributive shock, including the current stepwise approach to managing patients, and an overview of the renin angiotensin aldosterone system as another potential target to help manage hypotension.

Speaker: **H. Bryant Nguyen, MD, MS**, *John G. Peterson Professor of Medicine, Emergency Medicine and Basic Sciences; division head, pulmonary, critical care, hyperbaric, and sleep medicine; vice-chair, research, Loma Linda University Medical Center*

Company: La Jolla Pharmaceutical Company ■

Visit GSK Booth #1734

For patients with COPD taking fluticasone furoate/vilanterol who need additional lung function improvement

LESS TO TAKE.
MORE TO TAKE IN.

TRELEGY– the only once-daily triple therapy (ICS/LABA/LAMA) for COPD delivered in a single inhaler

COPD=chronic obstructive pulmonary disease; ICS=inhaled corticosteroid; LABA=long-acting beta$_2$-adrenergic agonist; LAMA=long-acting muscarinic antagonist.

INDICATION

TRELEGY is for maintenance treatment of patients with COPD, including chronic bronchitis and/or emphysema, who are on fluticasone furoate and vilanterol (FF/VI) and need additional treatment of airflow obstruction or who are already taking umeclidinium and FF/VI. TRELEGY is NOT indicated for relief of acute bronchospasm or asthma.

IMPORTANT SAFETY INFORMATION

WARNING: ASTHMA-RELATED DEATH

LABA, such as vilanterol, one of the active ingredients in TRELEGY, 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.

The safety and efficacy of TRELEGY in patients with asthma have not been established. TRELEGY is not indicated for the treatment of asthma.

Please see additional Important Safety Information for TRELEGY on the following pages.
Please see Brief Summary of Prescribing Information, including Boxed Warning, for TRELEGY following this ad.

INNOVIVA

TRELEGY ELLIPTA
(fluticasone furoate 100 mcg, umeclidinium 62.5 mcg, and vilanterol 25 mcg inhalation powder)

Patients experienced greater lung function with TRELEGY vs patients taking fluticasone furoate/vilanterol (FF/VI)

Primary endpoint: Change from baseline in trough FEV_1 at Day 85[1,2]

In patients with COPD run-in on FF/VI 100/25, TRELEGY provided

124 mL ADDITIONAL LUNG FUNCTION IMPROVEMENT

vs FF/VI
($P < 0.001$)

Similar results were demonstrated in a replicate study.

STUDY DESCRIPTION

Design: 12-week, randomized, double-blind, parallel-group study. Following a 4-week run-in period on FF/VI 100/25, patients were randomized to treatment with UMEC 62.5 mcg (n=206) or placebo (n=206) added to FF/VI 100/25 mcg (each administered once daily in the morning by the ELLIPTA inhaler). Treatment with TRELEGY refers to patients who received UMEC 62.5 added to FF/VI 100/25.

Patients: COPD patients (mean age: 64 years). At screening, patients had a mean postbronchodilator percent predicted FEV_1 of 46%, a mean postbronchodilator FEV_1/FVC ratio: 0.48, and a mean mMRC score of 2.5.

FEV_1=forced expiratory volume in 1 second; FVC=forced vital capacity; mMRC=modified Medical Research Council; UMEC=umeclidinium.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

- TRELEGY is contraindicated in patients with severe hypersensitivity to milk proteins or demonstrated hypersensitivity to fluticasone furoate, umeclidinium, vilanterol, or any of the excipients.

WARNINGS AND PRECAUTIONS

- TRELEGY should NOT be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD.
- TRELEGY is NOT a rescue medication and should NOT be used for the relief of acute bronchospasm or symptoms. Acute symptoms should be treated with an inhaled, short-acting $beta_2$-agonist.
- TRELEGY should not be used more often or at higher doses than recommended or with another LABA for any reason, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs, like LABA.
- Oropharyngeal candidiasis has occurred in patients treated with orally inhaled drug products containing fluticasone furoate. Advise patients to rinse their mouths with water without swallowing after inhalation.
- Physicians should remain vigilant for the possible development of pneumonia in patients with COPD, as clinical features of pneumonia and exacerbations frequently overlap. Lower respiratory tract infections, including pneumonia, have been reported following use of inhaled corticosteroids, like fluticasone furoate.
- 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.
- Particular care is needed for patients transferred from systemic corticosteroids to inhaled corticosteroids because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer. Taper patients slowly from systemic corticosteroids if transferring to TRELEGY.

Please see additional Important Safety Information for TRELEGY on the following pages.
Please see Brief Summary of Prescribing Information, including Boxed Warning, for TRELEGY following this ad.

Visit GSK Booth #1734

TRELEGY contains FF/VI, an ICS/LABA proven to reduce COPD exacerbations

This study did not evaluate the effect of TRELEGY on COPD exacerbations.

Primary endpoint: Annual rate of moderate/severe exacerbations[1,3]

In patients with a history of COPD exacerbations, FF/VI 100/25 provided

21% EXACERBATION REDUCTION

in annual rate vs vilanterol

0.90 vs 1.14 for FF/VI 100/25 and VI, respectively; $P=0.024$

Similar results were demonstrated in a replicate study.

STUDY DESCRIPTION

Design: 12-month, randomized, double-blind, parallel-group study that evaluated the effect of FF/VI 100/25 mcg (n=403) and VI 25 mcg* (n=409) (each administered once daily by the ELLIPTA inhaler) on the rate of moderate/severe exacerbations. Patients with a history of ≥1 moderate or severe exacerbation in the previous year were randomized to treatment following a 4-week run-in period on fluticasone propionate/salmeterol 250/50 mcg twice daily.

Patients: COPD patients (mean age: 64 years). At screening, patients had a mean postbronchodilator percent predicted FEV_1 of 46% and a mean postbronchodilator FEV_1/FVC ratio: 0.46.

Exacerbation severity criteria: Moderate if treatment with systemic corticosteroids and/or antibiotics was required and severe if hospitalization was required.

*Vilanterol is not approved as monotherapy.

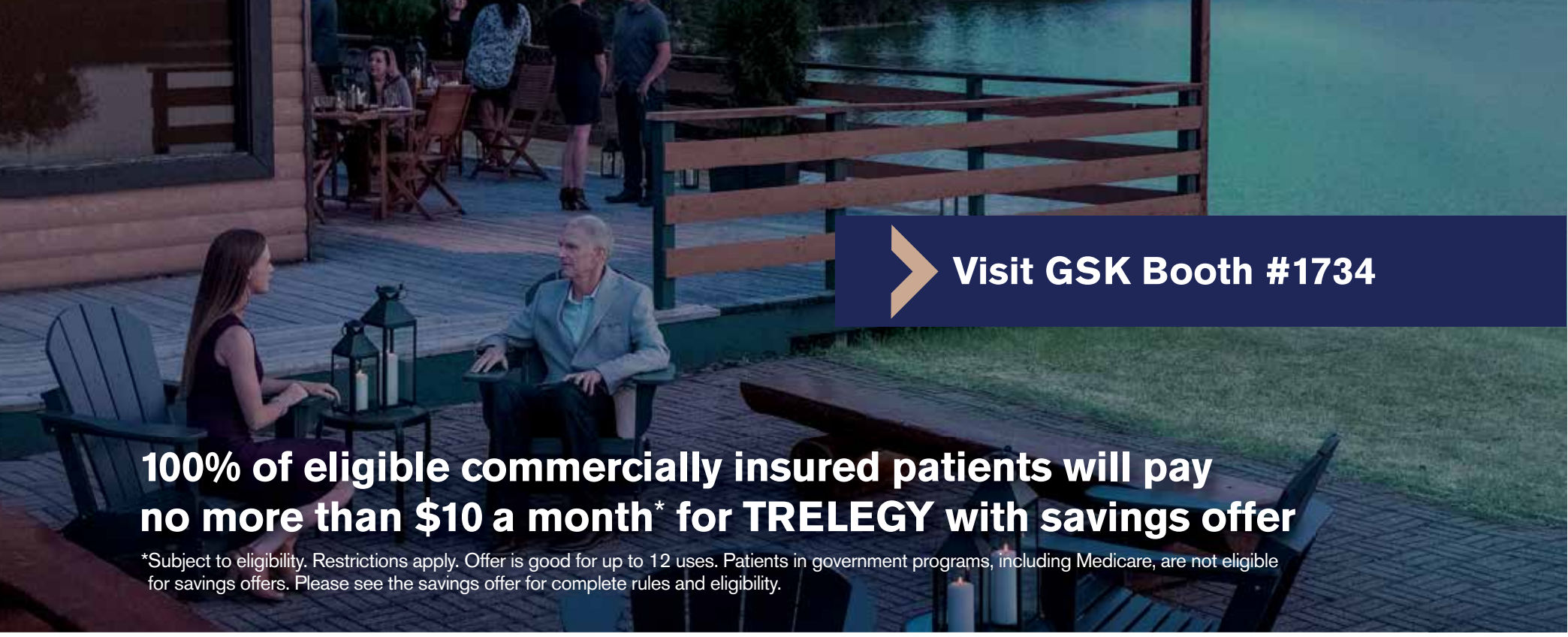
IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Hypercorticism and adrenal suppression may occur with higher than the recommended dosage or at the regular dosage of inhaled corticosteroids in susceptible individuals. If such changes occur, appropriate therapy should be considered.
- Caution should be exercised when considering the coadministration of TRELEGY with long-term ketoconazole and other known strong CYP3A4 inhibitors (eg, 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 TRELEGY and institute alternative therapy.
- Hypersensitivity reactions such as anaphylaxis, angioedema, rash, and urticaria may occur after administration of TRELEGY. Discontinue TRELEGY 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, TRELEGY may need to be discontinued. TRELEGY should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

To learn more, go to DiscoverTrelegy.com

TRELEGY ELLIPTA
(fluticasone furoate, umeclidinium, and vilanterol inhalation powder)



IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Decreases in bone mineral density 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 (eg, anticonvulsants, oral corticosteroids) should be monitored and treated with established standards of care prior to initiating TRELEGY and periodically thereafter.
- Glaucoma, increased intraocular pressure, and cataracts have been reported following the long-term administration of inhaled corticosteroids or inhaled anticholinergics; therefore, monitoring is warranted.
- Use with caution in patients with narrow-angle glaucoma. Instruct patients to contact a healthcare provider immediately if signs or symptoms of acute narrow-angle glaucoma develops.
- Use with caution in patients with urinary retention, especially in patients with prostatic hyperplasia or bladder-neck obstruction. Instruct patients to contact a healthcare provider immediately if signs or symptoms of urinary retention develops.
- 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.

ADVERSE REACTIONS

- The most common adverse reactions (≥1% and more common than placebo) reported in two 12-week clinical trials with umeclidinium + FF/VI, the components of TRELEGY, (and placebo + FF/VI) were: headache, 4% (3%); back pain, 4% (2%); dysgeusia, 2% (<1%); diarrhea, 2% (<1%); cough, 1% (<1%); oropharyngeal pain, 1% (0%); and gastroenteritis, 1% (0%).

DRUG INTERACTIONS

- TRELEGY 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 they may potentiate the effect of vilanterol on the cardiovascular system.
- Use beta-blockers with caution, as they not only block the pulmonary effect of beta-agonists, such as vilanterol, but may produce severe bronchospasm in patients with COPD.
- Use with caution in patients taking non–potassium-sparing diuretics, as ECG changes and/or hypokalemia associated with these diuretics may worsen with concomitant beta-agonists.
- Avoid coadministration of TRELEGY with other anticholinergic-containing drugs, as this may lead to an increase in anticholinergic adverse effects.

USE IN SPECIFIC POPULATIONS

- Use TRELEGY with caution in patients with moderate or severe hepatic impairment, as fluticasone furoate systemic exposure may increase by up to 3-fold. Monitor for corticosteroid-related side effects.

Please see additional Important Safety Information for TRELEGY on the previous pages.
Please see Brief Summary of Prescribing Information, including Boxed Warning, for TRELEGY following this ad.

References: 1. Data on file, GSK. **2.** Siler TM, Kerwin E, Sousa AR, Donald A, Ali R, Church A. Efficacy and safety of umeclidinium added to fluticasone furoate/vilanterol in chronic obstructive pulmonary disease: results of two randomized studies. *Respir Med*. 2015;109(9):1155-1163. **3**. Dransfield MT, Bourbeau J, Jones PW, et al. Once-daily inhaled fluticasone furoate and vilanterol versus vilanterol only for prevention of exacerbations of COPD: two replicate double-blind, parallel-group, randomised controlled trials. *Lancet Respir Med*. 2013;1(3):210-223.

To learn more, go to DiscoverTrelegy.com

TRELEGY ELLIPTA was developed in collaboration with INNOVIVA

Printed in USA. 1001205R0 March 2018

TRELEGY ELLIPTA
(fluticasone furoate, umeclidinium, and vilanterol inhalation powder)

BRIEF SUMMARY

TRELEGY ELLIPTA (fluticasone furoate, umeclidinium, and vilanterol inhalation powder), for oral inhalation

The following is a brief summary only; 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 TRELEGY, 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 *[see Warnings and Precautions (5.1)]*.

The safety and efficacy of TRELEGY in patients with asthma have not been established. TRELEGY is not indicated for the treatment of asthma *[see Warnings and Precautions (5.1)]*.

1 INDICATIONS AND USAGE

TRELEGY is indicated for the long-term, once-daily, maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, who are on a fixed-dose combination of fluticasone furoate and vilanterol for airflow obstruction and reducing exacerbations in whom additional treatment of airflow obstruction is desired or for patients who are already receiving umeclidinium and a fixed-dose combination of fluticasone furoate and vilanterol.

Important Limitations of Use

TRELEGY is NOT indicated for the relief of acute bronchospasm or for the treatment of asthma.

4 CONTRAINDICATIONS

The use of TRELEGY is contraindicated in the following conditions: severe hypersensitivity to milk proteins or demonstrated hypersensitivity to fluticasone furoate, umeclidinium, 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

Data from a large placebo-controlled trial in subjects with asthma showed that LABA may increase the risk of asthma-related death.

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 TRELEGY.

No trial adequate to determine whether the rate of asthma-related death is increased in subjects treated with TRELEGY has been conducted. The safety and efficacy of TRELEGY in patients with asthma have not been established. TRELEGY is not indicated for the treatment of asthma.

5.2 Deterioration of Disease and Acute Episodes

TRELEGY should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD. TRELEGY has not been studied in subjects with acutely deteriorating COPD. The initiation of TRELEGY in this setting is not appropriate.

TRELEGY should not be used for the relief of acute symptoms, ie, as rescue therapy for the treatment of acute episodes of bronchospasm. TRELEGY 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 TRELEGY, patients who have been taking oral or inhaled, short-acting beta$_2$-agonists on a regular basis (eg, 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.

COPD may deteriorate acutely over a period of hours or chronically over several days or longer. If TRELEGY no longer controls symptoms of bronchoconstriction; the patient's inhaled, short-acting beta$_2$-agonist becomes less effective; or the patient needs more short-acting beta$_2$-agonist than usual, these may be markers of deterioration of disease. In this setting, a re-evaluation of the patient and the COPD treatment regimen should be undertaken at once. Increasing the daily dose of TRELEGY beyond the recommended dose is not appropriate in this situation.

5.3 Excessive Use of TRELEGY and Use With Other Long-acting Beta$_2$-agonists

TRELEGY 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 TRELEGY should not use another medicine containing a LABA (eg, salmeterol, formoterol fumarate, arformoterol tartrate, indacaterol) for any reason.

5.4 Local Effects of Inhaled Corticosteroids

In clinical trials, the development of localized infections of the mouth and pharynx with *Candida albicans* has occurred in subjects treated with TRELEGY. When such an infection develops, it should be treated with appropriate local or systemic (ie, oral) antifungal therapy while treatment with TRELEGY continues, but at times therapy with TRELEGY 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.

5.5 Pneumonia

Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as clinical features of pneumonia and exacerbations frequently overlap. Lower respiratory tract infections, including pneumonia, have been reported following the inhaled administration of corticosteroids.

In two 12-week studies of subjects with COPD (N=824), the incidence of pneumonia was less than 1% for both treatment arms: umeclidinium 62.5 mcg + fluticasone furoate/vilanterol 100 mcg/25 mcg or placebo + fluticasone furoate/vilanterol 100 mcg/25 mcg. Fatal pneumonia occurred in 1 subject receiving placebo + fluticasone furoate/vilanterol 100 mcg/25 mcg.
In a mortality trial with fluticasone furoate/vilanterol with a median treatment duration of 1.5 years in 16,568 subjects with moderate COPD and cardiovascular disease, the annualized incidence rate of pneumonia was 3.4 per 100 patient-years for fluticasone furoate/vilanterol 100 mcg/25 mcg, 3.2 for placebo, 3.3 for fluticasone furoate 100 mcg, and 2.3 for vilanterol 25 mcg. Adjudicated, on-treatment deaths due to pneumonia occurred in 13 subjects receiving fluticasone furoate/vilanterol 100 mcg/25 mcg, 9 subjects receiving placebo, 10 subjects receiving fluticasone furoate 100 mcg, and 6 subjects receiving vilanterol 25 mcg (less than 0.2 per 100 patient-years for each treatment group).

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 TRELEGY may control COPD 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 or a severe COPD exacerbation, 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 or a severe COPD exacerbation.

Patients requiring oral corticosteroids should be weaned slowly from systemic corticosteroid use after transferring to TRELEGY. Prednisone reduction can be accomplished by reducing the daily prednisone dose by 2.5 mg on a weekly basis during therapy with TRELEGY. Lung function (forced expiratory volume in 1 second [FEV$_1$]), beta-agonist use, and COPD 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.

Continued on next page

Transfer of patients from systemic corticosteroid therapy to TRELEGY may unmask allergic conditions previously suppressed by the systemic corticosteroid therapy (eg, rhinitis, conjunctivitis, eczema, arthritis, eosinophilic conditions).

During withdrawal from oral corticosteroids, some patients may experience symptoms of systemically active corticosteroid withdrawal (eg, 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 fluticasone furoate in TRELEGY. 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 TRELEGY 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, appropriate therapy should be considered.

5.9 Drug Interactions With Strong Cytochrome P450 3A4 Inhibitors

Caution should be exercised when considering the coadministration of TRELEGY with long-term ketoconazole and other known strong CYP3A4 inhibitors (eg, 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, TRELEGY can produce paradoxical bronchospasm, which may be life threatening. If paradoxical bronchospasm occurs following dosing with TRELEGY, it should be treated immediately with an inhaled, short-acting bronchodilator; TRELEGY 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 TRELEGY. Discontinue TRELEGY 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 TRELEGY *[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, TRELEGY 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 *[see Clinical Pharmacology (12.2) of full prescribing information]*. Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.

TRELEGY, like other sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

In a mortality trial with fluticasone furoate/vilanterol with a median treatment duration of 1.5 years in 16,568 subjects with moderate COPD and cardiovascular disease, the annualized incidence rate of adjudicated cardiovascular events (composite of myocardial infarction, stroke, unstable angina, transient ischemic attack, or on-treatment death due to cardiovascular events) was 2.5 per 100 patient-years for fluticasone furoate/vilanterol 100 mcg/25 mcg, 2.7 for placebo, 2.4 for fluticasone furoate 100 mcg, and 2.6 for vilanterol 25 mcg. Adjudicated, on-treatment deaths due to cardiovascular events occurred in 82 subjects receiving fluticasone furoate/vilanterol 100 mcg/25 mcg, 86 subjects receiving placebo, 80 subjects receiving fluticasone furoate 100 mcg, and 90 subjects receiving vilanterol 25 mcg (annualized incidence rate ranged from 1.2 to 1.3 per 100 patient-years for the treatment groups).

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 (eg, anticonvulsants, oral corticosteroids) should be monitored and treated with established standards of care. Since patients with COPD often have multiple risk factors for reduced BMD, assessment of BMD is recommended prior to initiating TRELEGY and periodically thereafter. If significant reductions in BMD are seen and TRELEGY is still considered medically important for that patient's COPD therapy, use of medicine to treat or prevent osteoporosis should be strongly considered.

5.14 Glaucoma and Cataracts, Worsening of Narrow-Angle Glaucoma

Glaucoma, increased intraocular pressure, and cataracts have been reported in patients with COPD following the long-term administration of ICS or with use of inhaled anticholinergics. TRELEGY should be used with caution in patients with narrow-angle glaucoma. Prescribers and patients should also be alert for signs and symptoms of acute narrow-angle glaucoma (eg, eye pain or discomfort, blurred vision, visual halos, or colored images in association with red eyes from conjunctival congestion and corneal edema). Instruct patients to consult a healthcare provider immediately if any of these signs or symptoms develops. Close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, narrow- or open-angle glaucoma, and/or cataracts.

5.15 Worsening of Urinary Retention

TRELEGY, like all medicines containing an anticholinergic, should be used with caution in patients with urinary retention. Prescribers and patients should be alert for signs and symptoms of urinary retention (eg, difficulty passing urine, painful urination), especially in patients with prostatic hyperplasia or bladder-neck obstruction. Instruct patients to consult a healthcare provider immediately if any of these signs or symptoms develops.

5.16 Coexisting Conditions

TRELEGY, 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.

5.17 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.

6 ADVERSE REACTIONS

LABA, such as vilanterol, one of the active ingredients in TRELEGY, increase the risk of asthma-related death. TRELEGY is not indicated for the treatment of asthma. *[See Boxed Warning and Warnings and Precautions (5.1).]*

The following adverse reactions are described in greater detail in other sections:

- *Candida albicans* infection *[see Warnings and Precautions (5.4)]*
- Increased risk of pneumonia in COPD *[see Warnings and Precautions (5.5)]*
- Immunosuppression *[see Warnings and Precautions (5.6)]*
- Hypercorticism and adrenal suppression *[see Warnings and Precautions (5.8)]*
- Paradoxical bronchospasm *[see Warnings and Precautions (5.10)]*
- Cardiovascular effects *[see Warnings and Precautions (5.12)]*
- Reduction in bone mineral density *[see Warnings and Precautions (5.13)]*
- Worsening of narrow-angle glaucoma *[see Warnings and Precautions (5.14)]*
- Worsening of urinary retention *[see Warnings and Precautions (5.15)]*

6.1 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 with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of TRELEGY is based on the safety data from two 12-week treatment trials with the coadministration of umeclidinium and the fixed-dose combination fluticasone furoate/vilanterol, the components of TRELEGY, compared with placebo + fluticasone furoate/vilanterol, and on the long-term (≥12 months) safety profiles from the fixed-dose combination of fluticasone furoate/vilanterol, the fixed-dose combination of umeclidinium/vilanterol, and umeclidinium monotherapy. *[see Description (11), Clinical Pharmacology (12.3), and Clinical Studies (14.1) of full prescribing information]*.

Confirmatory Trials

Two 12-week treatment trials (Trial 1 and Trial 2) evaluated the coadministration of umeclidinium + fluticasone furoate/vilanterol, the components of TRELEGY, compared with placebo + fluticasone furoate/vilanterol. A total of 824 subjects with COPD across two 12-week, randomized, double-blind clinical trials received at least 1 dose of umeclidinium 62.5 mcg + fluticasone furoate/vilanterol 100 mcg/25 mcg or placebo + fluticasone furoate/vilanterol 100 mcg/25 mcg administered once daily (mean age: 64 years; 92% white, 66% male across all treatments) *[see Clinical Studies (14.1) of full prescribing information]*. The incidence of adverse reactions associated with the use of umeclidinium 62.5 mcg + fluticasone furoate/vilanterol 100 mcg/25 mcg presented in Table 1 is based upon the two 12-week trials.

Continued on next page

Table 1. Adverse Reactions With Umeclidinium + Fluticasone Furoate/Vilanterol With ≥1% Incidence and More Common Than Placebo + Fluticasone Furoate/Vilanterol (Trials 1 and 2)

Adverse Reaction	Umeclidinium + Fluticasone Furoate/ Vilanterol (n=412) %	Placebo + Fluticasone Furoate/ Vilanterol (n=412) %
Nervous system disorders		
Headache	4	3
Dysgeusia	2	<1
Musculoskeletal and connective tissue disorders		
Back pain	4	2
Respiratory, thoracic, and mediastinal disorders		
Cough	1	<1
Oropharyngeal pain	1	0
Gastrointestinal disorders		
Diarrhea	2	<1
Infections and infestations		
Gastroenteritis	1	0

Supporting Long-Term Safety Data

The long-term (≥12 months) safety profiles from the fixed-dose combination of fluticasone furoate/vilanterol, the fixed-dose combination of umeclidinium/vilanterol, and umeclidinium monotherapy are similar to that reported in the 12-week clinical trials described in Table 1. *[See full prescribing information for BREO ELLIPTA (fluticasone furoate and vilanterol inhalation powder), ANORO ELLIPTA (umeclidinium and vilanterol inhalation powder), and INCRUSE ELLIPTA (umeclidinium inhalation powder).]*

7 DRUG INTERACTIONS

7.1 Inhibitors of Cytochrome P450 3A4

Fluticasone furoate and vilanterol are 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 TRELEGY with long-term ketoconazole and other known strong CYP3A4 inhibitors (eg, 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, but may also produce severe bronchospasm in patients with COPD. Therefore, patients with COPD 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.

7.5 Anticholinergics

There is potential for an additive interaction with concomitantly used anticholinergic medicines. Therefore, avoid coadministration of TRELEGY with other anticholinergic-containing drugs as this may lead to an increase in anticholinergic adverse effects *[see Warnings and Precautions (5.14, 5.15)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are insufficient data on the use of TRELEGY or its individual components, fluticasone furoate, umeclidinium, and vilanterol, in pregnant women to inform a drug-associated risk.

Clinical Considerations

Labor and Delivery: TRELEGY should be used during late gestation and labor only if the potential benefit justifies the potential for risks related to beta-agonists interfering with uterine contractility.

8.2 Lactation

Risk Summary

There is no information available on the presence of fluticasone furoate, umeclidinium, or vilanterol in human milk; the effects on the breastfed child; or the effects on milk production. Umeclidinium is present in rat milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TRELEGY and any potential adverse effects on the breastfed child from fluticasone furoate, umeclidinium, or vilanterol, or from the underlying maternal condition.

8.5 Geriatric Use

Based on available data, no adjustment of the dosage of TRELEGY in geriatric patients is necessary, but greater sensitivity in some older individuals cannot be ruled out.

In Trials 1 and 2 (coadministration trials), 189 subjects aged 65 years and older, of which 39 subjects were aged 75 years and older, were administered umeclidinium 62.5 mcg + fluticasone furoate/vilanterol 100 mcg/25 mcg. 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

TRELEGY has not been studied in subjects with hepatic impairment. Information on the individual components is provided below.

Fluticasone Furoate/Vilanterol

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. Monitor patients for corticosteroid-related side effects *[see Clinical Pharmacology (12.3) of full prescribing information]*.

Umeclidinium

Patients with moderate hepatic impairment (Child-Pugh score of 7-9) showed no relevant increases in C_{max} or AUC, nor did protein binding differ between subjects with moderate hepatic impairment and their healthy controls. Studies in subjects with severe hepatic impairment have not been performed *[see Clinical Pharmacology (12.3) of full prescribing information]*.

10 OVERDOSAGE

No human overdosage data has been reported for TRELEGY.

TRELEGY contains fluticasone furoate, umeclidinium, and vilanterol; therefore, the risks associated with overdosage for the individual components described below apply to TRELEGY. Treatment of overdosage consists of discontinuation of TRELEGY 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 4000 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 Umeclidinium

High doses of umeclidinium may lead to anticholinergic signs and symptoms. However, there were no systemic anticholinergic adverse effects following a once-daily inhaled dose of up to 1000 mcg umeclidinium (16 times the maximum recommended daily dose) for 14 days in subjects with COPD.

10.3 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 (eg, 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 *of full prescribing information*).

Asthma-Related Death

Inform patients that LABA, such as vilanterol, one of the active ingredients in TRELEGY, increase the risk of asthma-related death. TRELEGY is not indicated for the treatment of asthma.

Not for Acute Symptoms

Inform patients that TRELEGY is not meant to relieve acute symptoms of COPD, 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.

Continued on next page

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 TRELEGY 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.

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 (ie, oral) antifungal therapy while still continuing therapy with TRELEGY, but at times therapy with TRELEGY 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.

Pneumonia

Patients with COPD have a higher risk of pneumonia; instruct them to contact their healthcare providers if they develop symptoms of pneumonia.

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 TRELEGY 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 TRELEGY.

Paradoxical Bronchospasm

As with other inhaled medicines, TRELEGY can cause paradoxical bronchospasm. If paradoxical bronchospasm occurs, instruct patients to discontinue TRELEGY and contact their healthcare provider right away.

Hypersensitivity Reactions, Including Anaphylaxis

Advise patients that hypersensitivity reactions (eg, anaphylaxis, angioedema, rash, urticaria) may occur after administration of TRELEGY. Instruct patients to discontinue TRELEGY 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 TRELEGY.

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.

Instruct patients to be alert for signs and symptoms of acute narrow-angle glaucoma (eg, eye pain or discomfort, blurred vision, visual halos, or colored images in association with red eyes from conjunctival congestion and corneal edema). Instruct patients to consult a physician immediately if any of these signs or symptoms develops.

Worsening of Urinary Retention

Instruct patients to be alert for signs and symptoms of urinary retention (eg, difficulty passing urine, painful urination). Instruct patients to consult a physician immediately if any of these signs or symptoms develops.

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.

TRELEGY ELLIPTA was developed in collaboration with INNOVIVA

GlaxoSmithKline
Research Triangle Park, NC 27709

Revised 09/2017 TRL:1BRS

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Printed in USA. 1001205R0 March 2018

TRELEGY ELLIPTA
(fluticasone furoate 100 mcg, umeclidinium 62.5 mcg, and vilanterol 25 mcg inhalation powder)

Earn MOC Points and CME Credits

Each year, the ATS Educational and the International Conference committees collaborate to ensure that International Conference symposia are eligible for Maintenance of Certification points.

ATS 2018 attendees are able to earn up to 44.5 American Board of Internal Medicine MOC Medical Knowledge points and 10 American Board of Pediatrics Part 2 MOC Self-Assessment points.

In addition to the adult and pediatric Core Curriculum, there are 20 symposia that are eligible for MOC and will cover adult pulmonary, critical care, and sleep medicine as well as pediatric pulmonary symposia. The Adult and Pediatric Symposia eligible for MOC at the conference can be found at **conference.thoracic.org/program/moc.php**.

HOW TO EARN MOC POINTS AT ATS 2018

- **During ATS 2018:** Attend any or all of the MOC symposia you are interested in. These sessions are highlighted in the Final Program.
- **After ATS 2018:** Take the post-session test. All the tests will be available on Wednesday, May 23, 2018, 4 p.m. PT and attendees can take the tests at no cost through July 31, 2018. Please note: audience response during a session does *not* count at the post-test.

HOW TO EARN CME ATS 2018

There are two separate pathways for claiming MOC and CME. In order to claim both CME and MOC, you will need to follow steps for both. You must pass the MOC post-test to earn MOC, and complete the CME evaluation to claim CME. Claiming one will not automatically transfer to the other.

CME AND NURSING CE

ATS is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. This live activity has been planned and implemented in accordance with the essential areas and policies of the ACCME and are free from the control of commercial interests. The ATS designates this activity for a maximum of 45 AMA PRA Category 1 Credits™. The designation of AMA PRA Category 1 Credit(s)™ per session is listed in the session pages. Physicians should only claim the credit commensurate with the extent of their participation in the activity.

The American Thoracic Society partners with National Jewish Health® to provide Nursing Contact Hours for selected sessions. Provider approved by the California Board of Registered Nursing, Provider Number CEP 12724.

Pediatric Clinical Core Curriculum 1 is supported by educational grants from Boehringer Ingelheim Pharmaceuticals, Inc. and Gilead Sciences, Inc. ■

Step Up to the ATS Walking Challenge

You still have time to participate in the ATS Walking Challenge. Free wireless activity trackers are available on a first-come, first-served basis at the ATS Walking Challenge Booth, located across from the Starbucks in Lobby B in the Convention Center. The ATS Walking Challenge Mobile App also supports attendees who prefer to use their own FitBit, Jawbone, or iPhone/Android smartphone step counters.

You can watch the results unfold in real-time on leaderboards in the Teva Respiratory booth, #2735, or at the ATS Walking Challenge booth. The top five overall steppers win a prize.

Don't forget, the ATS Walking Challenge also supports the ATS Foundation Research Program. For every participant who walks 30,000 steps during ATS 2018, Teva Respiratory makes a donation of $100 to the ATS Foundation, with a total maximum donation of $50,000 to fund new research awards in pulmonary, critical care, and sleep medicine. ■

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Bibbins-Domingo to Discuss Communities at Risk

The annual ATS Diversity Forum's featured speaker is Kirsten Bibbins-Domingo, MD, PhD, MAS, who will address career and diversity issues followed by a question-and-answer period.

Dr. Bibbins-Domingo co-founded and currently directs the University of California at San Francisco Center for Vulnerable Populations at Zuckerberg San Francisco General Hospital, a research center focused on discovery, implementation, policy, advocacy, and community engagement for communities at risk for poor health and inadequate health care.

A general internist at Zuckerberg San Francisco General Hospital, Dr. Bibbins-Domingo's work focuses on racial, ethnic, and income differences in manifestations of chronic disease and effective clinical, public health, and policy interventions aimed at prevention. She leads the UCSF Cardiovascular Disease Policy Model group that conducts simulation modeling, disease projections, and cost-effectiveness analyses related to cardiovascular disease in the U.S. and in other national contexts.

Also during today's forum, the Minority Trainee Development Scholarships, which recognize trainees who are members of underrepresented minority groups, will be presented. MTDS recipients are selected for the quality of the science in their submitted abstract, among other criteria.

All conference attendees, including past MTDS recipients, are invited to attend this forum, which provides an opportunity for discussion and networking among attendees. Attendees will find inspiration and valuable career insights.

ATS Diversity Forum

11:45 a.m.-1:15 p.m.

Sunday

Grand Hall B (off lobby), Manchester Grand Hyatt Hotel

The Diversity Forum is organized and presented by the ATS Membership Committee and will be hosted by its chair, Janet Lee, MD. The Minority Trainee Development Scholarships are supported by the American Thoracic Society.

Registration is required. There is no fee to attend this event, and tickets will not be issued; however, conference badges are required for admission. A plated lunch will be served. ■

Connect With Colleagues at Networking Events

Expanding your knowledge and network are primary objectives of the ATS 2018 International Conference, where you will find world-class educational programming as well as numerous opportunities for networking. Here are some of the opportunities. Be sure to check the program onsite for specific times and locations.

ASSEMBLY AND SECTION MEETINGS

All assembly and section members and other conference attendees are invited to attend any of the 14 ATS Assembly Annual Membership Meetings on May 20 and 21 or three section meetings during the conference. Assembly leaders will provide updates on the assembly's activities, and members will give input, get involved, and network during the meetings.

ATS FOUNDATION DONOR APPRECIATION SUITE

As a way to thank donors, the ATS Foundation will again feature its ATS Foundation Donor Appreciation Suite at ATS 2018. Conference attendees who contribute $250 or more between June 2017 and May 2018 are invited to the suite, located in the convention center's Sails Pavilion (Upper Level) to enjoy complimentary coffee, tea and snacks, internet access, printers, the use of Microsoft Office software, and private meeting rooms. (Be sure to reserve these ahead of time.)

ATS WOMEN'S AND DIVERSITY FORUMS

Take the opportunity to support women and diversity during two separate luncheon forums at ATS 2018. The Diversity Forum takes place Sunday, May 20, and the Women's Forum takes place Monday, May 21. Both forums are free and include a plated lunch. Pre-registration is required but there are usually seats available at the door on a first-come, first-served basis.

CLINICIANS CENTER

All clinicians are invited to meet, network, relax, refresh, and learn in the Clinicians Center and Learning Lab located in the Sails Pavilion (Upper Level) of the San Diego Convention Center.

On Monday, May 21, don't miss the ATS Outstanding Clinician Award Reception from 4 to 5 p.m.

Educational programs kick off at the Center on Sunday, May 20, with a session on shark tank lung nodules and another on coding and billing. On Monday, May 21, there is a session on ICU rounds and a session on pulmonary hypertension. On Tuesday, topics include health policy and advanced disease state.

Center hours are 7 a.m. to 5 p.m. Sunday, May 20, through Tuesday, May 22, and 7 a.m. to 1 p.m. Wednesday, May 23. Every morning coffee and a light breakfast will be available from 7 to 9 a.m.

EARLY CAREER PROFESSIONALS

Whether you are a graduate or medical student, medical resident, clinical or postdoctoral fellow, or junior faculty member, the ATS is committed to your pursuit of a successful career in pulmonary, critical care, and sleep medicine. To foster career development among early career professionals, ATS has developed a number of networking opportunities.

The Center for Career Development also provides networking opportunities, including the Trainee Educators ATS Camaraderie Hour Medical Educational Fellows' Mixer, on Sunday, May 20. Each day, the CCD will serve a complimentary breakfast at 7 a.m. and offer a themed Professional Networking Hour from 4:30 to 5 p.m.

INTERNATIONAL PARTICIPANTS CENTER

All international attendees are invited to stop by the International Participants Center, located in the Sails Pavilion (upper level) of the San Diego Convention Center. The center is open 7 a.m. to 5 p.m. Sunday, May 20, through Tuesday, May 22, and 7 a.m. to 1 p.m. Wednesday, May 23.

The center is designed to enhance the conference experience for participants from outside North America, as well as provide opportunities to become more knowledgeable about ATS international activities. Use the center to connect with colleagues, network, or just relax while enjoying complimentary snacks, coffee, and soda.

Don't miss the reception to recognize international attendees and honor this year's International Trainee/MECOR award recipients from 4:15 to 6:30 p.m. on Tuesday, May 22, at the center. The reception is open to all international attendees, current and former International Trainee/MECOR award recipients, and their colleagues.

Also plan to attend the educational opportunities available at the Center. These include an interactive session on global health careers in pulmonary and critical care medicine from 11:45 a.m. to 1:15 p.m. on Sunday, May 20, and a discussion on grant writing for beginners from 12 to 2 p.m. on Tuesday, May 22.

SCIENCE AND INNOVATION CENTER

Scientists and researchers looking to network, learn, and relax should head over to the Science and Innovation Center located in the Sails Pavilion (upper level) of the San Diego Convention Center.

A complimentary breakfast will be served daily in the SIC at 7 a.m., and light refreshments will be served each day at noon.

If you need to catch up on basics of a topic before attending a symposium, you can attend a SIC 101 series presentation. ■

Please join us for an evening symposium

Consider the Risk:
A Case-based Look at Risk Assessment in PAH Management

Sunday, May 20, 2018

6:30 PM–7:00 PM Registration and Dinner
7:00 PM–8:30 PM Symposium

Agenda and Faculty

Welcome and Introductions
Vallerie McLaughlin, MD, Chair
University of Michigan
Ann Arbor, Michigan

Overview of PAH
Vallerie McLaughlin, MD

Current Considerations About Clinical Decision-Making in PAH
Vallerie McLaughlin, MD

Evaluating Risk in a Previously Diagnosed IPAH Patient: Case Study and Discussion
Nick H. Kim, MD
University of California, San Diego
La Jolla, California

Evaluating Risk in a Previously Diagnosed PAH-CTD Patient: Case Study and Discussion
Lana Melendres-Groves, MD
University of New Mexico
School of Medicine
Albuquerque, New Mexico

Panel Discussion
All Faculty

Concluding Remarks
Vallerie McLaughlin, MD

Hilton San Diego Bayfront

Indigo Ballroom A/E,
Second Floor
1 Park Blvd
San Diego, California

Register on-site or online at: www.PAHsymposium.com

This promotional program is sponsored by Actelion Pharmaceuticals US, Inc., a Janssen Pharmaceutical Company of Johnson & Johnson.

Dinner will not be provided to physicians and other healthcare professionals licensed in Vermont or other states where gifts and meals are prohibited. Dinner provided to physicians will be subject to reporting under Federal law. Federal, state, and local government employees should abide by their respective meal limits. We regret that spouses and other guests cannot be accommodated.

An Industry-Organized Symposium at the ATS 2018 International Conference. A non-CME educational program sponsored by Actelion Pharmaceuticals US, Inc., a Janssen Pharmaceutical Company of Johnson & Johnson, open to all ATS 2018 International Conference attendees.

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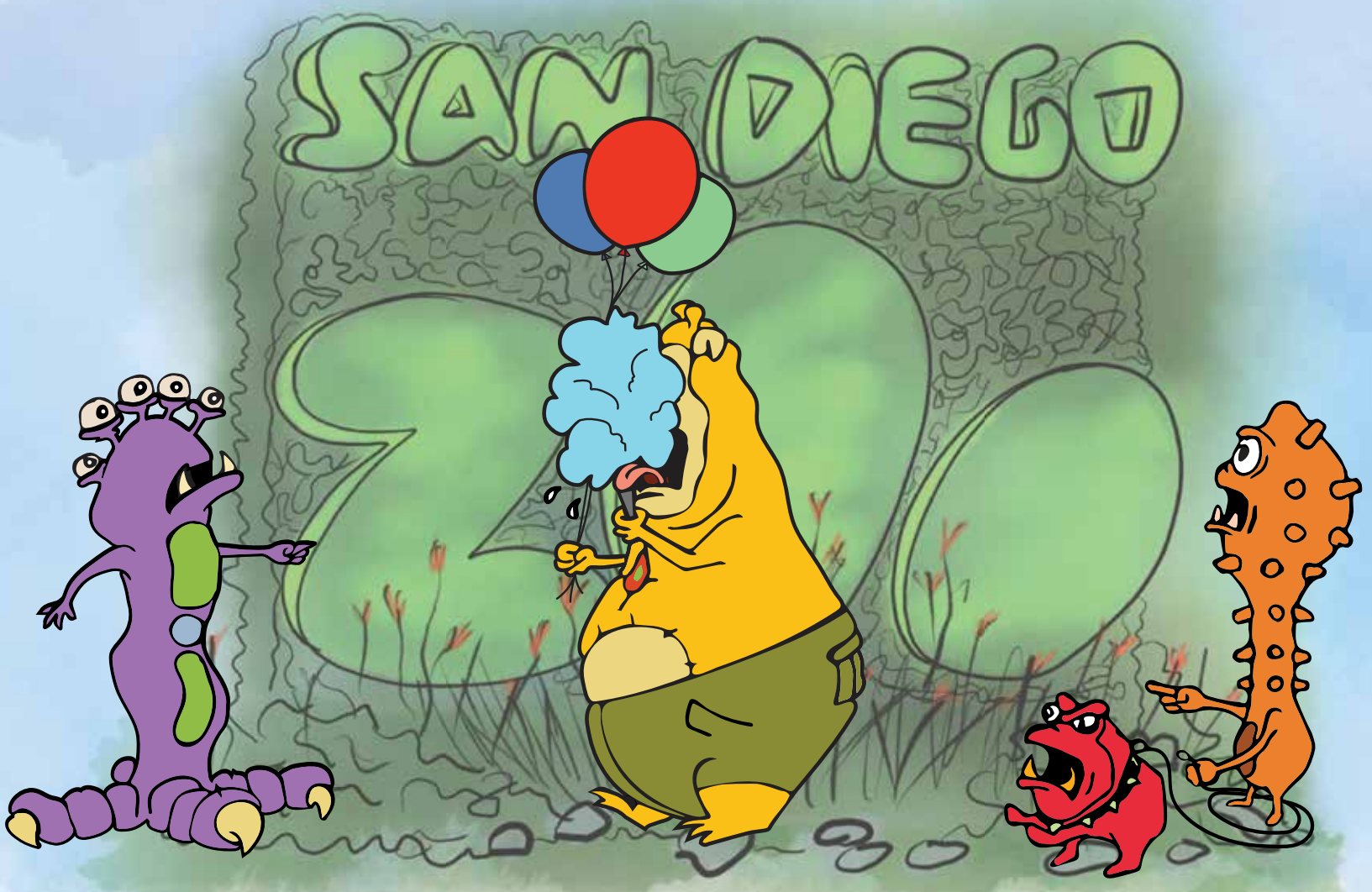

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Gastrointestinal Panel: Quickly ruling in or out enteric pathogens may improve patient care by preventing misdiagnosis and mistreatment.

Meningitis/Encephalitis Panel: Quickly identifying a CNS infection as viral, bacterial or fungal may reduce patient mortality.

Pneumonia Panel (Investigational Use Only): This panel will test for 18 Bacteria, 8 Viruses, and 7 genetic markers of antibiotic resistance, all in one hour!

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Question of the Day

How do co-morbidities affect whether to offer low-dose CT screening for lung cancer?

Todd Bull, MD
Aurora, Colorado
"It is important to identify the underlying co-morbidities, identify the type of lung cancer, and understand the wants and needs of the patient. It should not be a knee-jerk decision."

Susan Murin, MD, MSC, MPH
Sacramento, California
"If the co-morbidities are so severe that it would not affect the outcome or life expectancy is less than three years, it would be of limited use."

Kenneth Ramos, MD, PhD, PharmD
Tucson, Arizona
"You basically do not check on co-morbidities. Low-dose CT scan sticks to prescribed guidelines of age and smoking history."

Chelsea Davis, PA
Springfield, Oregon
"Co-morbidities tell you what the patient might be able to handle, what kind of treatment they can tolerate. If they have bad co-morbidities that would keep them from receiving therapies, it's a risk-benefit conversation about the diagnosis of the lung cancer and what's realistic."

Joseph Friedberg, MD
Baltimore, Maryland
"It shouldn't. There's no risk for two seconds in a CT scanner, which is all it takes. There should not be a reason you wouldn't want to know if someone has lung cancer. You would act on the info, unless they were imminently dying."

HOW ARE WE DIAGNOSING AND MANAGING OUR PATIENTS WITH IPF?

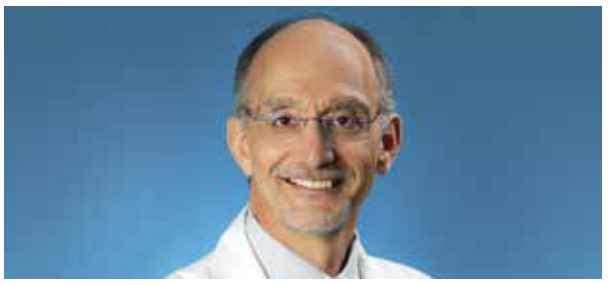
AN EXPERT-GUIDED DISCUSSION

Join Us for a Dinner Symposium

6:30-8:30 P.M., SUNDAY, MAY 20, 2018

SAN DIEGO MARRIOTT MARQUIS AND MARINA, MARINA BALLROOM F-G

333 West Harbor Drive, San Diego, CA 92101



STEVEN D. NATHAN, MD
Inova Fairfax Hospital
Falls Church, VA

SHYAM SUBRAMANIAN, MD
Sutter Gould Medical Foundation
Tracy, CA

ALISON G. WILCOX, MD, FSCCT
University of Southern California
Los Angeles, CA

Join us for a collaborative discussion with a multidisciplinary team of renowned interstitial lung disease (ILD) experts to investigate the key barriers and benefits to timely diagnosis and management of patients with IPF.

An Industry-Organized Symposium at the ATS 2018 International Conference.

A non-CME educational program sponsored by Genentech. Due to regulatory restrictions, this program is only available to attendees from the United States.

Minnesota, New Jersey, Vermont, and Federal Entities (e.g., the Department of Defense and the Department of Veterans Affairs) have restrictions on receiving in-kind benefits (e.g., meals, valet parking) at company-sponsored events. You are accountable for understanding such restrictions and complying with them. If you are licensed in or affiliated with any of these states or federal agencies, Genentech policies may restrict you from consuming any portion of the Genentech-sponsored meal at this program or from receiving any other in-kind benefit from Genentech (e.g., valet parking) in connection with the program.

Indication

Esbriet® (pirfenidone) is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

Select Important Safety Information

Elevated liver enzymes: Increases in ALT and AST >3× ULN have been reported in patients treated with Esbriet. In some cases these have been associated with concomitant elevations in bilirubin. Patients treated with Esbriet had a higher incidence of elevations in ALT or AST than placebo patients (3.7% vs 0.8%, respectively). No cases of liver transplant or death due to liver failure that were related to Esbriet have been reported. However, the combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that could lead to death or the need for liver transplants in some patients. Conduct liver function tests (ALT, AST, and bilirubin) prior to initiating Esbriet, then monthly for the first 6 months and every 3 months thereafter. Dosage modifications or interruption may be necessary.

Photosensitivity reaction or rash: Patients treated with Esbriet had a higher incidence of photosensitivity reactions (9%) compared with patients treated with placebo (1%). Patients should avoid or minimize exposure to sunlight (including sunlamps), use a sunblock (SPF 50 or higher), and wear clothing that protects against sun exposure. Patients should avoid concomitant medications that cause photosensitivity. Dosage reduction or discontinuation may be necessary.

Gastrointestinal disorders: Gastrointestinal events of nausea, diarrhea, dyspepsia, vomiting, gastroesophageal reflux disease, and abdominal pain were more frequently reported in patients treated with Esbriet. Dosage reduction or interruption for gastrointestinal events was required in 18.5% of patients in the 2403 mg/day group, as compared to 5.8% of patients in the placebo group; 2.2% of patients in the Esbriet 2403 mg/day group discontinued treatment due to a gastrointestinal event, as compared to 1.0% in the placebo group. The most common (>2%) gastrointestinal events that led to dosage reduction or interruption were nausea, diarrhea, vomiting, and dyspepsia. Dosage modifications may be necessary in some cases.

Adverse reactions: The most common adverse reactions (≥10%) are nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsia, dizziness, vomiting, anorexia, gastroesophageal reflux disease, sinusitis, insomnia, weight decreased, and arthralgia.

Drug interactions: Concomitant administration with strong inhibitors of CYP1A2 (eg, fluvoxamine) significantly increases systemic exposure of Esbriet and is not recommended. Discontinue prior to administration of Esbriet. If strong CYP1A2 inhibitors cannot be avoided, dosage reductions of Esbriet are recommended. Monitor for adverse reactions and consider discontinuation of Esbriet as needed.

Concomitant administration of Esbriet and ciprofloxacin (a moderate inhibitor of CYP1A2) moderately increases exposure to Esbriet. If ciprofloxacin at the dosage of 750 mg twice daily cannot be avoided, dosage reductions are recommended. Monitor patients closely when ciprofloxacin is used.

Agents that are moderate or strong inhibitors of both CYP1A2 and CYP isoenzymes involved in the metabolism of Esbriet should be avoided during treatment.

The concomitant use of a CYP1A2 inducer may decrease the exposure of Esbriet, and may lead to loss of efficacy. Concomitant use of strong CYP1A2 inducers should be avoided.

Specific populations: Esbriet should be used with caution in patients with mild to moderate (Child Pugh Class A and B) hepatic impairment. Monitor for adverse reactions and consider dosage modification or discontinuation of Esbriet as needed. The safety, efficacy, and pharmacokinetics of Esbriet have not been studied in patients with severe hepatic impairment. Esbriet is not recommended for use in patients with severe (Child Pugh Class C) hepatic impairment.

Esbriet should be used with caution in patients with mild (CL^{cr} 50–80 mL/min), moderate (CL^{cr} 30–50 mL/min), or severe (CL^{cr} less than 30 mL/min) renal impairment. Monitor for adverse reactions and consider dosage modification or discontinuation of Esbriet as needed. The safety, efficacy, and pharmacokinetics of Esbriet have not been studied in patients with end-stage renal disease requiring dialysis. Use of Esbriet in patients with end-stage renal diseases requiring dialysis is not recommended.

Smoking causes decreased exposure to Esbriet, which may alter the efficacy profile of Esbriet. Instruct patients to stop smoking prior to treatment with Esbriet and to avoid smoking when using Esbriet.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

Please see full Prescribing Information for additional Important Safety Information.

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Esbriet® (pirfenidone) tablets 267 mg 801 mg

ATS Lauds 3 Scientists at Opening Ceremony

ATS presented its annual Respiratory Health Awards during the opening ceremony on Saturday. George Thurston, MD, received the Public Service Award; Eric D. Bateman, MB, ChB, received the World Lung Health Award; and Yohannes T. Ghebre, PhD, received the Jo Rae Wright Award for Outstanding Science.

PUBLIC SERVICE AWARD

George Thurston, MD

Dr. Thurston's pioneering research has made substantial contributions to the health effects of particular matter exposure. He was among the first to report the association between PM2.5 exposure and mortality, work that was critical to current PM2.5 exposure standards and classification of PM2.5 as a cause of human lung cancer as it increases the risk of ischemic heart disease, acute cardiac events, asthma, and other respiratory diseases.

Dr. Thurston has worked tirelessly to translate science into effective policy that can improve the health of individuals and populations. He seldom turns down an opportunity to speak to the press about clean air and the importance of air quality standards.

WORLD LUNG HEALTH AWARD

Eric D. Bateman, MB, ChB

Professor Bateman has spent two decades promoting global lung health from within the ATS and representing the organization internationally. He founded the University of Cape Town Lung Institute in 1999. Recognizing that achieving maximum impact in lung disease means integrating lung care and disease prevention into primary health care, the UCT Knowledge Translation Unit has standardized and improved primary care delivery by nurses, physicians, and health workers using a standardized format of algorithms and checklists tailored to local priorities in the care of common infectious and non-communicable chronic conditions.

The resulting Practical Approach to Care Kit has been translated and adapted for use around the world. Professor Bateman has played key roles in GINA, the Global Initiative for Asthma, and has had an active and prolific academic research career with more than 300 peer-reviewed publications.

OUTSTANDING SERVICE

Yohannes T. Ghebre, PhD

Dr. Ghebre emerged from war-torn Eritrea to win a World Bank Scholarship. He earned a BSc from the University of Cape Town, then a PhD in medical microbiology. Moving to Stanford University, he worked on the effects of tobacco smoke on cardiovascular health. He developed a robotic assay to screen more than 130,000 compounds to uncover the handful that regulate nitric oxide synthase (NOS) to develop drug leads for interstitial lung disease. His hits included proton pump inhibitors, which are effective NOS antagonists.

Given the pathobiologic role of the NOS pathway in lung inflammation and fibrosis, Dr. Ghebre pioneered the concept of PPIs as antifibrotic drugs. He has been awarded a number of NHLBI and American Heart Association grants in support of his research. ■

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We help the world breathe
PULMONARY • CRITICAL CARE • SLEEP

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RESTORING JOY IN HEALTH CARE

How can we make burnout better? Explore the Restoring Joy in Health Care booth (#904). While you're there, visit with a therapy dog. Therapy dogs are in the booth from 11 a.m. to 2 p.m. each day.

OPENING SESSION

Continued from page 1

"That is an existential challenge to medicine," Dr. Kirch said. "The best people to speak to the value of science are the people who do it."

The third challenge is education. Not education spending, but the process of education.

"Our students are tired of the sage on the stage," Dr. Kirch said. "They are ready to adapt new technology, apps, artificial intelligence, virtual reality, and high-definition simulation to learning."

Inequality is the fourth key challenge. There is a straight line between income disparities and health disparities, Dr. Kirch noted. One of the best predictors of health status is income and educational status.

"Health inequalities are some of the most pernicious challenges to health," he said.

The fifth challenge is burnout and depression. Just as "to err is human" focused attention on quality in health care, the spotlight today must shine on the reality that physicians are not immune to human frailties.

Lack of leadership is the final challenge.

"We must face the brutal realities and set the course to prevail against these challenges," Dr. Kirch said. "It is so easy to get inspired to lead in health care because of our foundation in clinical ethics. Do good for patients, avoid harm, respect their autonomy, and build social justice. It is not ethically correct to have haves and have-nots in health care." ■

KEYNOTE SERIES

Continued from page 1

how heart, lung, and blood research can be expected to change dramatically over the next several decades in response to major drivers of research activity.

Dr. Kiley joined the NHLBI, in the NIH, as a health scientist administrator in the Institutes Division of Lung Diseases. He subsequently served as chief of the Division's Airways Diseases Branch, director of the NIH National Center on Sleep Disorders Research, and currently serves as director of the Division of Lung Diseases. Dr. Kiley's primary research interests include obstructive lung diseases and sleep.

Victoria Sweet, MD

Slow Medicine: The Key to Post-ICU Recovery? (K2)
Room 6 C/F (Upper Level), San Diego Convention Center

Victoria Sweet, MD, associate clinical professor of medicine at the University of California, San Francisco, and a prize-winning historian with a PhD in history, will discuss a radical new understanding of how medicine is best practiced, based on her book, Slow Medicine.

Dr. Sweet practiced medicine for more than 20 years at Laguna Honda Hospital in San Francisco, where she began writing. Her second book focuses on what she calls Slow Medicine. The premise of Slow Medicine is that medicine works best—that is, arrives at the right diagnosis and the right treatment for the least amount of money—when it is personal and face-to-face; when the doctor has enough time to do a good job, and pays attention not only to the patient but to what's around the patient. ■

KEYNOTE SERIES LINEUP

Monday: Macrophages in Health and Disease

Reducing Burnout and Promoting Engagement

Tuesday: Hypoxemic and Ischemic Protection in Deep-Diving Seals

Bacteriophage Therapy

Wednesday: On Pharma: The Complexity of Innovation

The Pulmonologist as Medical Educator

Applications Now Being Accepted

Gilead Sciences Research Scholars Program In Cystic Fibrosis

The program supports innovative scientific research that will advance knowledge in the field of cystic fibrosis, and provides support for 3 junior faculty researchers in Canada, Europe, or the United States for a 2-year period

Each award will be funded up to USD130,000, to be paid in annual installments of up to USD65,000

Awards are subject to separate terms and conditions

SCIENTIFIC REVIEW COMMITTEE

Applications will be reviewed by a committee comprised of internationally recognized experts in basic and clinical research in the field of cystic fibrosis

Application Deadline:
Friday, July 20, 2018, 11:59 PM Daylight Savings Time

For more information and to apply for an award, please visit:
http://researchscholars.gilead.com
Click on the CF program logo

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