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REVIEW

# Brodalumab for Moderate-to-Severe Psoriasis: A Comprehensive Review of Efficacy, Safety, and Clinical Positioning

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**Abstract:** Brodalumab is a monoclonal antibody that targets interleukin-17 receptor A (IL-17RA), offering a novel approach to treating moderate-to-severe psoriasis. By blocking IL-17RA, brodalumab inhibits the activity of multiple pro-inflammatory IL-17 isoforms, including IL-17A, IL-17F, and IL-17C, which are critical in the pathogenesis of psoriasis. This review synthesizes data from Phase I–IV clinical trials and real-world studies to provide a comprehensive overview of brodalumab's efficacy, safety, and clinical role in the treatment of moderate-to-severe psoriasis. Clinical trial data consistently demonstrate its rapid onset of action, high rates of skin clearance, and durability of response. Real-world evidence supports its effectiveness in treatment-resistant cases and among patients with previous biologic failures. Safety considerations include the need for monitoring suicidality, although no causal relationship has been confirmed. Despite being one of the most effective biologic agents available for psoriasis, brodalumab remains underutilized, highlighting the need for improved awareness of its potential clinical advantages. Further research is warranted to better define its role in treatment algorithms and to assess long-term outcomes in broader patient populations.

**Keywords:** brodalumab, psoriasis, Il-17RA, psoriasis treatment

## Introduction

Psoriasis is a chronic, immune-mediated disease that primarily affects the skin, presenting both physical and psychological challenges to affected individuals.[1] This prevalent condition impacts approximately 2–4% of the global population and manifests in various forms, including plaque, nail, inverse, guttate, and pustular psoriasis, with plaque psoriasis being the most common.[2,3] The hallmark of plaque psoriasis is the presence of sharply demarcated, erythematous, pruritic plaques covered with silvery scales, which can coalesce to cover large areas of the skin, particularly on the trunk and extensor surfaces.[4]

Given the chronic and relapsing nature of the disease, long-term management is often required. Biologic therapies, which target specific cytokines involved in the pathogenesis of psoriasis, have emerged as effective treatment options.[5] Compared to traditional systemic treatments, such as methotrexate, cyclosporin A, and retinoids, biologics offer a more targeted approach with fewer side effects. Among the biologics targeting the interleukin-17 (IL-17) pathway, brodalumab is unique in that it binds to the IL-17 receptor A (IL-17RA), thereby blocking multiple pro-inflammatory IL-17 isoforms, rather than a single cytokine.[6] This broader inhibition may translate into distinct clinical outcomes compared to other IL-17 inhibitors such as secukinumab and ixekizumab, which target IL-17A alone, or bimekizumab, which targets both IL-17A and Il-17F.

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Despite advances in treatment, challenges remain in psoriasis management. Many patients experience suboptimal responses, adverse effects, or relapse, and the disease significantly impairs quality of life, particularly when lesions affect visible or functionally critical areas such as the scalp, nails, palms, and soles. Therapeutic fatigue is common in patients cycling through multiple therapies with insufficient clearance or durability.

Brodalumab is approved by the US Food and Drug Administration (FDA) for the treatment of moderate-to-severe plaque psoriasis in adults who have failed to respond or have lost response to other systemic treatments.[7] This review critically examines brodalumab's pharmacology, clinical trial data, real-world effectiveness, and safety profile to clarify its role in the therapeutic landscape for moderate-to-severe psoriasis.

## Role of IL-17 in Psoriasis

Psoriasis is driven by activated T-cells, overexpression of pro-inflammatory cytokines, and the IL-23/T helper 17 (TH17) pathway.[8–11] IL-23 is responsible for the differentiation of TH17 cells, a subpopulation of CD4+ cells that preferentially produce IL-17.[10] It is known that unregulated TH17 responses or overwhelming IL-17 production from T-cells and other sources is associated with chronic inflammation and severe immunopathologic conditions.[9]

The IL-17 family comprises six isoforms (IL-17A–IL-17F),[12] with IL-17A and IL-17F being the primary contributors to psoriasis pathogenesis, alongside IL-17C and IL-17E.[13–15] The expression of IL-17A, IL-17C, and IL-17F is significantly elevated in psoriatic lesions, with their protein levels increasing 6.7-fold, 4.1-fold, and 8-fold, respectively, compared to nonlesional skin.[14] IL-17A, the most biologically active isoform, exists as a homodimer or a heterodimer with IL-17F, binding to the same IL-17R receptor complex (IL-17RA/IL-17RC), but with greater potency than IL-17F.

IL-17 directly stimulates keratinocytes, driving their proliferation and triggering the release of psoriasis-associated cytokines, chemokines, and antimicrobial peptides.[16] These keratinocyte-derived factors amplify the inflammatory feedback loop by recruiting more immune cells and promoting the production of IL-17. Additionally, IL-17 acts synergistically with other cytokines, like IL-1 and tumor necrosis factor alpha (TNF-α), enhancing the inflammatory response and further upregulating the expression of psoriasis-related genes.[8]

Brodalumab stands out among other IL-17 inhibitors with its unique mechanism of action, targeting IL-17RA rather than directly inhibiting IL-17A like secukinumab and ixekizumab, or both IL-17A and IL-17F like bimekizumab. This human monoclonal antibody selectively binds to IL-17RA, effectively blocking signaling pathways mediated by multiple IL-17 cytokines, including IL-17A, IL-17F, IL-17C, IL-17A/F heterodimer, and IL-25. By inhibiting IL-17RA, brodalumab prevents the activation of proinflammatory cascades that drive keratinocyte proliferation and cytokine release.

Brodalumab's effectiveness in treating moderate-to-severe plaque psoriasis was established in Phase 2 and 3 trials, leading to its FDA approval in 2017.[6] The recommended dosage involves an initial induction phase of 210 mg administered subcutaneously at weeks 0, 1, and 2, followed by a maintenance dose of 210 mg every two weeks.[17] This formulation is provided as a prefilled syringe containing 210 mg of brodalumab in a 1.5 mL solution, ensuring convenience and consistent dosing for patients.

## Clinical Efficacy

### Phase I Studies

In a Phase I study of AMG 827, or brodalumab, 25 patients with psoriasis received a single dose of AMG 827 at 140 mg or 350 mg subcutaneously or 700 mg intravenously, while five patients received a placebo.[18] Results showed a dose-dependent improvement in Psoriasis Area and Severity Index (PASI) scores, with the 700 mg IV group achieving the highest response rates. By day 29, all patients in this cohort had at least PASI 50, with 88% achieving PASI 75 and 38% reaching PASI 90 by day 43. Similarly, the 350 mg SC group showed notable improvements, with 75% achieving PASI 50 and 38% reaching PASI 75. In contrast, the 140 mg SC cohort demonstrated a limited response, and no placebo recipients achieved PASI 50.

Biomarker analysis confirmed rapid reductions in epidermal thickness, keratin 16 expression, and inflammatory markers, indicating early disease resolution at the molecular level. Notably, lesional skin mRNA levels for IL-17-modulated factors, including DEFB4, cAMP, and CCL20, significantly decreased within two weeks of treatment.

## Phase II Studies

In a 12-week, Phase II, dose-ranging, randomized, double-blind, placebo-controlled trial, brodalumab was assessed for its efficacy and safety in patients with moderate-to-severe plaque psoriasis (NCT00975637).[19] The study included a total of 198 patients randomly assigned to receive brodalumab at doses of 70 mg, 140 mg, 210 mg, or 280 mg, administered subcutaneously on day 1 and at weeks 1, 2, 4, 6, 8, and 10, or placebo. The primary endpoint was the percentage improvement in the PASI score at week 12, with secondary endpoints including PASI 75, PASI 90, and static physician's global assessment (sPGA) scores.

At week 12, the mean percentage improvements in PASI scores were significantly greater in all brodalumab groups compared to the placebo group ($P<0.001$). Specifically, the mean improvements were 45.0% for the 70 mg group, 85.9% for the 140 mg group, 86.3% for the 210 mg group, and 76.0% for the 280 mg group, versus 16.0% for placebo. The proportion of patients achieving PASI 75 and PASI 90 at week 12 was also significantly higher in the 140 mg and 210 mg brodalumab groups, with PASI 75 achieved by 77% and 82%, respectively, and PASI 90 achieved by 72% and 75%, compared to 0% in the placebo group ($P<0.001$ for all comparisons). Additionally, 85% of patients in the 140 mg group and 80% in the 210 mg group were assessed as having clear or minimal disease (sPGA score of 0 or 1) at week 12, compared to 3% in the placebo group ($P<0.01$). Notably, the study observed a rapid onset of clinical response, with improvements seen as early as week 2.

Following the initial trial, an interim analysis at treatment week 120 of a 264-week open-label extension (OLE) was designed to evaluate the long-term efficacy and safety of brodalumab (NCT01101100).[20] This phase II OLE study initially provided all participants with brodalumab 210 mg subcutaneously every two weeks (Q2W), with a protocol amendment later reducing the dose to 140 mg for patients weighing 100 kg or less, and subsequently allowing an increase back to 210 mg for those with inadequate responses.

The study found that 72% of patients maintained a sPGA score of 0 or 1 (clear or almost clear) at week 120, while PASI-75, PASI-90, and PASI-100 response rates were 86%, 70%, and 51%, respectively.

The 264-week OLE study demonstrated that brodalumab treatment resulted in rapid improvements in sPGA, PASI, and dermatology quality of life index (DLQI) scores that were maintained through week 264.[21] Achieving PASI 90 to < 100 or PASI 100 at weeks 12, 240, and 264 was associated with a greater likelihood of achieving DLQI 0 or 1 compared with achieving PASI 75 to < 90. Over the 5-year period, one adverse event of suicidal ideation was reported, no suicides occurred, and no new safety signals emerged. The study concluded that brodalumab demonstrated sustained skin clearance and improved quality of life with an acceptable safety profile throughout the 5-year treatment period.

## Phase III Studies

In AMAGINE-1, a Phase III, randomized, double-blind, placebo-controlled trial (NCT01708590), brodalumab was assessed for efficacy and safety in patients with moderate-to-severe plaque psoriasis.[22] Patients underwent a 12-week induction period followed by a withdrawal-retreatment phase lasting up to 52 weeks. 661 patients were randomized to receive brodalumab 210 mg, 140 mg, or placebo Q2W, with an additional dose at week 1. After achieving an sPGA score of 0 or 1 by week 12, patients were rerandomized to continue their induction dose or switch to placebo. Those who experienced a return of disease (sPGA $\geq 3$) from week 16 onward were eligible for retreatment with their induction dose. Patients with inadequate response after 12 weeks of retreatment qualified for open-label brodalumab 210 mg Q2W. At week 12, all patients initially receiving brodalumab with sPGA $\geq 2$ or placebo were transitioned to brodalumab 210 mg Q2W.

The co-primary endpoints were the percentage of patients achieving PASI 75 and sPGA success at week 12. Results showed that 60% of patients in the 140 mg group and 83% in the 210 mg group achieved PASI 75, compared to 3% in the placebo group. Similarly, 54% of the 140 mg group and 76% of the 210 mg group achieved sPGA success, compared to 1% for placebo.

In AMAGINE-2 and AMAGINE-3, two phase III, randomized, double-blind, placebo- and active-comparator-controlled trials (NCT01708603 and NCT01708629), brodalumab was further evaluated for its efficacy and safety in patients with psoriasis.[23] These trials enrolled over 3700 patients across 142 sites globally. Patients were randomized in

a 2:2:1:1 ratio to receive brodalumab 210 mg or 140 mg every two weeks (Q2W), ustekinumab (45 mg or 90 mg based on body weight), or placebo. The trials included a 12-week induction phase followed by a 40-week maintenance phase. At week 12, patients receiving brodalumab were rerandomized into four maintenance regimens, while those on placebo were transitioned to brodalumab 210 mg Q2W, and ustekinumab patients continued their treatment.

The co-primary endpoints were the percentage of patients achieving PASI 75 and an sPGA score of 0 or 1 (clear or almost clear skin) at week 12. Brodalumab 210 mg achieved PASI 75 response rates of 86% (AMAGINE-2) and 85% (AMAGINE-3) compared to 8% and 6% for placebo. PASI 100 response rates for brodalumab 210 mg were 44% and 37%, significantly higher than ustekinumab (22% and 19%) in AMAGINE-2 and AMAGINE-3, respectively.

### Phase IV Studies

In the CHANGE trial, a Phase IV, randomized, open-label, assessor-blinded, multicenter study (NCT03331835), brodalumab was compared to fumaric acid esters (FAE) in systemic-naïve adults with moderate-to-severe plaque psoriasis.[24] A total of 210 patients were randomized 1:1 to receive brodalumab 210 mg subcutaneously Q2W following an initial induction dose, or FAE tablets, up to 240 mg three times daily with individual dose titration. The trial spanned 24 weeks, with efficacy assessed using PASI 75 and sPGA scores of 0 or 1 as co-primary endpoints.

At week 24, 81.0% of patients receiving brodalumab achieved PASI 75 compared to 38.1% in the FAE group ($P<0.001$). Similarly, sPGA 0/1 responses were higher in the brodalumab group (64.8%) compared to the FAE group (20.0%, $P<0.001$). Brodalumab demonstrated a significantly faster median time to PASI 75 (4.1 weeks) and PASI 90 (7.4 weeks) compared to FAE (16.4 weeks and 24.4 weeks, respectively, $P<0.0001$ for both). Patients treated with brodalumab also reported greater improvements in quality of life, with 66.7% achieving a DLQI score of 0 or 1, versus 25.7% for FAE.

## Brodalumab Is Effective After Inadequate Response to Other IL-17 Biologics

In a multicenter, multinational retrospective study, Gasslitter et al evaluated the efficacy of switching to brodalumab in patients with moderate-to-severe psoriasis who had an inadequate response to other IL-17 inhibitors.[25] Among those who switched from secukinumab to brodalumab, 57% achieved PASI 75 after 12 weeks. Similarly, 66% of patients who switched from ixekizumab to brodalumab achieved PASI 75. In an open-label study of 39 patients with moderate-to-severe psoriasis who previously failed treatment with IL-17 inhibitors, brodalumab demonstrated significant effectiveness. By week 16, 76% of patients who completed the study achieved PASI 75. Additionally, 71% achieved a sPGA score of 0 (clear) or 1 (almost clear).[26] In a retrospective multicenter chart review, Kromer et al reported that 47.8% (11/23) of patients who failed IL-17 therapy achieved PASI 75 after week 12 and at week 24.[27] In a study of 16 patients with psoriasis who failed treatment with secukinumab, all patients achieved an sPGA score of 0 or 1 by week 12 after switching to brodalumab. PASI-90 and PASI-100 responses were observed in 80% and 20% of patients, respectively.[28]

Another study assessed effectiveness of brodalumab in 20 psoriasis patients who previously failed treatment with IL-17A inhibitors.[29] Patients had either primary failure (PASI <50% after 3 months) or secondary failure (initial response followed by loss of efficacy) with secukinumab and/or ixekizumab. After 12 weeks, 70% achieved PASI 75 or an absolute PASI ≤2, 40% achieved PASI 90, and 15% achieved PASI 100. By week 52, 35% maintained PASI 75, while 25% achieved PASI 90 and 15% achieved PASI 100. Additionally, 50% of patients achieved DLQI of 0 or 1 by week 12. Yeung et al further explored the efficacy of brodalumab in 47 patients with chronic plaque psoriasis who discontinued secukinumab or ixekizumab due to nonresponse (44/47), response optimization (2/47), or adverse events (1/47).[30] After 16 weeks of brodalumab treatment, 20 (42.5%) achieved PASI 100, while 22 (46.8%) and 29 (61.7%) reached PASI 90 and PASI 75, respectively. Notably, patients switching from secukinumab had a higher PASI 100 response rate (57%) compared with those switching from ixekizumab (31%). Subgroup analysis also revealed that secondary nonresponders were more likely to achieve PASI 100 compared to primary nonresponders.

## Brodalumab Is Effective Regardless of Previous Biologic History

Brodalumab's efficacy and safety have been well established in the Phase 3 AMAGINE-1, AMAGINE-2, and AMAGINE-3 trials.[22,23] Notably, prior biologic exposure did not impact treatment outcomes, as demonstrated in the AMAGINE-2/3 trials. Among patients who received brodalumab 210 mg every two weeks during the 12-week induction period, 27% had prior biologic exposure, primarily to TNF-α inhibitors, while 73% were biologic-naïve.[31] By week 12, PASI 75 response rates were comparable between biologic-experienced and biologic-naïve patients (81.7% vs 87.1%), with similar trends for PASI 90 and PASI 100.

Long-term data from 3625 patients further confirmed sustained efficacy, with PASI 75 and PASI 100 response rates maintained through 120 weeks regardless of prior biologic use.[32] At week 120, PASI 75 was achieved by 84.2% of biologic-experienced and 91.3% of biologic-naïve patients, while PASI 100 rates were 52.5% and 59.8%, respectively.

Additionally, brodalumab demonstrated effectiveness in patients with prior TNF-α inhibitor use, including those who failed or responded inadequately to adalimumab.[32] At week 52, PASI 75, PASI 90, and PASI 100 were achieved by 86.1%, 74.8%, and 47.7% of patients with prior adalimumab failure, and by 90.8%, 63.8%, and 40.4% of those who had a prior response. Moreover, brodalumab maintained efficacy even in patients who had failed one or multiple biologics.

## Brodalumab Is Effective After Inadequate Response to Ustekinumab

An additional analysis of the AMAGINE-2 and AMAGINE-3 trials further highlighted brodalumab's superior efficacy compared to ustekinumab, an IL-12/IL-23 inhibitor, regardless of prior treatment history.[33] By week 52, brodalumab achieved significantly higher rates of complete clearance (PASI 100) across all treatment subgroups, including systemic/biologic-naïve patients (76% vs 58% with ustekinumab) and those with prior biologic failure (70% vs 30%). The cumulative benefit of brodalumab, assessed through area-under-the-curve (AUC) analysis, was greater across all subgroups, with the most pronounced differences observed in biologic-treated patients. For example, in biologic-treated patients without prior failure, the AUC ratio for PASI 100 was 2.44 in favor of brodalumab. Additionally, brodalumab demonstrated a faster onset of action, with more patients achieving complete clearance earlier in the treatment course.

## Safety

Reich et al conducted an integrated safety analysis using pooled data from five Phase II/III clinical trials to evaluate the safety profile of brodalumab 140 mg and 210 mg.[34] The study included a total of 4464 patients, representing 8891.6 patient-years of exposure. Data were assessed across multiple time periods, including a 12-week placebo-controlled induction phase, a 52-week ustekinumab-controlled period, and long-term open-label extension trials.

Brodalumab was well tolerated with a safety profile comparable to ustekinumab. The incidence of serious adverse events (SAEs) was slightly higher in the brodalumab 210 mg group but remained within an acceptable range. No increased risk was observed for malignancy, major adverse cardiac events (MACE), suicidal ideation and behavior (SIB), or fatal events. The most common treatment-emergent adverse events (TEAEs) included nasopharyngitis, upper respiratory infections, arthralgia, and headache. Infections were the most frequent SAEs, with slightly higher rates in the brodalumab 210 mg group, particularly for fungal infections (eg, Candida). However, serious infections were rare, and no tuberculosis cases were reported.

Four suicide events were reported, three of which occurred in patients receiving brodalumab.[35] As a result, the FDA issued a black box warning for brodalumab, highlighting the potential risk of SIB. However, all affected individuals had pre-existing risk factors, such as depression or significant life stressors, and no causal relationship was established. Furthermore, the incidence of suicidal behavior or completed suicides did not increase over time in the brodalumab treatment group. A six-year US pharmacovigilance report found no completed suicides and no new suicide attempts throughout the entire period.[36] Notably, the AMAGINE-1 trial demonstrated greater improvements in depression and anxiety scores with brodalumab compared to placebo.[22] Similarly, MACE rates were low, with most cases occurring in patients with pre-existing cardiovascular risk factors like hypertension, obesity, diabetes, and smoking, suggesting psoriasis itself may contribute to cardiovascular risk rather than brodalumab treatment.

No increased risk of malignancy was observed in brodalumab-treated patients. While some inflammatory bowel disease cases were reported, no new-onset Crohn's disease occurred in those receiving brodalumab 210 mg. Neutropenia cases were mostly mild, transient, and not linked to serious infections. Hypersensitivity reactions were rare and occurred less frequently in the brodalumab 210 mg group, while injection-site reactions were mild and comparable across treatment groups.

## Discussion

Brodalumab is the first drug that targets IL-17RA, rather than individual IL-17 ligands. This unique mechanism of action enables broader inhibition across multiple IL-17 isoforms, including IL-17A, IL-17F, and IL-17E.[18] This broader inhibition may be particularly advantageous for patients with aggressive, refractory, or multifocal disease where IL-17A blockade alone proves insufficient.

Clinical trials, including the pivotal AMAGINE studies, have shown that brodalumab achieves significantly higher rates of complete skin clearance (PASI 100) compared to placebo and ustekinumab.[22,23] Furthermore, brodalumab has proven effective in patients with inadequate responses to other IL-17 inhibitors, like secukinumab and ixekizumab, underscoring its unique mechanism of action through IL-17RA blockade.[24–30] This degree of efficacy, particularly in achieving complete clearance, can have profound implications for patient confidence, quality of life, and long-term adherence, especially for those who have cycled through multiple therapies with only partial relief.

Beyond clinical trial settings, real-world evidence has further validated brodalumab's long-term effectiveness and safety profile. In a multicenter Italian study, Gargiulo et al reported that 65.2% of patients maintained complete skin clearance (PASI 100) and 91.3% achieved an absolute PASI $\leq 2$ after three years of continuous treatment.[37] The study also highlighted brodalumab's effectiveness across key subgroups, including those with difficult-to-treat areas (scalp, face, palms, soles, nails, and genitals), along with a high drug survival rate (85.6% at 36 months) and no new safety signals.

Similarly, the prospective BrIDGE study from Greece reported PASI 100 responses in 51.3% of patients at week 52 and 65% at week 104, with substantial improvements in quality of life measures.[38] The analysis revealed statistically significant differences in outcomes between biologic-naïve and biologic-experienced patients, favoring the former.

In a 52-week observational study focusing on difficult-to-treat regions, brodalumab demonstrated marked improvement in PASI, DLQI, Psoriasis Scalp Severity Index (PSSI), and palmoplantar PASI (ppPASI), along with reductions in inflammatory biomarkers and dermoscopic signs of disease.[39] Furthermore, a retrospective study comparing IL-17 and IL-23 inhibitors in palmoplantar psoriasis found that both classes, including brodalumab, were effective over 104 weeks, with no statistically significant differences in treatment outcomes.[40]

Despite its advantages, brodalumab is not without limitations. Safety concerns, particularly the boxed warning for SIB, remain a consideration. While no causal relationship has been established, clinicians must carefully screen and monitor patients with a history of depression or psychiatric disorders.[34] As a precaution, brodalumab is available only through a Risk Evaluation and Mitigation Strategy (REMS) program, which requires prescriber certification, patient enrollment, and pharmacy authorization to ensure appropriate monitoring and patient education.[41] Patients must also be informed about psychiatric symptoms that require immediate medical evaluation.

Additionally, there is a slightly increased risk of infections, particularly fungal infections, which necessitates vigilance in immunocompromised patients.[34] IBD remains another area of concern, as IL-17 inhibition has been linked to potential IBD exacerbation.[42] However, real-world data suggest that new-onset Crohn's disease is rare in brodalumab-treated patients.

## Expert Opinion

Clinical trial and real-world evidence position brodalumab among the most effective biologic agents currently available for moderate-to-severe psoriasis, particularly in achieving complete skin clearance. Its high PASI 100 rates, even in bio-experienced populations, underscore its unique therapeutic potential. While concerns regarding SIB led to a boxed warning, this signal has not been confirmed in long-term registry or post-marketing surveillance data. In clinical practice, with appropriate patient selection and monitoring, brodalumab can offer life-changing outcomes for patients with recalcitrant or high-impact disease.

## Conclusion

In conclusion, brodalumab remains a highly effective and reliable treatment option for moderate-to-severe psoriasis, particularly for patients with prior biologic failure or challenging clinical presentations. Its rapid onset, deep clearance rates, and growing real-world support its clinical value for dermatologists tailoring treatment to individual patient needs.

## Disclosure

Dr. Wu is or has been an investigator, consultant, or speaker for AbbVie, Almirall, Amgen, Arcutis, Aristea Therapeutics, Bausch Health, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Codex Labs, Dermavant, DermTech, Dr. Reddy's Laboratories, Eli Lilly, EPI Health, Galderma, Incyte, Janssen, LEO Pharma, Mindera, Novartis, Pfizer, Regeneron, Samsung Bioepis, Sanofi Genzyme, Solius, Sun Pharmaceutical, UCB, and Zerigo Health.

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