

BOEHRINGER INGELHEIM

RESPIRATORY RESEARCH & DEVELOPMENT TIMELINE

1921

Lobelin, the first stimulant-based respiratory product, is introduced as an emergency drug for arrested breathing



1975

Ipratropium Bromide aerosol is launched, a short-acting anti-cholinergic for the treatment of patients with chronic obstructive pulmonary disease (COPD)



1995

Launch of Ipratropium Bromide+Salbutamol for the treatment of COPD

2005

Tiotropium becomes the world's most prescribed COPD maintenance treatment¹



2011

Initiation of TOViTO[®] phase III clinical trial programme investigating efficacy and safety of Tiotropium/Olodaterol Respimat[®] in COPD



2013

Nintedanib receives orphan medicinal product designation from the European Commission in IPF

2013

First approval of Olodaterol Respimat[®] – an effective LABA specifically designed as a preferred combination partner to Tiotropium^{3,5}



2014

Nintedanib receives FDA approval



2015

Start of large-scale DYNAGITO[®] trial assessing potential benefit of Tiotropium+Olodaterol Respimat[®] compared to Tiotropium Respimat[®] on exacerbations in patients with COPD⁷

Tiotropium+Olodaterol Respimat[®] receives first approvals as a once-daily COPD maintenance treatment in countries worldwide



2015

First patient enrolled in the Phase III SENSICIST[™] (Safety and Efficacy of Nintedanib in Systemic Sclerosis) study investigating Nintedanib in people with systemic sclerosis who also develop interstitial lung disease (SSc-ILD)⁹

2016

To date, Tiotropium has acquired 50 million patient-years of real-life experience across all COPD severities which has helped to shape COPD clinical practice worldwide¹²

2017

First patient enrolled in the Phase III PF-ILD (progressive fibrosing interstitial lung disease) trial investigating the efficacy and safety of Nintedanib in a range of progressive fibrosing lung conditions other than idiopathic pulmonary fibrosis¹³

1941

Isoproterenol is launched, an anti-asthmatic treatment breaking new ground in asthma treatment



1985

Development of Tiotropium Bromide begins

2002

First launches of Tiotropium HandiHaler[®] in COPD take place in several European and Asian countries



2007

Nintedanib (OFEV[®]) starts clinical development programme for the treatment of IPF²

2012

Launch of Ipratropium Bromide+Salbutamol Respimat[®] for the treatment of COPD in the US

2013

Results from TIOSPIR[®] confirm similar safety and efficacy of Tiotropium HandiHaler[®] and Tiotropium Respimat[®]3



2014

Results from Phase III INPULSIS[®] trials show Nintedanib significantly slows disease progression in patients with IPF compared to placebo⁶



2014

Approval of Tiotropium Respimat[®] for use in adult asthma patients by regulatory authorities in the EU, Japan and many other countries



2015

Nintedanib receives approval in EU, Japan and many other countries

Nintedanib included in the updated International Treatment Guidelines for IPF⁸

2015

Approval of Tiotropium Respimat[®] for use in asthma patients 12+ in the US and inclusion of Tiotropium Respimat[®] for adults with asthma in the updated 2015 Global Strategy for Asthma Management and Prevention (GINA)¹⁰

2016

Updated GINA 2016 strategy includes Tiotropium Respimat[®] as an add-on option for patients aged 12+¹¹

2016

Nintedanib receives orphan-drug designation from FDA for treatment of systemic sclerosis (including the associated interstitial lung disease)

To date more than 20,000 patients worldwide have been treated with Nintedanib¹²

2017

Approval of Tiotropium Respimat[®] as asthma maintenance treatment for children aged 6+ in the US / Paediatric approvals in further countries for patients 1+¹⁴

References:

1. IMS Health MIDAS[®]. Top 20 Global Products 2015. December 2015
2. Safety and Efficacy of BIBF 1120 in Idiopathic Pulmonary Fibrosis. Available at <https://clinicaltrials.gov/ct2/show/study/NCT00514683?term=nintedanib+IPF&phase=1&rank=2> [last accessed July 2016]
3. Buhl R, Maltais F, Abrahams R, et al. Tiotropium and olodaterol –fixed-dose combination versus mono-components in COPD (GOLD 2–4). Eur Respir J. 2015;45(4):969–979
4. Szeller S, Harper III T, Laki I, et al. Once-daily tiotropium Respimat[®] Add-on Therapy Improves Lung Function in Children with Severe Symptomatic Asthma. ATS 2016 International Conference.
5. Bouyssou T, Casarosa P, Naline E, et al. Pharmacological characterization of olodaterol, a novel inhaled beta2-adrenoceptor agonist exerting a 24-hour-long duration of action in preclinical models. J Pharmacol Exp Ther. 2010;334(1):53–62
6. Raghu G, Wells A, Nicholson AG, et al. Consistent effect of nintedanib on decline in FVC in patients across subgroups based on HRCT diagnostic criteria: results from the INPULSIS[®] trials in IPF. Poster presented at the 110th American Thoracic Society Conference; Denver, Colorado, May 15–20, 2015. <http://clinicaltrials.gov/ct2/results?term=dyragito&Search=Search> [last accessed July 2017]
7. Raghu G, et al. An Official ATS/ERS/JRS/ALAT Clinical Practice Guidelines: Treatment of Idiopathic Pulmonary Fibrosis: Executive Summary. American Journal of Respiratory and Critical Care Medicine Volume 192 (2):238 – 248, July 2015
8. Raghu G, et al. An Official ATS/ERS/JRS/ALAT Clinical Practice Guidelines: Treatment of Idiopathic Pulmonary Fibrosis. Available at <https://clinicaltrials.gov/ct2/show/study/NCT02597933?term=Nintedanib+systemic+sclerosis+lung&rank=1> [last accessed July 2017]
9. ClinicalTrials.gov. A Trial to Compare Nintedanib with Placebo for Patients With Scleroderma Related Lung Fibrosis. Available at <https://clinicaltrials.gov/ct2/show/study/NCT02597933?term=Nintedanib+systemic+sclerosis+lung&rank=1> [last accessed July 2017]
10. GINA Strategy for asthma management and prevention report. Updated 2015. http://ginasthma.org/wp-content/uploads/2016/01/GINA_Report_2015_Aug11-1.pdf [last accessed July 2017]
11. GINA strategy for asthma management and prevention report updated 2016. <http://ginasthma.org/2016-gina-report-global-strategy-for-asthma-management-and-prevention/> [last accessed July 2017].
12. Boehringer Ingelheim. IPF data on file, 2016
13. ClinicalTrials.gov. Efficacy and Safety of Nintedanib in Patients with Progressive Fibrosing Interstitial Lung Disease (PF-ILD). Available at: <https://clinicaltrials.gov/ct2/show/NCT02999178> [last accessed July 2017]
14. Boehringer Ingelheim. Data on file, 2017

For further Boehringer Ingelheim media information please visit <https://www.boehringer-ingelheim.com/press>