The Cosentyx® clinical trial programme[1-11]

- There are eight pivotal trials (four in psoriasis, two in psoriatic arthritis, two in ankylosing spondylitis)
- There are two head-to-head trials in psoriasis showing superiority of Cosentyx® over Enbrel®* and Stelara®†
- More than 9,600 patients have been treated with Cosentyx across multiple indications in the clinical trial program
- There have been four major publications in The New England Journal of Medicine (NEJM) and The Lancet

Clinical trials in psoriasis

The Cosentyx® (secukinumab) clinical trial program in psoriasis was made up of 10 Phase II and Phase III studies.

Pivotal studies: strength, speed and sustainability

The approval of Cosentyx in psoriasis is based on four pivotal Phase III trials: ERASURE[2], FIXTURE[2], FEATURE[3] and JUNCTURE[4], which involved 2,403 patients with moderate-to-severe plaque psoriasis[1]. Across all trials, the co-primary endpoints were the proportion of patients who achieved a reduction in Psoriasis Area Severity Index (PASI) score of at least 75% (PASI 75 response) from baseline to Week 12 and treatment success (clear or almost clear skin) on the Investigator's Global Assessment modified 2011 (IGA 0/1)[1].

ERASURE: A randomized, double-blind, placebo-controlled study, in 738 patients with moderate-to-severe chronic plaque-type psoriasis, to assess safety and efficacy at 12 weeks of either Cosentyx 300 mg or 150 mg with long-term follow up to 52 weeks[1,2].

FIXTURE: A randomized, double-blind, double-dummy study, in 1,306 patients with moderate-to-severe chronic plaque type psoriasis, to assess the safety and efficacy at 12 weeks of either Cosentyx 300 mg or 150 mg, Enbrel (etanercept) 50 mg, or placebo with long-term follow up to 52 weeks[1,2].

FEATURE: A randomized, double-blind, placebo-controlled study, in 117 patients, to assess the safety, tolerability and usability of a self-administered pre-filled syringe of Cosentyx 300 mg or 150 mg or placebo over 12 weeks[1,3].

JUNCTURE: A randomized, double-blind, placebo-controlled study, in 182 patients, to assess the safety, tolerability and usability of the SensoReady pen in patients who self-administered of either Cosentyx 300 mg or 150 mg or placebo over 12 weeks[1,4].

Results

- All primary endpoints were achieved with Cosentyx 300 mg and 150 mg

*Enbrel is a registered trademark of Amgen Inc. †Stelara is a registered trademark of Janssen Biotech Inc.

PASI 75 response achieved at Week 12[1]

	150 mg	300 mg	Placebo
ERASURE	72%	82%	5%
FIXTURE	67%	77%	5%
FEATURE	70%	76%	0%
JUNCTURE	72%	87%	3%

IGA mod 2011 0/1 scores (clear or almost clear skin)[1]

	150 mg	300 mg	Placebo
ERASURE	51%	55%	2%
FIXTURE	51%	62%	3%
FEATURE	53%	69%	0%
JUNCTURE	53%	73%	0%

- In the ERASURE study, Cosentyx was associated with a fast onset of efficacy with a 50% reduction in mean PASI response by Week Three for the 300 mg dose[1,2]

Extension studies exploring sustainability

Researchers are following patients in the ERASURE, FIXTURE, SCULPTURE and STATURE trials which have all been extended to capture long-term safety and efficacy data for Cosentyx over five years[1,2,8].

Results so far from the SCULPTURE study[8]:

- Clear or almost clear skin (PASI 90 response) was achieved by 69% of patients at Year One and by 66% of patients at Year Four
- Completely clear skin (PASI 100 response) was achieved by 44% of patients at Year One and this rate was maintained to Year Four
- With Cosentyx almost 100% of PASI 90 and PASI 100 response rates are maintained from Year One to Year Four
- The current treatment goal of PASI 75 response was achieved by 89% of patients at Year Four

CLEAR study: Cosentyx shows superiority to Stelara

A 52-week, randomized, double-blind, head-to-head study, in 669 patients with moderate-to-severe plaque psoriasis, comparing the efficacy, long-term safety and tolerability of Cosentyx 300 mg versus Stelara (ustekinumab, dosing per label)[9,10].

Results so far[9,10]:

- Cosentyx was superior to Stelara in achieving and sustaining PASI 90 response (79% versus 58%) at Week 16
- Cosentyx remained consistently superior to Stelara in achieving and sustaining a PASI 90 response (76% versus 61%) and significantly better in achieving PASI 100 (clear skin) response (46% versus 36%) at Week 52*

*Exploratory endpoint

- Cosentyx showed significantly greater and sustained Dermatology Life Quality Index (DLQI) 0/1 responses versus Stelara (72% versus 59%) at Week 52*

Clinical trials in psoriatic arthritis (PsA) and ankylosing spondylitis (AS)

Pivotal studies: speed, sustainabilty, structure and safety

Cosentyx was assessed in more than 1,003 adult patients, in two randomized, double-blind, placebo-controlled studies (FUTURE 1 and FUTURE 2) in adult patients with active PsA, and in 590 patients in two randomized, double-blind, placebo-controlled studies (MEASURE 1 and MEASURE 2) in adult patients aged 18 years and older with active AS[5-7].

Psoriatic arthritis

FUTURE 1: A randomized, double-blind, placebo-controlled study, in 606 patients with active PsA, to demonstrate the 24 week efficacy and assess the long-term safety, tolerability and efficacy up to two years of a 10 mg/kg intravenous loading dose followed by subcutaneous doses of Cosentyx 75 mg, 150 mg[5].

FUTURE 2: A randomized, double-blind, placebo-controlled study, in 397 patients with active PsA, to demonstrate the efficacy of subcutaneous Cosentyx 75 mg, 150 mg, 300 mg in prefilled syringes at 24 weeks and to assess the long-term efficacy, safety and tolerability for up to five years[6].

Both studies included patients who were anti-TNF therapy naïve or inadequate responders; randomization was stratified so that approximately 70% and 65% were required to be anti-TNF therapy naïve in FUTURE 1 and FUTURE 2, respectively. In both trials, the primary endpoint was the percentage of patients achieving an ACR20 response (American College of Rheumatology response criteria) at Week 24. Extension of both studies are currently ongoing to investigate long-term efficacy of Cosentyx.

Results so far[5,6,12]:

- The primary endpoint was achieved in both studies with 50-51% of patients on Cosentyx 150 mg achieving an ACR20 response at Week 24 compared with 15-17% on placebo
- Clinical improvements were observed within one to three weeks of treatment
- In FUTURE 2 significantly more Cosentyx patients, 54% on 300 mg and 51% on 150 mg, achieved an ACR20 at Week 24, compared to 15% on placebo
- In FUTURE 2 improvements seen with Cosentyx 150 mg and 300 mg were sustained over one year of treatment in 64% of patients as measured using ACR 20. ACR 50 response rates were also sustained to one year; 39% in the 150 mg group and 44% in the 300 mg group
- In the extension of FUTURE 1, data show no progression in joint damage in 84% of patients in the Cosentyx groups
- The results from the FUTURE 1 study represent the longest Cosentyx Phase III study in PsA to date

Ankylosing spondylitis

MEASURE 1: A randomized, double-blind, placebo-controlled study, in 371 patients with active AS, to demonstrate the 16 week efficacy and assess the long-term safety, tolerability and efficacy up to two years of a 10 mg/kg intravenous loading dose followed by subcutaneous doses of Cosentyx 75 mg or 150 mg[7]. The study has now entered a three year extension period.

*Exploratory endpoint

MEASURE 2: A randomized, double-blind, placebo-controlled study, in 219 patients with active AS, to demonstrate the efficacy of subcutaneous Cosentyx 75 mg or 150 mg in prefilled syringes, and to assess long-term efficacy, safety and tolerability up to five years[7].

The primary end point in both studies was the proportion of patients with at least 20% improvement in Assessment of Spondyloarthritis International Society (ASAS20) response criteria at Week 16†.

Results[7,13,14,15]:

- Cosentyx is the first IL-17A inhibitor to demonstrate efficacy in Phase III studies in AS patients
- Cosentyx demonstrated rapid and statistically significant improvements versus placebo in the signs and symptoms of AS at Week 16 in both studies
- The primary endpoint was met in both studies. In MEASURE 1 the ASAS20 response rates at Week 16 were 60%, 61%, and 29% for Cosentyx 75 mg and 150 mg and for placebo, respectively. In MEASURE 2, the rates were 41%, 61%, and 28% for 75 mg and 150 mg Cosentyx and for placebo, respectively
- In MEASURE 2 the onset of action of 150 mg Cosentyx occurred as early as Week One for ASAS20 and Week Two for ASAS40 (superior to placebo)
- In MEASURE 2, Cosentyx provided sustained improvement in the signs and symptoms, physical function and quality of life. 74% of patients achieved ASAS20 response at both 52 weeks and 104 weeks
- In an extension of MEASURE 1, Cosentyx demonstrated a sustained response in improvements of signs and symptoms, physical function and quality of life in AS patients over two years
- In MEASURE 1, up to 80% of patients with AS treated with Cosentyx had no radiographic progression in the spine on x-ray assessments

Safety

- Cosentyx has been shown to have a favorable safety profile in clinical trials across multiple indications in which more than 9,600 patients have been treated with Cosentyx. A further 18,000 patients have been treated with Cosentyx in the post-marketing setting[11]
- The risk-benefit assessment for Cosentyx has not changed in the post-market setting
- The most common side effects in psoriasis studies were nasopharyngitis, headache and upper respiratory tract infection[1,2]
- The most common side effects in PsA studies were the common cold, headache and upper respiratory tract infections[1,5,6]
- The most common side effects in AS studies were upper respiratory tract infection and

The Cosentyx clinical trial program includes long-term extension studies that will continue to collect safety information and data over an extended period of time. In addition, an eight-year psoriasis registry study consisting of more than 3,000 patients exposed to Cosentyx will also provide long-term safety data[11].

†ASAS 20 is improvement of ≥20% and ≥1 unit on a 10-unit scale in at least three of the four core ASAS domains, with no worsening of ≥20% and ≥1 unit in the fourth at 104 weeks

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