

## Health Technology Briefing September 2024

### Astegolimab for treating chronic obstructive pulmonary disease in people aged 40 to 80 years

Company/Developer

Roche Products Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 27685

NICE ID: Not available

UKPS ID: 672225

#### Licensing and Market Availability Plans

Currently in phase III/II clinical trials.

#### Summary

Astegolimab is currently in clinical development for the treatment of chronic obstructive pulmonary disease (COPD) in patients aged 40 to 80 years who are former or current smokers and have a history of frequent exacerbations. COPD is the name for a group of lung conditions that cause breathing difficulties. It is a disease that causes obstructed airflow to and from the lungs. It is typically caused by long-term exposure to irritating gasses or matter, most often from cigarette smoke. There may be periods when the symptoms suddenly get worse, known as a flare-up or exacerbation. Many patients continue to have exacerbations despite the use of current therapies to address the symptoms of COPD, and there is a lack of treatments to improve lung function or stop disease progression.

Astegolimab is a fully human monoclonal antibody (a type of protein) designed to prevent binding of interleukin-33 (IL-33 – a protein involved in inflammation) to the ST2 receptor (a protein which binds to IL-33). IL-33 and its receptor ST2 have been implicated in airway inflammation and infection. Therefore, preventing them from binding to one another could ease COPD symptoms by reducing airway inflammation and infection that are present in patients with the disease. Astegolimab is administered subcutaneously (SC). If licensed, astegolimab will offer an additional treatment option as an add-on to standard therapies for adult patients with COPD.

## Proposed Indication

Treatment of chronic obstructive pulmonary disease (COPD) in patients aged 40 to 90 years who are former or current smokers and have a history of frequent exacerbations.<sup>1,2</sup>

## Technology

### Description

Astegolimab (anti-ST2, AMG 282, RG6149) is a fully human monoclonal antibody designed to inhibit binding of interleukin-33 (IL-33) to the ST2 receptor.<sup>3</sup> IL-33, an alarmin cytokine, is released from the epithelium following damage and is increased in the airway in COPD. The epithelial-derived IL-33 and its receptor ST2 have been implicated in airway inflammation and infection.<sup>4</sup> Therefore, preventing them from binding to one another could ease COPD symptoms by reducing airway inflammation and infection that are present in patients with the disease.<sup>5</sup>

Astegolimab is currently in phase III clinical development for the treatment of COPD in patients aged 40 to 80 years who are former or current smokers and have a history of frequent exacerbations. In the phase III clinical trial (ARNASA, NCT05595642), participants receive subcutaneous (SC) astegolimab every 2 weeks or every 4 weeks.<sup>1</sup> There is a supporting ongoing pivotal Phase 2b study (ALIENTO, NCT05037929) with a similar trial design to ARNASA in patients aged 40 to 90 years.<sup>2</sup>

### Key Innovation

Current treatments for COPD are still based on inhaled corticosteroids and bronchodilators. This kind of medication is beneficial in reducing the acuteness of the symptoms; however, it does not improve lung function or stop disease progression.<sup>6</sup> Prevention of exacerbations is a major aim of disease management for patients with COPD, but, despite maximal inhaled therapy (inhaled corticosteroids, long-acting  $\beta$ 2-agonists, and long-acting muscarinic antagonists), many patients with COPD continue to have exacerbations.<sup>4</sup> The IL-33/ST2 pathway has been demonstrated to orchestrate, at least in part, the inflammatory and remodelling processes taking part in COPD. However, the mechanisms by which IL-33/ST2 is involved in the disease are more complex and heterogeneous than those already reported in allergic airway inflammation (like in asthma), meaning that its role in COPD is rather defined by the context and progression of the disease.<sup>6</sup> The results of the phase II trial COPD-ST2OP in 80 patients (NCT03615040) showed that using astegolimab in patients with moderate to severe COPD did not significantly reduce the rate of exacerbations but did improve health status compared with the placebo.<sup>4</sup>

If licensed, astegolimab will offer an additional treatment option for COPD in adult patients.

### Regulatory & Development Status

Astegolimab does not currently have Marketing Authorisation in the EU/UK for any indication. Astegolimab is also in phase II clinical development for uncontrolled severe asthma, moderate to severe atopic dermatitis and severe COVID-19 pneumonia.<sup>7</sup>

## Patient Group

### Disease Area and Clinical Need

COPD is the name for a group of lung conditions that cause breathing difficulties. It includes emphysema (damage to the air sacs in the lungs) and chronic bronchitis (long-term inflammation of the airways). It is a

common condition that mainly affects middle-aged or older adults who smoke. COPD happens when the lungs become inflamed, damaged, and narrowed. The main cause is smoking, although the condition can sometimes affect people who have never smoked. The main symptoms of COPD are shortness of breath, a persistent chesty cough with phlegm, frequent chest infections, and persistent wheezing. Without treatment, the symptoms usually get progressively worse. There may also be periods when they get suddenly worse, known as a flare-ups or exacerbations.<sup>8</sup> COPD exacerbations can be triggered by viral infections, allergies, or irritants (such as chemicals or dust) which damage cells that line the airways of the lungs and causes them to release the protein IL-33. IL-33 helps the body's immune system to fight infections. However, in people with COPD, it can cause too much inflammation that affects the airways. This makes breathing more difficult and causes extra mucus production.<sup>9</sup>

An estimated at least 1.2 million people in the UK are living with diagnosed COPD. In terms of diagnosed cases, this makes COPD the second most common lung disease in the UK, after asthma. Around 2% of the whole population – 4.5% of all people aged over 40 – live with diagnosed COPD. The number of people who have ever had a diagnosis of COPD has increased by 27%, from under 1,600 to nearly 2,000 per 100,000 (estimated numbers of people ever diagnosed with COPD 2004–12).<sup>10</sup> Reported mortality rates following hospitalisation for an acute exacerbation vary from 23–80% with a 5-year mortality rate of around 50%.<sup>11</sup> In England 2022-23, there were 55,877 finished consultant episodes (FCEs) and 30,340 admissions for COPD with acute exacerbation, unspecified (ICD-10 code J44.1) which resulted in 141,475 FCE bed days and 153 day cases.<sup>12</sup>

#### Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends roflumilast as an add-on to bronchodilator therapy, for treating severe COPD in adults with chronic bronchitis.<sup>13</sup>

Other potential pharmacological treatment options can include:<sup>14</sup>

- Inhalers:
  - o Short-acting bronchodilator inhalers, long-acting bronchodilator inhalers, steroid inhalers
- Tablets:
  - o Theophylline tablets, mucolytics, steroid tablets, antibiotics

#### Clinical Trial Information

Trial	<p><b>ARNASA, <a href="#">NCT05595642</a></b>; A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Astegolimab in Patients With Chronic Obstructive Pulmonary Disease</p> <p><b>Phase III – Recruiting</b></p> <p><b>Locations:</b> 16 EU countries, UK, USA, Canada, and other countries</p> <p><b>Primary completion date:</b> June 2025</p>
Trial Design	Randomised, parallel assignment, double masking
Population	N=1290 (planned); subjects with COPD who are former or current smokers and have a history of frequent exacerbations; aged 40 to 80 years.
Intervention(s)	<ul style="list-style-type: none"> <li>• SC astegolimab</li> <li>• alternating SC astegolimab and placebo</li> </ul>
Comparator(s)	SC placebo

Outcome(s)	Primary outcome: annualised rate of moderate and severe COPD exacerbations over the 52-week treatment period [Time frame: 52 weeks]  See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-
Clinical Trial Information	
Trial	<a href="#">NCT05878769</a> ; A Phase III Open-Label Extension Study to Evaluate the Long-Term Safety of Astegolimab in Patients With Chronic Obstructive Pulmonary Disease <b>Phase III</b> – Recruiting <b>Locations:</b> 11 EU countries, UK, USA, Canada, and other countries <b>Primary completion date:</b> June 2027
Trial Design	Single group assignment, open label
Population	N=2000 (planned); subjects with COPD who have completed the 52-week placebo-controlled treatment period in parent studies GB43311 or GB44332; aged 40 to 90 years.
Intervention(s)	SC astegolimab
Comparator(s)	No comparator
Outcome(s)	Primary outcome: incidence of all adverse events (AEs) [Time frame: up to 12 weeks after last dose of study treatment]
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	<a href="#">NCT05037929</a> , <a href="#">EudraCT 2021-002045-15</a> ; A Phase IIb, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Astegolimab in Patients With Chronic Obstructive Pulmonary Disease <b>Phase II</b> – Active, not recruiting <b>Locations:</b> 11 EU countries, UK, USA, Canada, and other countries <b>Primary completion date:</b> February 2025
Trial Design	Randomised, parallel assignment, double masking
Population	N=1440 (planned); subjects with COPD who are former or current smokers and have a history of frequent exacerbations; aged 40 to 90 years.
Intervention(s)	<ul style="list-style-type: none"> <li>• SC astegolimab</li> <li>• alternating SC astegolimab and placebo</li> </ul>
Comparator(s)	SC placebo

Outcome(s)	Primary outcome: annualised rate of moderate and severe COPD exacerbations over the 52-week treatment period [Time frame: baseline up to week 52]  See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	<b>COPD-ST2OP, <a href="#">NCT03615040</a></b> ; A Randomised Placebo-controlled Trial of Anti-ST2 in COPD <b>Phase II – Completed</b> <b>Location:</b> UK <b>Actual study completion date:</b> December 2020
Trial Design	Single-centre, double-blinded, placebo-controlled, parallel group, randomised controlled trial
Population	N=81 (actual); subjects with moderate to very severe COPD (GOLD II-IV); aged 40 years and older.
Intervention(s)	Astegolimab received as SC injection by infusion pump at 490mg
Comparator(s)	Placebo received as SC injection by infusion pump at 490mg
Outcome(s)	Primary outcome: number of moderate to severe exacerbations (defined as requiring treatment with systemic corticosteroids and/or antibiotics in the community or hospital or hospitalisation) [Time frame: 0-48 weeks]  See trial record for full list of other outcomes
Results (efficacy)	See trial record
Results (safety)	See trial record

Estimated Cost
The cost of astegolimab is not yet known.

Relevant Guidance
NICE Guidance
<ul style="list-style-type: none"> <li>• NICE technology appraisal. Dupilumab for treating moderate to severe chronic obstructive pulmonary disease [ID6235] (TA11246). Expected publication date to be confirmed.</li> <li>• NICE technology appraisal. Mepolizumab for treating chronic obstructive pulmonary disease [ID1237] (TA10239). Expected publication date to be confirmed.</li> <li>• NICE technology appraisal. Roflumilast for treating chronic obstructive pulmonary disease (TA461). July 2017.</li> </ul>

- NICE guideline. Chronic obstructive pulmonary disease (acute exacerbation): antimicrobial prescribing (NG114). December 2018. Last updated September 2019.
- NICE guideline. Chronic obstructive pulmonary disease in over 16s: diagnosis and management (NG115). December 2018. Last updated July 2019.
- NICE quality standard. Chronic obstructive pulmonary disease in adults (QS10). July 2011. Last updated September 2023.

#### NHS England (Policy/Commissioning) Guidance

No relevant guidance found.

#### Other Guidance

- BMJ Best Practice. Chronic obstructive pulmonary disease (COPD). 2023.<sup>15</sup>
- NHS RightCare. RightCare Pathway: COPD. 2017.<sup>16</sup>
- NHS Improvement. Lung: National Improvement Projects. Improving earlier diagnosis and the long-term management of COPD: Testing the case for change. 2011.<sup>17</sup>

### Additional Information

### References

- 1 Clinicaltrials.gov. *A Study to Evaluate Astegolimab in Participants With Chronic Obstructive Pulmonary Disease (ARNASA)*. Trial ID: NCT05595642. 2022. Available from: <https://clinicaltrials.gov/study/NCT05595642> [Accessed 19 July 2024].
- 2 Clinicaltrials.gov. *A Study to Evaluate the Efficacy and Safety of Astegolimab in Participants With Chronic Obstructive Pulmonary Disease*. Trial ID: NCT05037929. 2021. Status: Active, not recruiting. Available from: <https://clinicaltrials.gov/study/NCT05037929?intr=Astegolimab&aggFilters=phase:2%203,status:not%20rec%20act%20com%20enr&rank=3> [Accessed 3 September 2024].
- 3 Roche. *Product Development Portfolio*. 2024. Available from: <https://www.roche.com/solutions/pipeline> [Accessed 19 July 2024].
- 4 Yousuf AJ, Mohammed S, Carr L, Yavari Ramsheh M, Micieli C, Mistry V, et al. Astegolimab, an anti-ST2, in chronic obstructive pulmonary disease (COPD-ST2OP): a phase 2a, placebo-controlled trial. *Lancet Respir Med*. 2022;10(5):469-77. Available from: [https://doi.org/10.1016/s2213-2600\(21\)00556-7](https://doi.org/10.1016/s2213-2600(21)00556-7).
- 5 Maia M. *Astegolimab Lifts Quality of Life For Those With Frequent Flare-ups*. Press release. Available from: <https://copdnewstoday.com/news/astegolimab-lifts-quality-of-life-copd-patients-with-frequent-flare-ups/> [Accessed 24 July 2024].
- 6 Riera-Martínez L, Cànaves-Gómez L, Iglesias A, Martín-Medina A, Cosío BG. The Role of IL-33/ST2 in COPD and Its Future as an Antibody Therapy. *Int J Mol Sci*. 2023;24(10). Available from: <https://doi.org/10.3390/ijms24108702>.
- 7 Clinicaltrials.gov. *Search for: Astegolimab | Not yet recruiting, Recruiting, Active, not recruiting, Completed, Enrolling by invitation studies | Phase: 2, 3 | Card Results | ClinicalTrials.gov*. 2024. Available from: <https://clinicaltrials.gov/search?intr=Astegolimab&aggFilters=phase:2%203,status:not%20rec%20act%20com%20enr> [Accessed 16 August 2024].

- 8 NHS UK. *Overview - Chronic obstructive pulmonary disease (COPD)*. 2019. Available from: <https://www.nhs.uk/conditions/chronic-obstructive-pulmonary-disease-copd/> [Accessed 21st November 2022].
- 9 ForPatients by Roche. *A clinical trial to see how well different doses of astegolimab plus standard treatment work compared with a placebo plus standard treatment to reduce certain symptoms of chronic obstructive pulmonary disease*. 2024. Available from: <https://forpatients.roche.com/en/trials/respiratory-disorder/copd/a-study-to-evaluate-astegolimab-in-participants-with-ch-57511.html> [Accessed 19 July 2024].
- 10 British Lung Foundation. *Chronic obstructive pulmonary disease (COPD) statistics*. c2024. Available from: <https://statistics.blf.org.uk/copd> [Accessed 19 July 2024].
- 11 National Institute for Health and Care Excellence (NICE). *Chronic obstructive pulmonary disease: What is the prognosis?* 2024. Available from: <https://cks.nice.org.uk/topics/chronic-obstructive-pulmonary-disease/background-information/prognosis/> [Accessed 24 July 2024].
- 12 NHS England. *Hospital Admitted Patient Care Activity, 2022-23: Diagnosis*. 2022-23. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2022-23> [Accessed 23 July 2024].
- 13 National Institute for Health and Care Excellence (NICE). *Roflumilast for treating chronic obstructive pulmonary disease*. 2017. Available from: <https://www.nice.org.uk/guidance/ta461>.
- 14 NHS UK. *Treatment - Chronic obstructive pulmonary disease (COPD)*. Available from: <https://www.nhs.uk/conditions/chronic-obstructive-pulmonary-disease-copd/treatment/> [Accessed 21st November 2022].
- 15 BMJ Best Practice. *Chronic obstructive pulmonary disease (COPD)*. 2023. Available from: <https://bestpractice.bmj.com/topics/en-gb/7/management-approach> [Accessed 24 July 2024].
- 16 NHS RightCare. *RightCare Pathway: COPD*. 2017. Available from: <https://www.england.nhs.uk/rightcare/wp-content/uploads/sites/40/2017/12/nhs-rightcare-copd-pathway-v18.pdf> [Accessed 24 July 2024].
- 17 NHS Improvement - Lung. *Improving earlier diagnosis and the long term management of COPD: Testing the case for change*. 2011. Available from: <https://www.england.nhs.uk/improvement-hub/wp-content/uploads/sites/44/2017/11/Early-Diagnosis-of-COPD-Testing-the-Case-for-Change.pdf> [Accessed 24 July 2024].

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