Il portfolio Novartis: attualità e prospettive future in ambito respiratorio

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Omalizumab: 10 years of experience

Past, present and future for our patients

2006

Lancio con registro AIFA on-line

Prescrivibilità dai 12 anni

Range IgE per trattamento: da 30-700 UI/ml

2010

Espansione della Tabella posologica: da 30-1500 UI/ml (IgE totali)

Indicazione Pediatrica: Omalizuamb è prescrivibile sin dall'età di 6 anni.

Chiusura del Registro web-based: Piano Terapeutico Cartaceo

Classe di rimborsabilità da H ad A
Prescrizione da parte di specialisti **allergologo-immunologo-pneumologo** del territorio

2014

2015

Indicazione in Orticaria Cronica Spontanea

Estensione della prescrivibilità a Dermatologo

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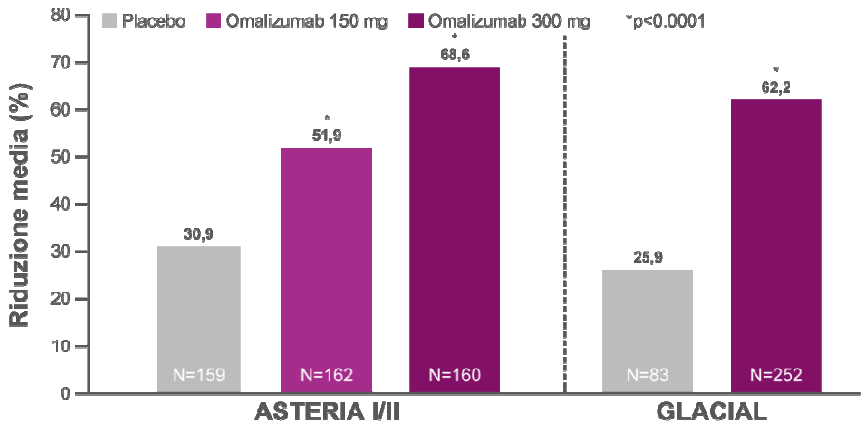
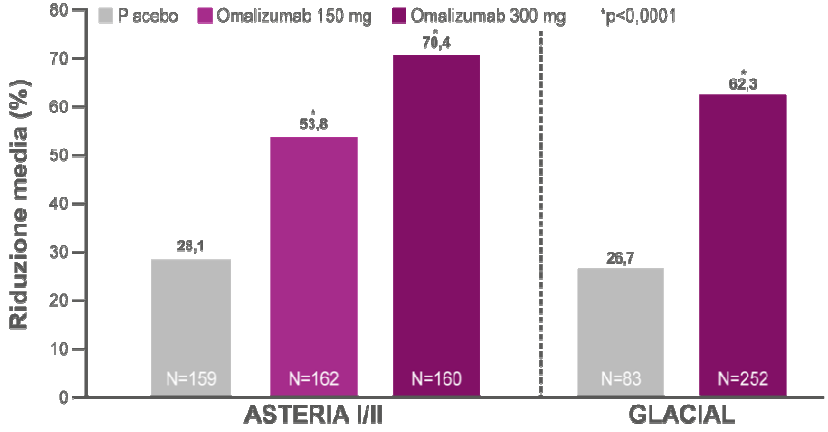
First approved biologic in CSU management

Fast onset of action, efficacy in symptoms reduction

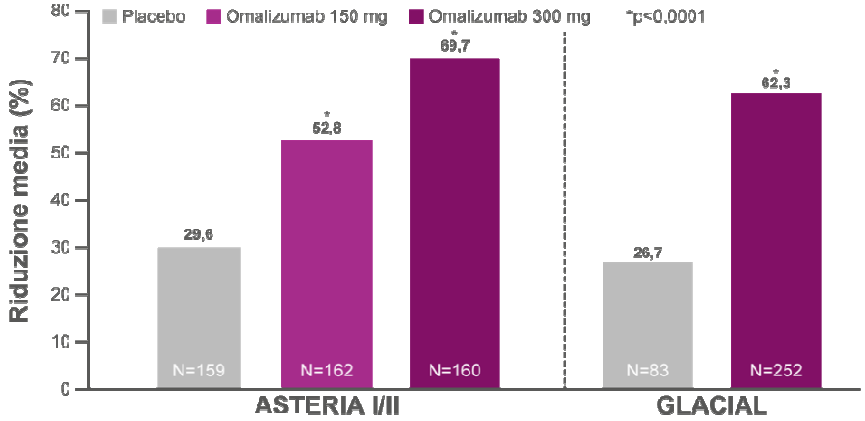
-69% PRURITO con 300 mg di omalizumab



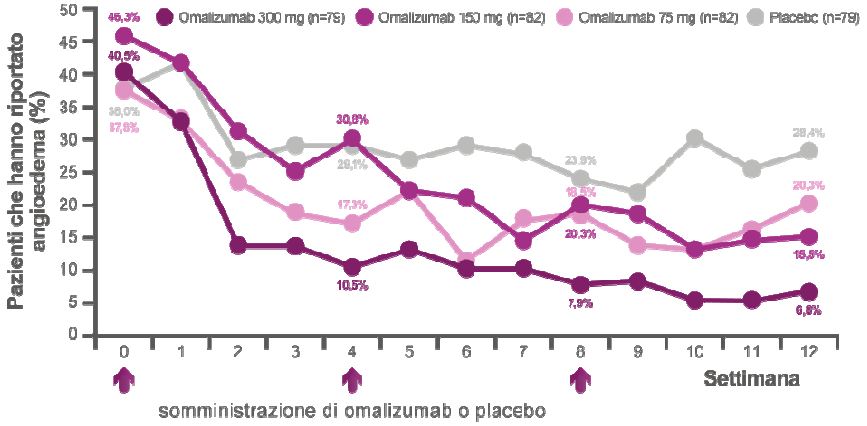
-70% POMFI con 300 mg di omalizumab



-70% UAS7 con 300 mg di omalizumab



Riduzione di pazienti con Angioedema



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Clinical Pipeline

Novartis is consistently rated as having one of the industry's most respected development pipelines, with more than 200 projects in clinical development, as of December 31, 2016.

Many of these projects, which include new molecular entities as well as additional indications and different formulations for marketed products, are for potentially best-in-class or first-in-class medicines that could significantly advance treatment standards for patients worldwide.

This table provides an overview of selected projects in confirmatory development. We use the traditional pipeline model as a platform (e.g., Phase I-III). However, we have tailored the process to be simpler, more flexible and more efficient

.For a detailed review of selected projects in confirmatory development, download the complete Novartis Pipeline chart (PDF 92 KB):

Major development projects

Project/product	Common name	Mechanism of action	Potential indication/disease area	Route of administration	Planned filing dates [2]	PHASE I	PHASE II	PHASE III	SUBMISSION
Oncology									
ABL001	asciminib	BCR-ABL inhibitor	Chronic myeloid leukemia (CML), 3rd line	Oral	2020	PHASE I			
PIM447	–	Pan-PIM inhibitor	Hematologic tumors	Oral	≥2021	PHASE I			
CTL019	tisagenlecleucel-T	CD19-targeted chimeric antigen receptor T-cell immunotherapy	Pediatric acute lymphoblastic leukemia [lead indication]; diffuse large B-cell lymphoma	Intravenous infusion	2017		PHASE II		
INC280	capmatinib	c-MET inhibitor	Non-small cell lung cancer (NSCLC) [lead indication]; NSCLC (EGFRm)	Oral	2018		PHASE II		
BYL719	alpelisib	PI3Kα inhibitor	Hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (postmenopausal women), 2nd line (+ fulvestrant)	Oral	2019			PHASE III	
Jakavi	ruxolitinib	JAK1/2 inhibitor	Graft-versus-host disease [lead indication]; early myelofibrosis	Oral	2019			PHASE III	
LCI699	osilodrostat	Aldosterone synthase inhibitor	Cushing's disease	Oral	2018			PHASE III	
Promacta/Revolade	eltrombopag	Thrombopoietin receptor agonist	Severe aplastic anemia, 1st line	Oral	2017			PHASE III	
SEG101	crizanlizumab	P-selectin inhibitor	Sickle cell disease	Intravenous infusion	2020			PHASE III	
Arzerra	ofatumumab	Anti-CD20 monoclonal antibody	Refractory non-Hodgkin's lymphoma	Oral	2018			PHASE III	
LEE011	ribociclib	CDK4/6 inhibitor	HR+/HER2- advanced breast cancer (postmenopausal women), 1st line (+ letrozole) [lead indication]; HR+/HER2- advanced breast cancer (postmenopausal women), 1st/2nd line (+ fulvestrant); HR+/HER2- advanced breast cancer (premenopausal women), 1st line (+ tamoxifen + goserelin or NSAP + goserelin); HR+/HER2- breast cancer (adjuvant)	Oral	US/EU registration				SUBMISSION
PKC412	midostaurin	Signal transduction inhibitor	Acute myeloid leukemia (AML) [lead indication]; advanced systemic mastocytosis; AML (FLT3 wild type)	Oral	US/EU registration				SUBMISSION
Signifor LAR	pasireotide	Somatostatin analogue	Cushing's disease	Long-acting release/ intramuscular injection	US/EU registration[4]				SUBMISSION
Tafinlar + Mekinist	dabrafenib + trametinib	BRAF inhibitor + MEK inhibitor	BRAF V600+ NSCLC [lead indication]; BRAF V600+ melanoma (adjuvant); BRAF V600+ colorectal cancer	Oral	US/EU registration				SUBMISSION
Zykadia	ceritinib	ALK inhibitor	ALK+ advanced NSCLC (1st line, treatment naïve) [lead indication]; ALK+ NSCLC (brain metastases)	Oral	US/EU registration				SUBMISSION
Afinitor/Votubia	everolimus	mTOR inhibitor	Tuberous sclerosis complex seizures	Oral	EU registration US 2017				SUBMISSION
Tasigna	nilotinib	BCR-ABL inhibitor	CML treatment-free remission	Oral	EU registration US 2017				SUBMISSION

[1] Filings that have received approval in either the US or EU but are awaiting approval in the other market
[2] Phase and planned filing dates refer to the lead indication in development.
[3] Non-steroidal aromatase inhibitor
[4] Submission pending acceptance by the FDA

Clinical research: leadership in Italy since 2005

Best-in-class position in the ranking of trials per sponsor

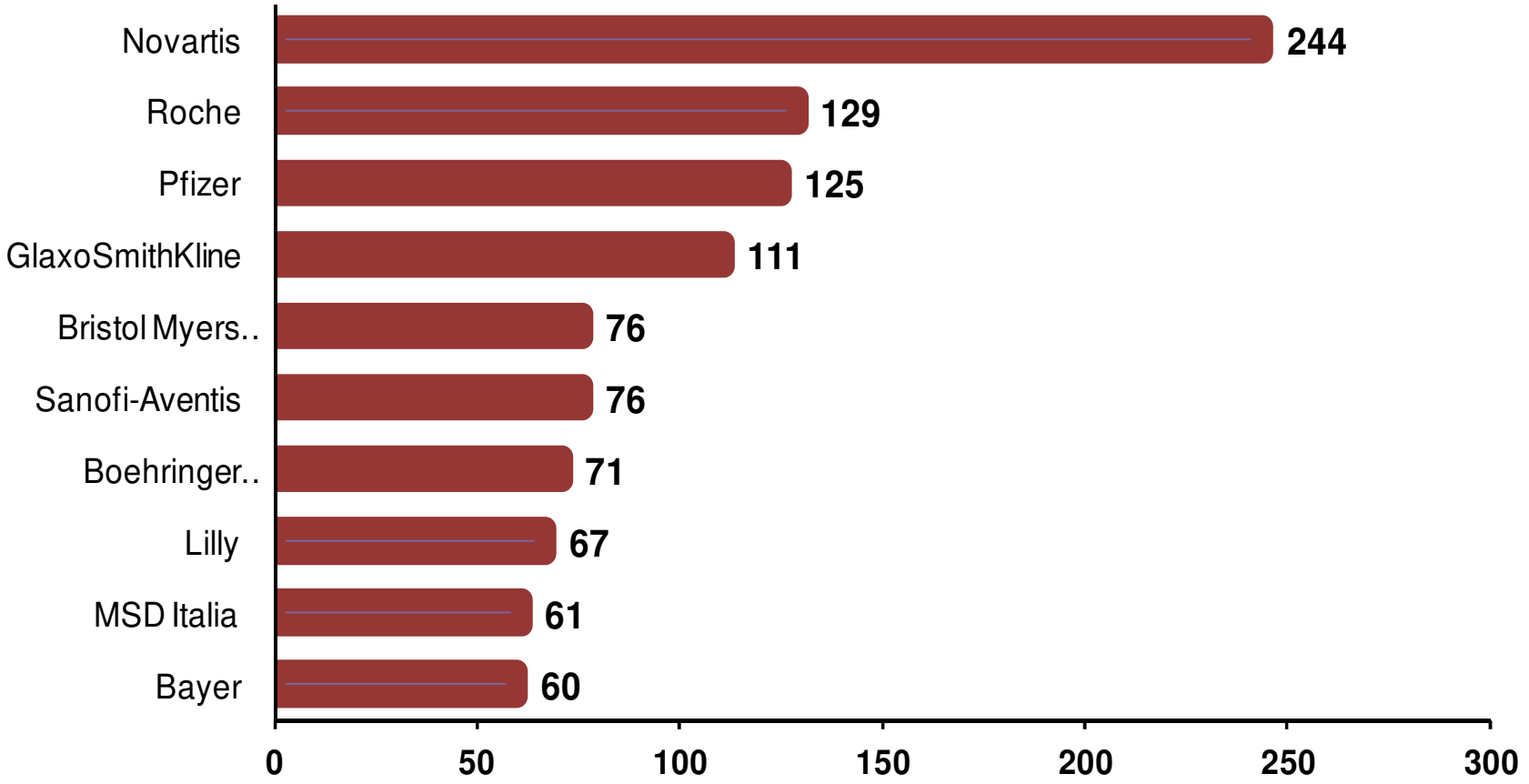

Grafico tratto da: 11° Rapporto Nazionale - AIFA, 2012. La sperimentazione clinica dei medicinali in Italia. Dati dal 1/1/2007 al 31/12/2011

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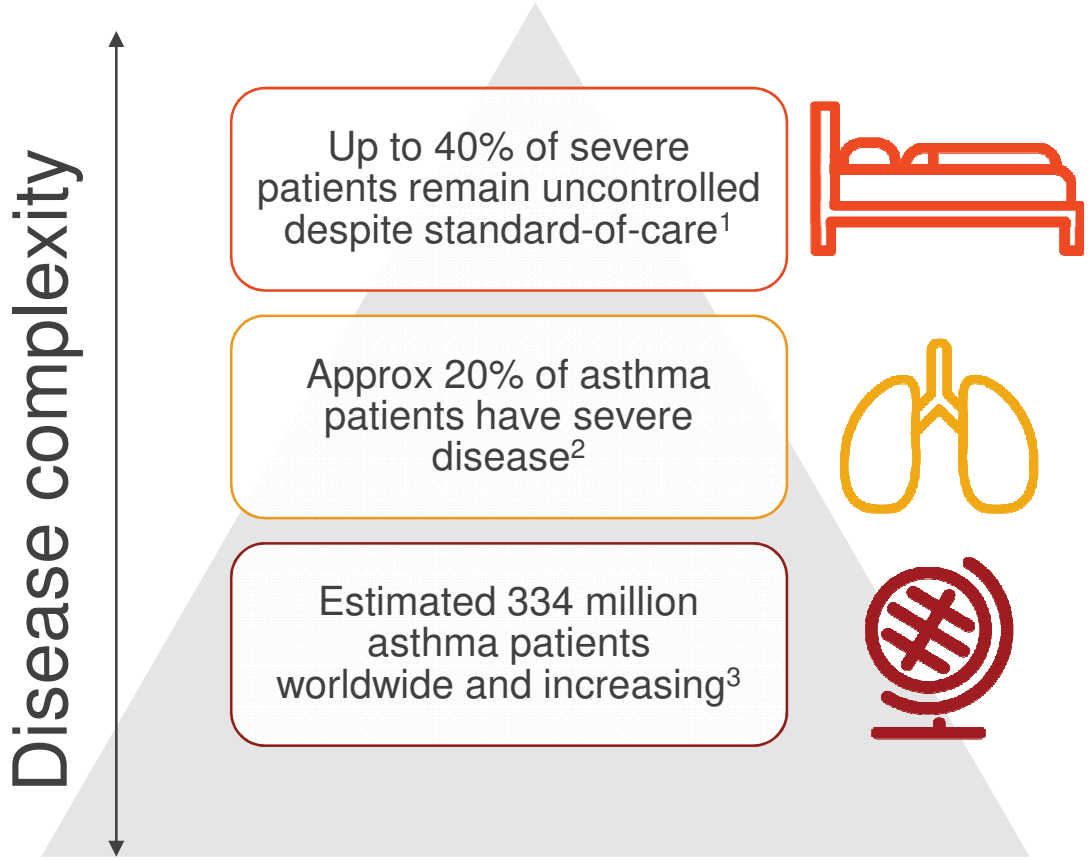
Severe asthma:

A relatively low prevalence but high burden



1. Price D et al. npj Prim Care Resp Med 2014;24:14009; 2. Peters SP et al. Respir Med 2006;100:1139–51; 3. The Global Asthma Report 2014. Available at: http://www.globalasthmareport.org/resources/resources.php, accessed 06/01/16.

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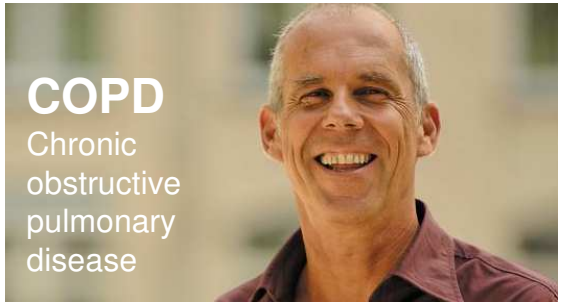
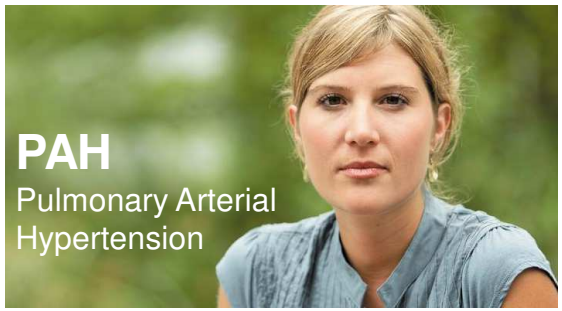
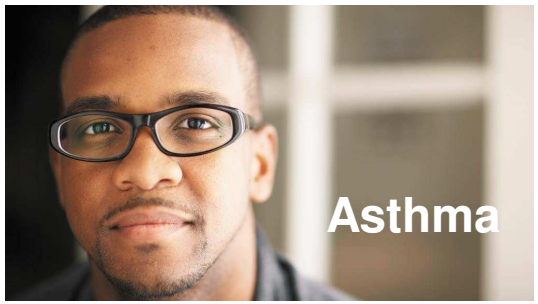
Novartis Respiratory focus Areas

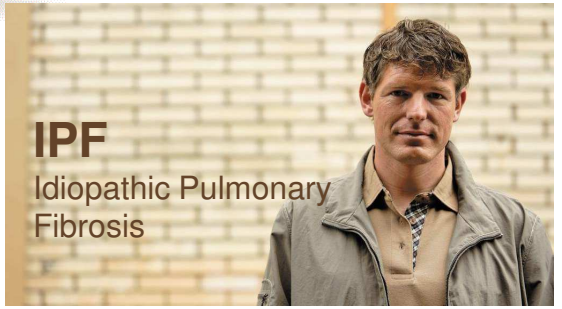
Place patient unmet need at the center of medicines development







Novartis Respiratory



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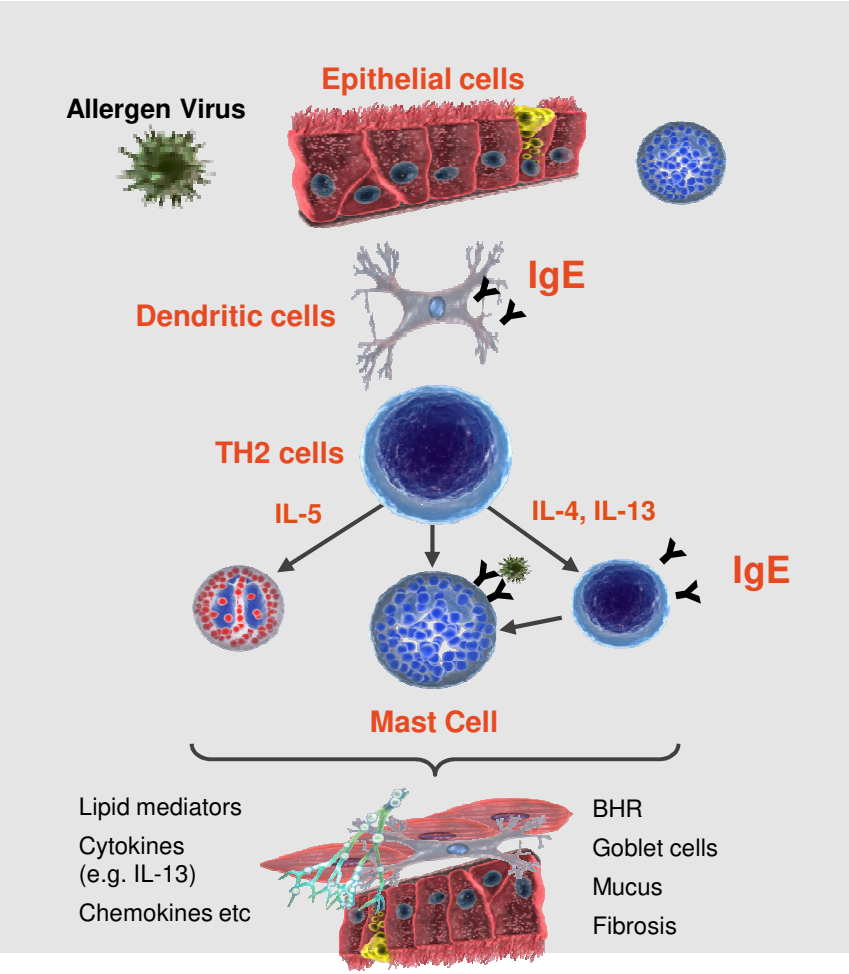
Asthma: a complex disease

There is no one single target in asthma



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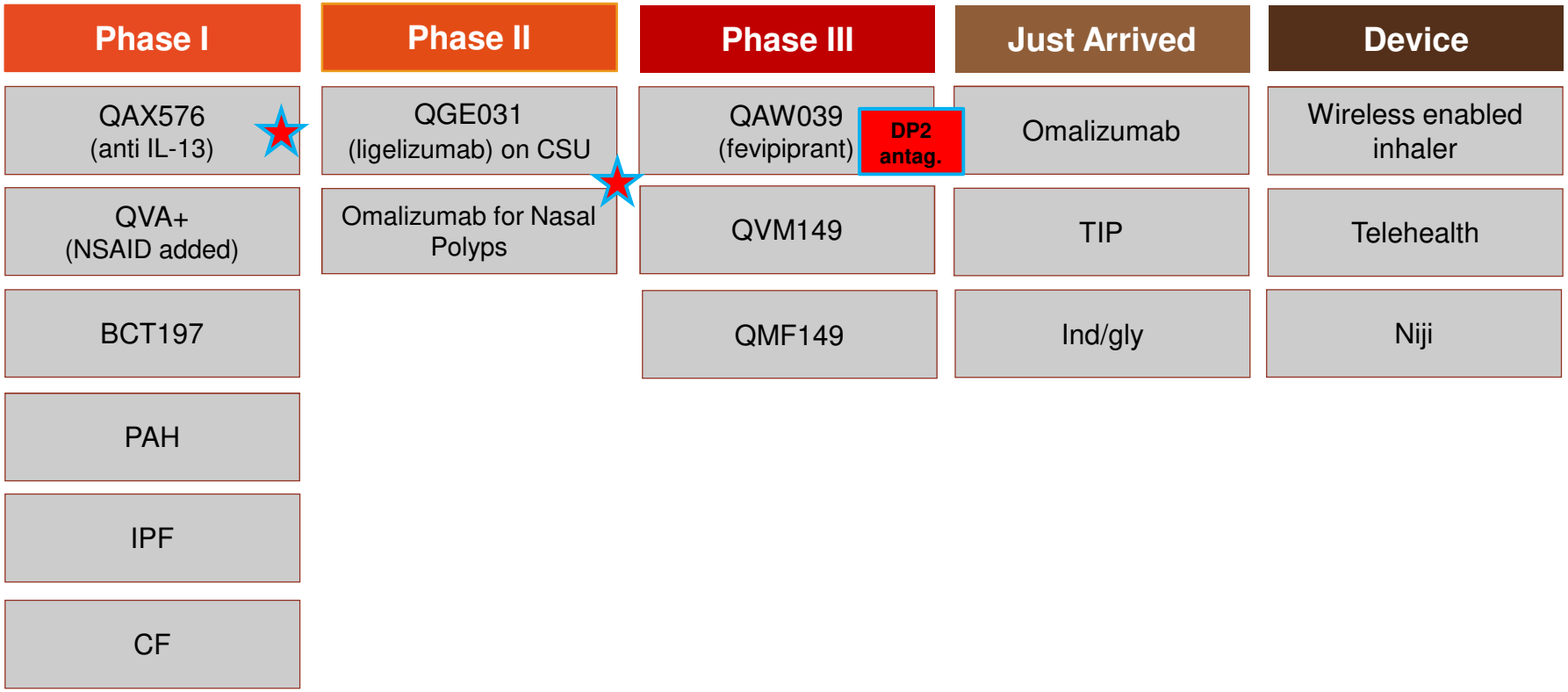
A Nice Present; an Even Better Future

Robust efforts on pipeline and innovation for patients' benefit



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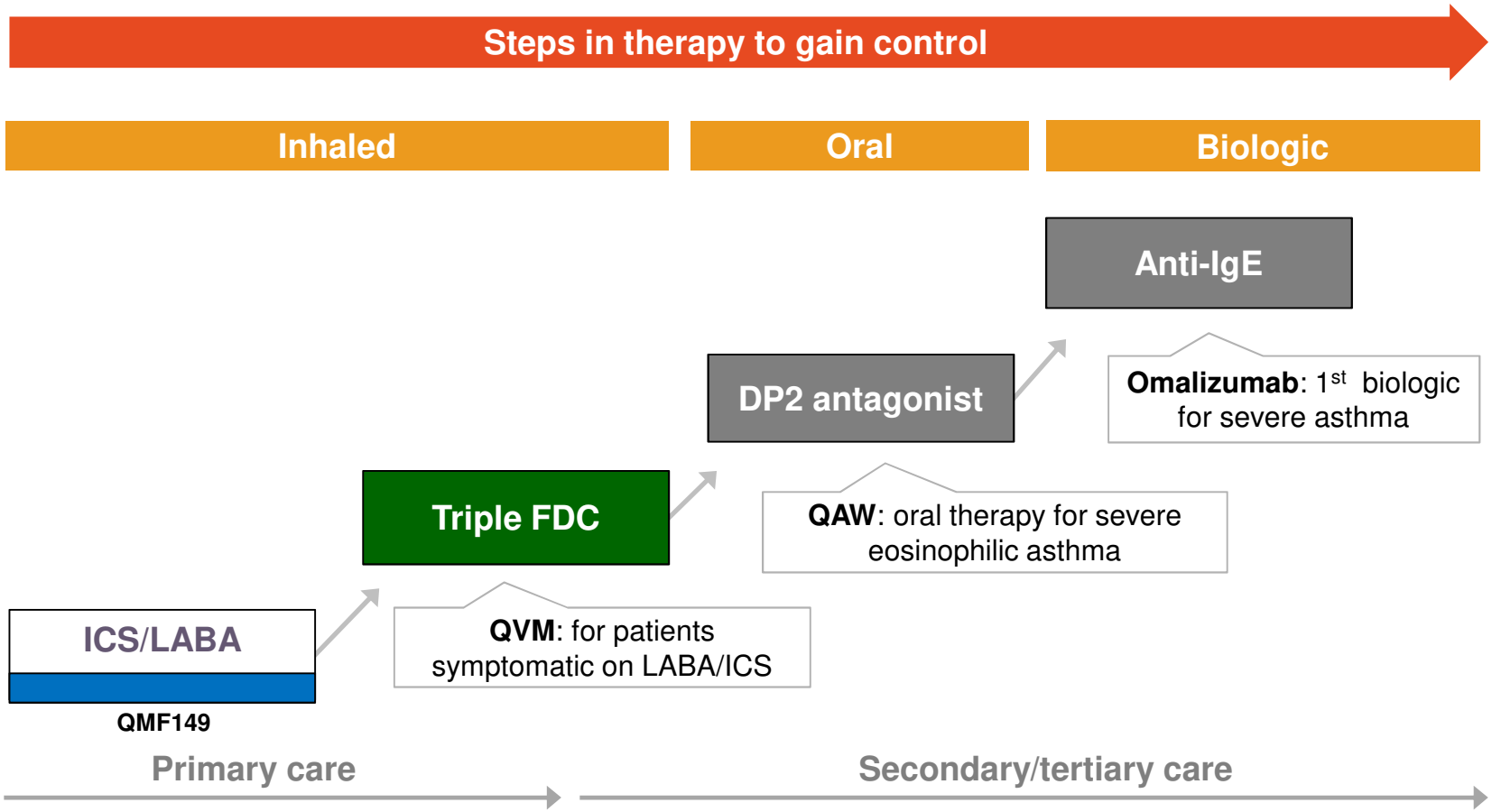
Novartis is well positioned to provide tailored solutions for patients with moderate to severe asthma



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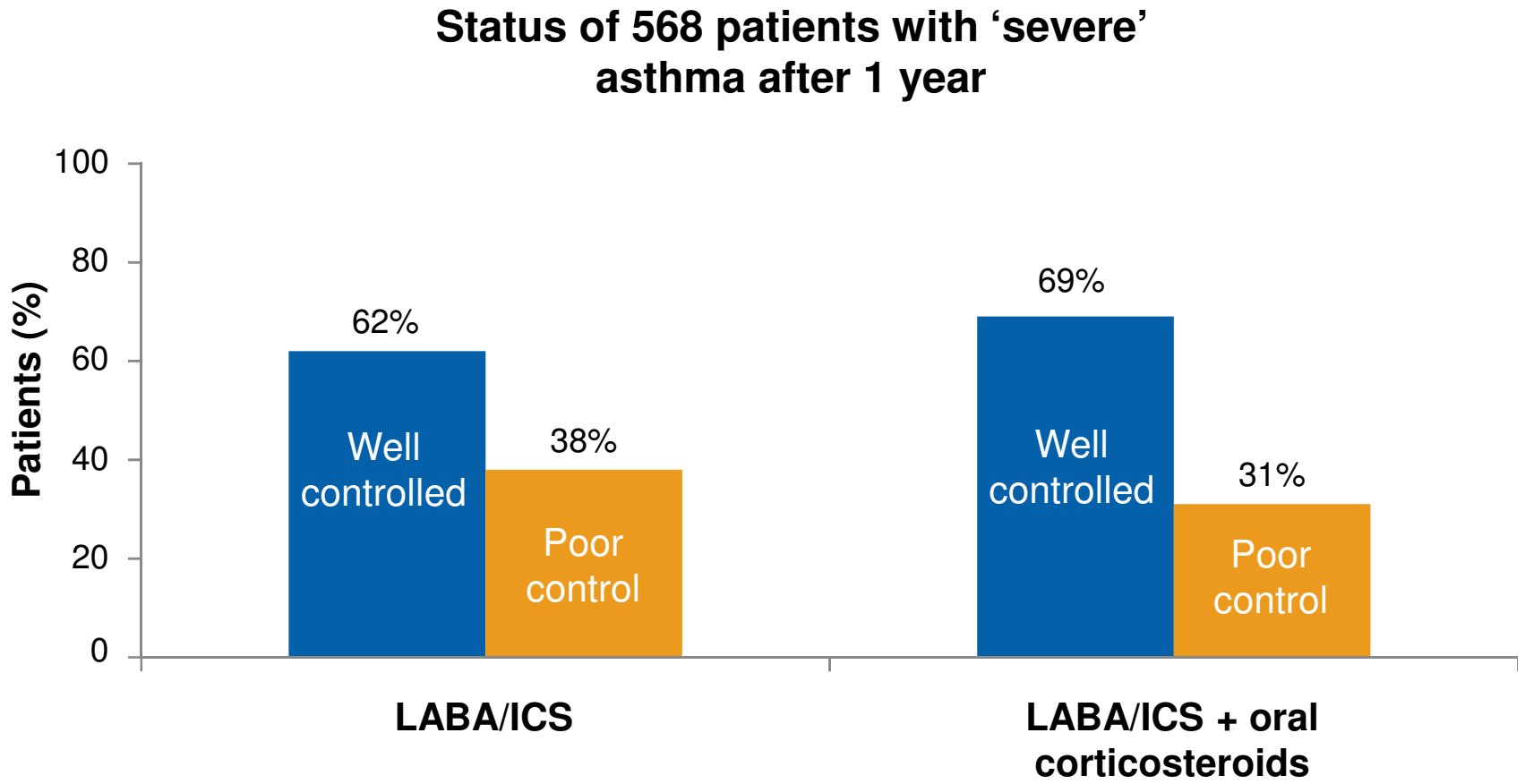
Unmet Need: Many Severe Asthma patients do not achieve control with LABA/ICS



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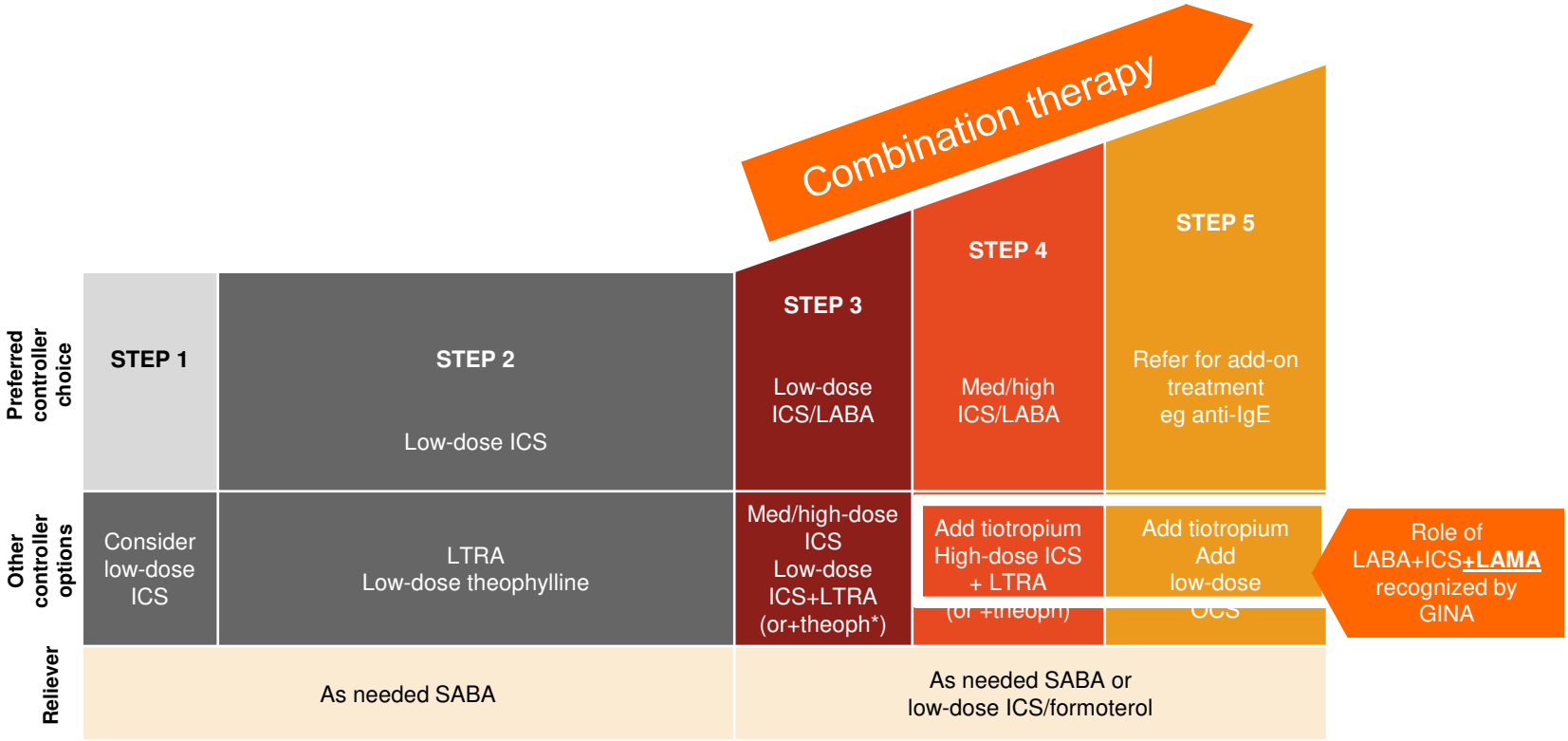
Bateman ED et al. Am J Respir Crit Care Med 2004;170:836–44

Role of triple combination therapy in asthma

New GINA Guidelines recognize LAMA add-on to LABA/ICS in Step 4 & 5



Adapted from GINA 2015. www.ginasthma.org

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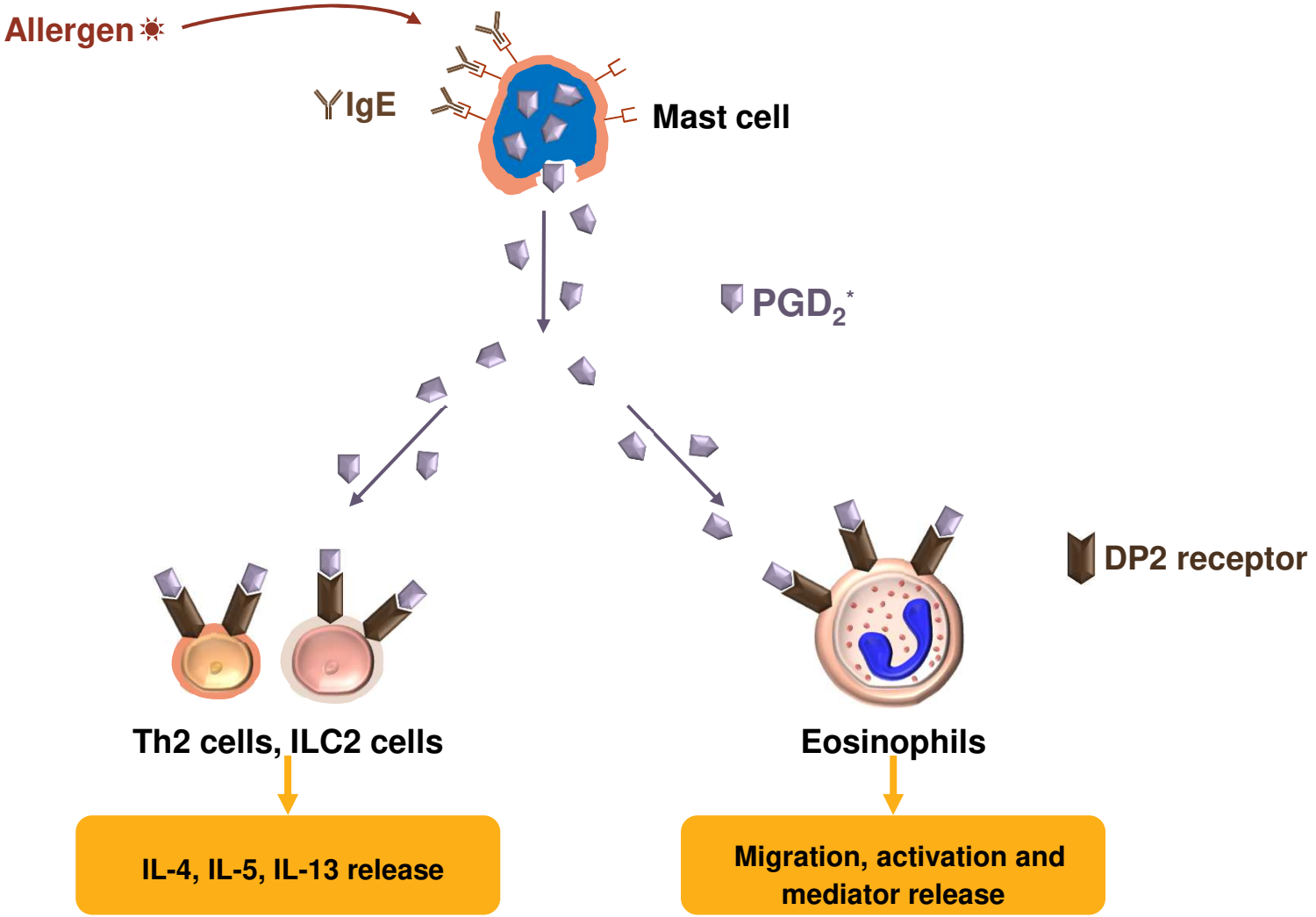
PGD2 binding to DP2 receptors on effector cells mediates the inflammatory response[1]



*PGD_2 is produced predominantly from mast cells

1. Townley, et al. Ann Allergy Asthma Immunol 2012

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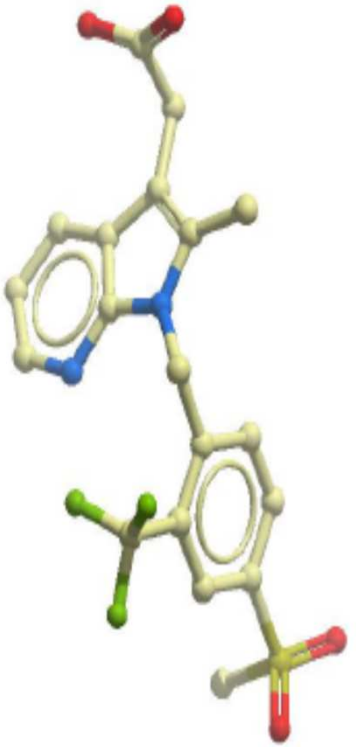
Fevipiprant is an oral, selective, competitive and reversible DP2 antagonist

- Highly selective, reversible, small-molecule, competitive antagonist of DP2
- Shows slower receptor dissociation than other DP2 antagonists tested (AZD-1981, OC-459, BI-671800, setipiprant and ramatroban)[2]
- Inhibits DP2-driven functional effects of PGD_2 on effector cells[3–6]
- High affinity for DP2 receptor (K_d 1.1 nM)[1] - Superior potency than the DP2 antagonists mentioned[1]



1. Willard L et al. Eur Respir J 2014;44(Suppl 58):P4072; 2. Sykes D et al Mol Pharmacol 2016 DOI: 10.1124/mol.115.101832; 3. Barnes et al. Clin Exp Allergy 2012 42: 38-48;
4. Gonem et al. ERS 2014; 5. Berair ATS 2015; 6. Stinson et al. J Allergy Clin Immunol 2015 135: 395-406.

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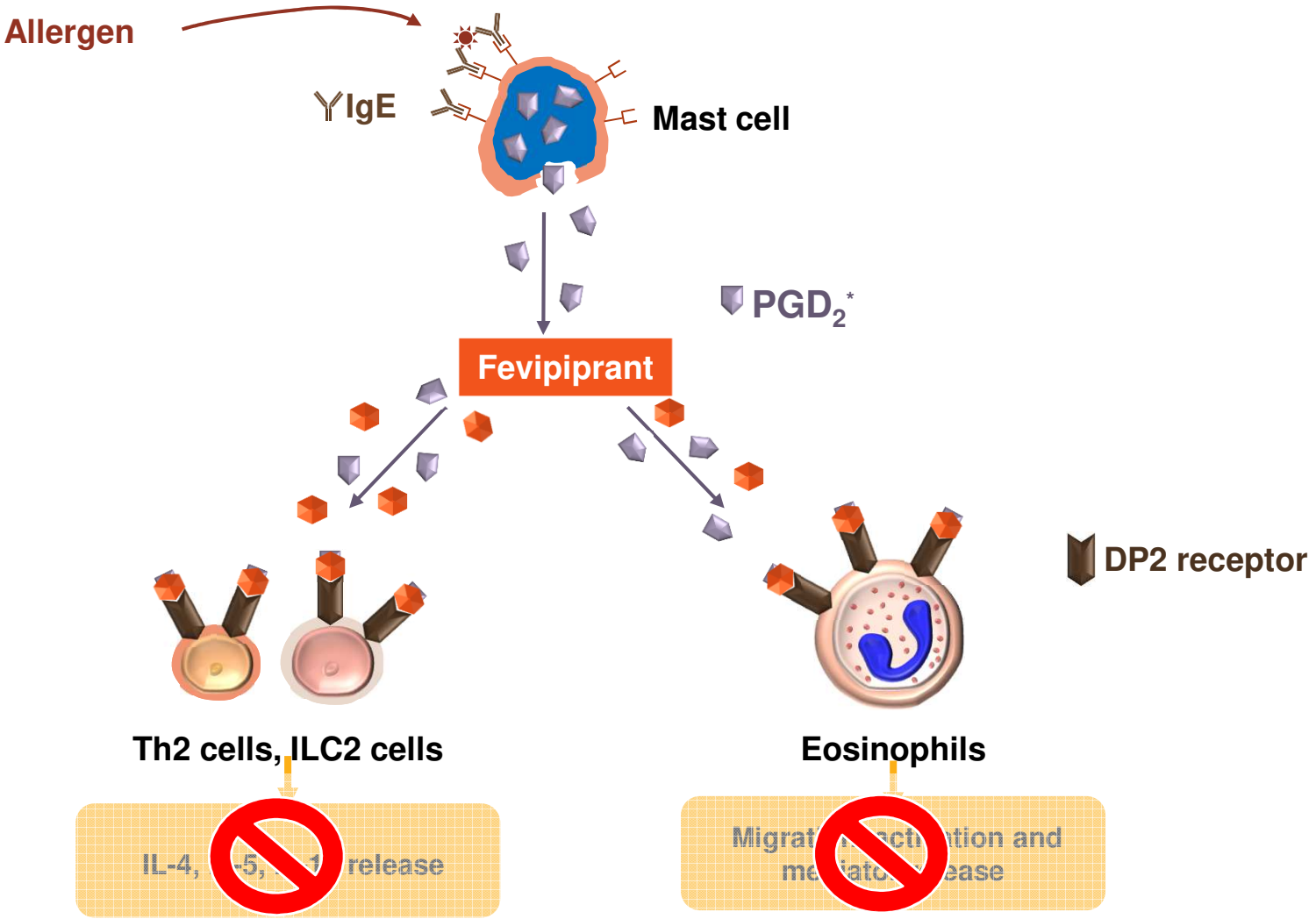
Fevipiprant inhibits the binding of PGD2 on effector cells such as Th2, ILC2 and eosinophils[1]



*PGD_2 is produced predominantly from mast cells

1. Townley, et al. Ann Allergy Asthma Immunol 2012

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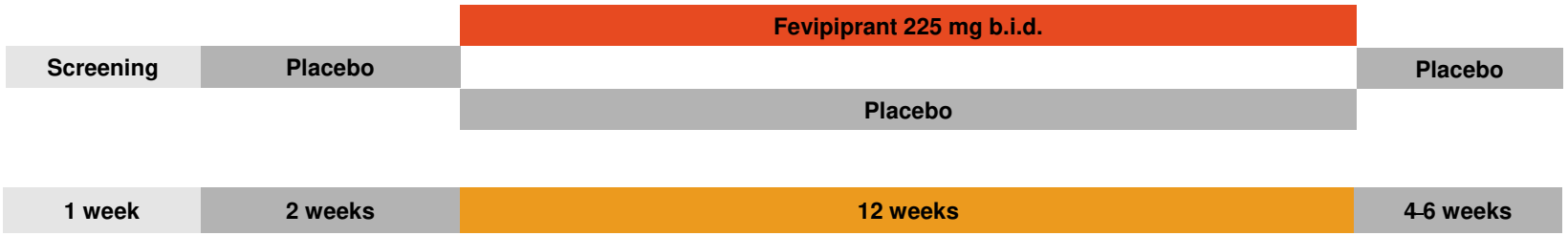
Study A2208: (Eosinophilic asthma study)



Design	Randomized, double-blind, parallel-group, placebo-controlled study
Treatment duration	12 weeks
Population	Treatment-resistant, moderate-to-severe eosinophilic asthma on ICS therapy (GINA treatment steps 2-5);age>18 years FEV_1 % predicted-No requirement; Atopy-not specified; sputum eosinophils ≥2%; ACQ ≥1.5 at baseline and/or 1 asthma exacerbations in last year
Randomized patient number	Fevipiprant 225 mg b.i.d.: 30 patients; placebo: 31 patients
Primary objective	To demonstrate reduction in sputum eosinophils in inadequately controlled, moderate-to-severe asthmatics with sputum eosinophilia after 12 weeks of treatment with fevipiprant compared to placebo.
Primary endpoint	Reduction in sputum eosinophil levels
Secondary and other objectives	• Asthma control (as measured by the Asthma Control Questionnaire, ACQ) • Asthma Quality of Life (QoL) as measured by AQLQ • FEV_1 • Safety

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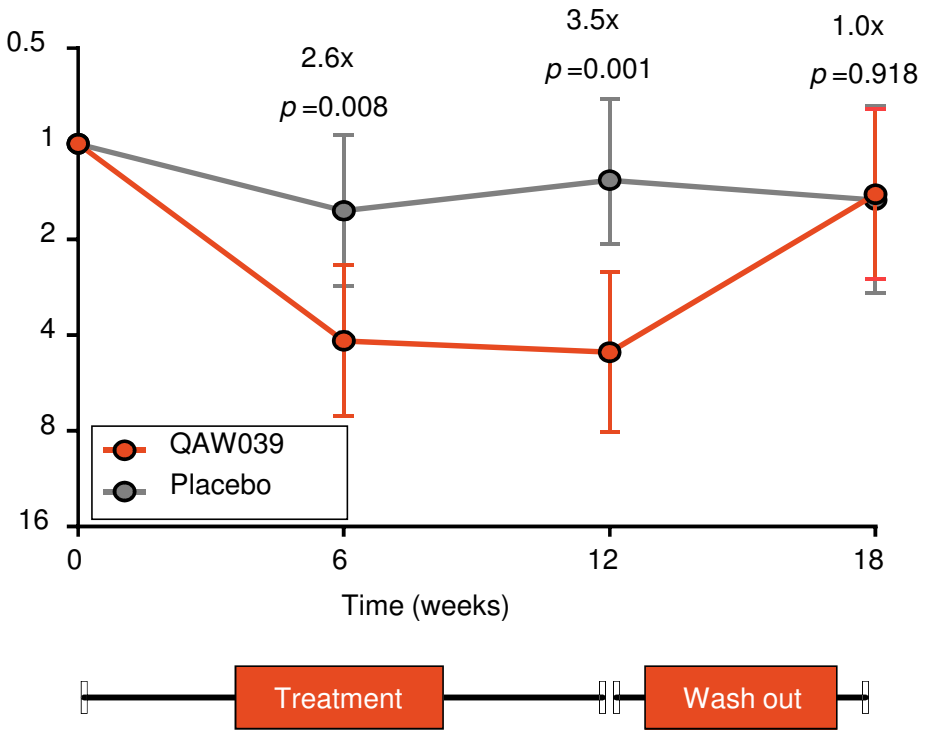
Gonem S et al, Lancet Respir Med. 2016 Sep;4(9):699-707.

Primary endpoint 2208:
Fevipiprant significantly reduces sputum eosinophilia[1]

Fold reduction from baseline in eosinophil count

(Geometric mean (95% CI); LOCF)



- **Primary endpoint:** Sputum Eos 3.5-fold lower for fevipiprant compared with Pbo
- Clinical improvement in asthma control in those uncontrolled at baseline (i.e., 42/61 patients with ACQ7 score ≥1.5) improved by 0.56 points compared with placebo **(p=0.046)**

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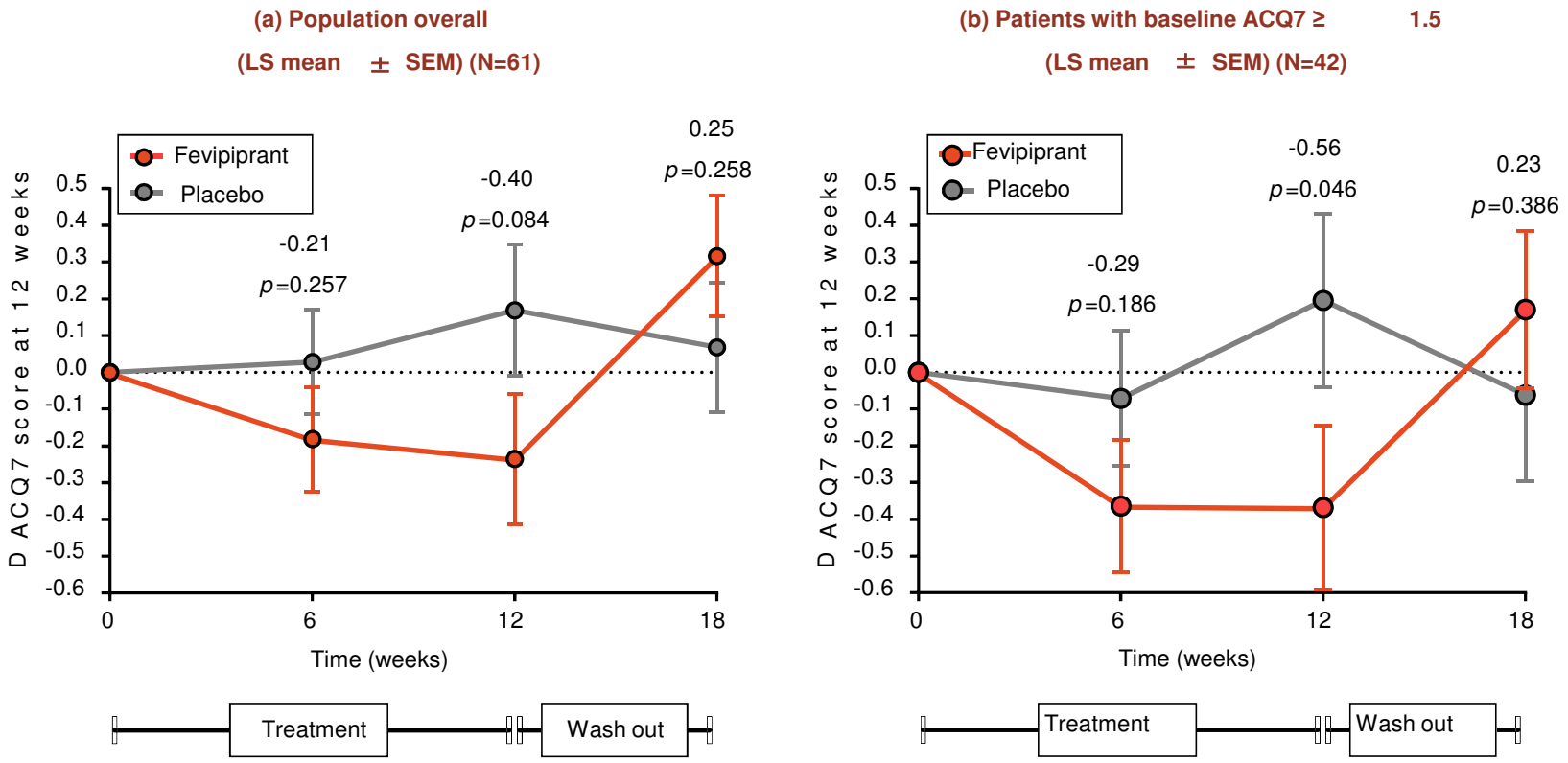
Gonem S et al, Lancet Respir Med. 2016 Sep;4(9):699-707.

Secondary endpoint 2208:

Significant improvement in ACQ7 at 12 weeks in patients uncontrolled at baseline[1]



Gonem S et al, Lancet Respir Med. 2016 Sep;4(9):699-707.

Novartis' Commitment in Cystic Fibrosis

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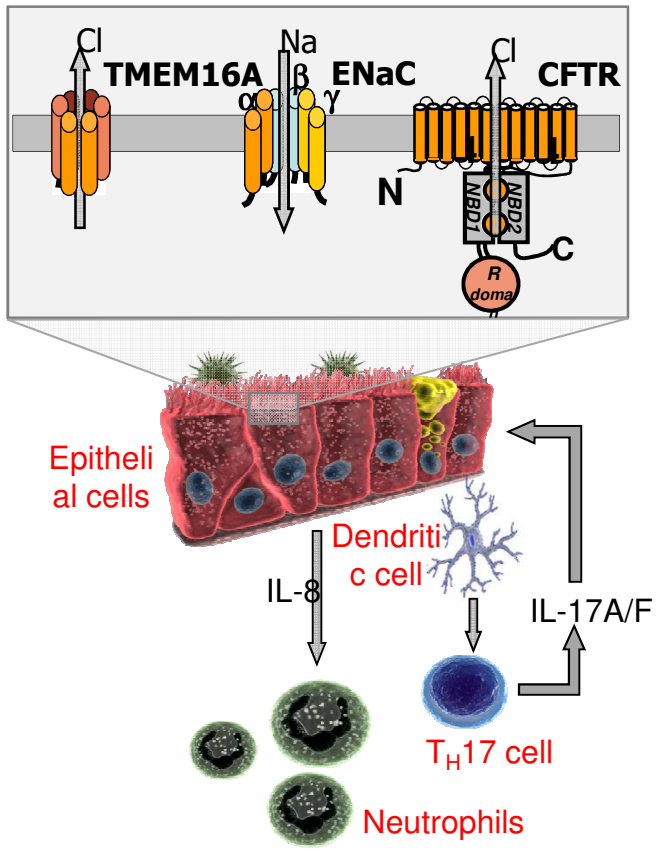
Cystic Fibrosis

Cellular pathways, targets and strategy



Strategic Approaches

1) to enhance the function of mutant CFTR addressing the genetic defect in CF
2) to improve mucociliary clearance by increasing airway surface liquid, improving lung function
3) to inhibit goblet cell formation and reduce mucus burden.
4) to reduce inflammation in CF by modulating neutrophil function
5) ongoing basic research is aimed at understanding how the immune system is dysregulated in CF

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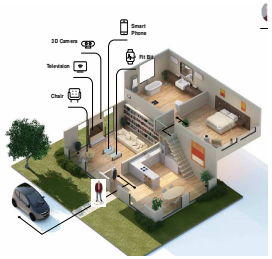
Key Ongoing Respiratory Digital & Devices Projects



eBreezhaler: Electronic enabled inhaler to improve adherence and possible outcomes. eBreezhaler fills a critical launch gap in our Respiratory Portfolio & paves the way for next generation devices.

Life is Calling: COPD Patient consumer online and Facebook campaign.
1st to support activity changes as well as education: **www.copdlifeiscalling.com**

AirSmart (Medical device registered in Italy by Novartis): Mobile Spirometer aids tracking of respiratory function, already distributed to specialists and GPs

Smart Health House: Interactive concept house to demonstrate the seamless patient monitoring invisibly

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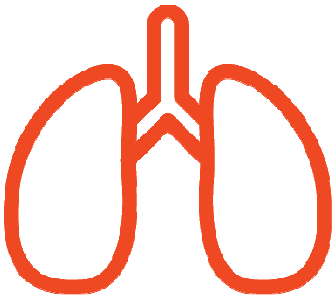
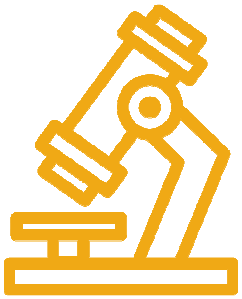
Conclusions



Respiratory is a key area for Novartis



We are committed to develop innovative medicines and health solutions for patients with respiratory diseases to improve their lives

We are exploring existing along with new therapeutic approaches across different respiratory diseases

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Thank You

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