Deucravacitinib in plaque psoriasis: maintenance of response over 4 years in the phase 3 POETYK PSO-1, PSO-2, and LTE trials

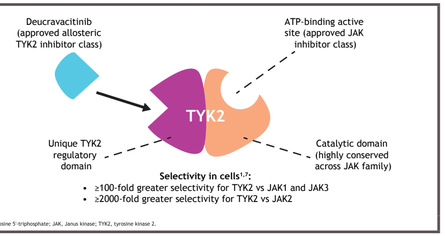
Bruce Strober,[1] Shinichi Imafuku,[2] Carle Paul,[3] Melinda Gooderham,[4] Lynda Spelman,[5] Seong Jun Seo,[6] Thierry Passeron,[7] Kim Hoyt,[8] Matthew J. Colombo,[8] Subhashis Banerjee,[8] Matthias Augustin,[9] Linda Stein Gold,[10] Andrew F. Alexis,[11] Diamant Thaçi,[12] Mark Lebwohl,[13] Naiem T. Issa,[14] Michael C. Cameron[13,15]

[1]Yale University School of Medicine, New Haven, and Central Connecticut Dermatology Research, Cromwell, CT, USA; [2]Fukuoka University Hospital, Fukuoka, Japan; [3]Toulouse University and CHU, Toulouse, France; [4]SKiN Centre for Dermatology, Peterborough, Queen's University, Kingston, and Probity Medical Research, Waterloo, ON, Canada; [5]Veracity Clinical Research, Brisbane, QLD, Australia; [6]Chun Hyang University Cheonan Hospital, Cheonan, South Korea; [7]Université Côte d'Azur, University Hospital of Nice, Nice, France; [8]Bristol Myers Squibb, Princeton, NJ, USA; [9]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [10]Henry Ford Health System, West Bloomfield, MI, USA; [11]Weill Cornell Medicine, New York, NY, USA; [12]University of Lübeck, Lübeck, Germany; [13]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [14]Forefront Dermatology, Vienna, VA, University of Miami Miller School of Medicine, Miami, FL, and George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [15]Cameron Dermatology, New York, NY, USA

Introduction

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of select inflammatory cytokines (eg, interleukin [IL]-23, IL-12, Type I interferons [IFNs])[1]
  - IL-23 and Type I IFNs are involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy[2-6]
- Deucravacitinib uniquely binds to the TYK2 regulatory domain rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] **(Figure 1)**, driving its selectivity for TYK2 and representing the first in a new class of oral drugs

Figure 1. Mechanism of action of deucravacitinib



ATP, adenosine 5′-triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

- Two global, 52-week, phase 3 trials, POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751), in patients with moderate to severe plaque psoriasis showed that deucravacitinib 6 mg once daily (QD) was well tolerated and was significantly more efficacious than placebo and apremilast at Week 16 based on the key endpoints[8,9]:
  - PASI 75 (≥75% reduction from baseline in Psoriasis Area and Severity Index)
  - sPGA 0/1 (static Physician Global Assessment score of 0 [clear] or 1 [almost clear])
- Patients who completed the POETYK PSO-1 and PSO-2 parent trials could enroll in the ongoing POETYK long-term extension (LTE) (NCT04036435) trial and receive open-label deucravacitinib
- Clinical efficacy was previously reported to be maintained well through 3 years (1 year in the parent trials and 2 additional years in the POETYK LTE trial) in deucravacitinib-treated patients[10,11]

Objective

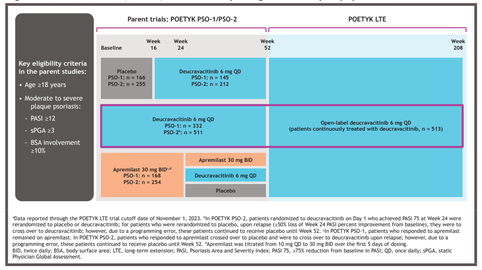
- To evaluate clinical efficacy for up to 4 years (208 weeks) in 2 cohorts of patients who received continuous deucravacitinib treatment from Day 1 in the parent trials (POETYK PSO-1 and PSO-2), achieved PASI 75 at Week 16 (primary endpoint) or at Week 24 (peak response), and entered the POETYK LTE trial

Methods

Study designs

- In the POETYK PSO-1 and PSO-2 trials, adults with moderate to severe plaque psoriasis (PASI ≥12, sPGA ≥3, and body surface area involvement ≥10% at baseline) were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg QD, or apremilast 30 mg twice daily (BID) **(Figure 2)**
- Blinded treatment switches occurred at Week 16 and Week 24:
  - Patients randomized to placebo crossed over to deucravacitinib at Week 16
  - Patients randomized to apremilast who failed to meet trial-specific efficacy thresholds (≥50% reduction from baseline in PASI [PASI 50] in POETYK PSO-1; PASI 75 in POETYK PSO-2) switched to deucravacitinib at Week 24
  - Patients randomized to deucravacitinib who achieved PASI 75 at Week 24 in POETYK PSO-2 were rerandomized 1:1 to placebo or deucravacitinib through Week 52
- At Week 52, eligible patients were allowed to enroll in the POETYK LTE trial and receive open-label deucravacitinib 6 mg QD

Figure 2. POETYK PSO-1, PSO-2, and LTE study designs and analysis populations[a]



[a]Data reported through the POETYK LTE trial cutoff date of November 1, 2023. [b]In POETYK PSO-2, patients randomized to deucravacitinib on Day 1 who achieved PASI 75 at Week 24 were rerandomized to placebo or deucravacitinib; for patients who were rerandomized to placebo, upon relapse (≥50% loss of Week 24 PASI percent improvement from baseline), they were to cross over to deucravacitinib; however, due to a programming error, these patients continued to receive placebo until Week 52. [c]In POETYK PSO-1, patients who responded to apremilast remained on apremilast. In POETYK PSO-2, patients who responded to apremilast crossed over to placebo and were to cross over to deucravacitinib upon relapse; however, due to a programming error, these patients continued to receive placebo until Week 52. ↑apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
BID, twice daily; BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily; sPGA, static Physician Global Assessment.

Patient population

- Patients pooled from the POETYK PSO-1 and PSO-2 trials who received continuous deucravacitinib from Day 1, achieved PASI 75 at Week 16 or at Week 24, and enrolled in the POETYK LTE trial

Outcomes

- Efficacy of deucravacitinib and maintenance of response through Week 208 (4 years) by achievement of:
  - PASI 75
  - PASI 90 (≥90% reduction from baseline in PASI)
  - sPGA 0/1

Statistical analysis

- Efficacy was analyzed through the data cutoff of November 1, 2023 (Week 208, 4 years)
- In addition to as-observed analysis, two methods of imputation for missing data were used to evaluate long-term efficacy, as recently done with other agents
  - **Treatment failure rules (TFR)**[12]: patients who discontinued treatment due to lack of efficacy or worsening of psoriasis were imputed as nonresponders; all other missing data were not imputed
  - **Modified nonresponder imputation (mNRI)**[13]: patients who either discontinued prior to Week 208 or reached Week 208 were included; patients with missing data who discontinued treatment due to worsening of psoriasis were imputed as nonresponders; all other missing data were imputed by multiple imputation
- The Clopper-Pearson method was used to calculate 95% confidence intervals (CIs) when there were no missing data or for nonresponder imputation; otherwise, the Rubin method was used for multiple imputation

Results

Patients

- Baseline demographics and disease characteristics for patients who received continuous deucravacitinib in POETYK PSO-1 or PSO-2 and enrolled in the POETYK LTE trial (n = 513) are presented in **Table 1**
  - 313 (61.0%) patients achieved PASI 75 at Week 16
  - 336 (65.5%) patients achieved PASI 75 at Week 24

Table 1. Baseline patient demographics and disease characteristics

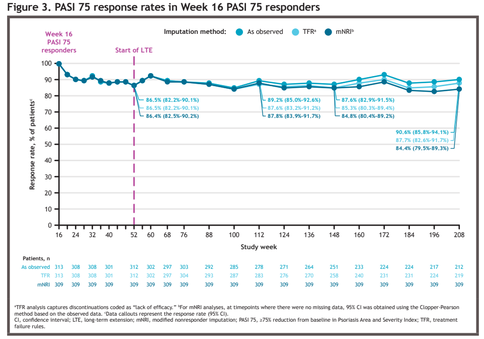
Parameter	Continuous deucravacitinib treatment in POETYK PSO-1 + PSO-2 + LTE[a]		
	All patients (n = 513)	Week 16 PASI 75 responders (n = 313)	Week 24 PASI 75 responders (n = 336)
Age, mean (SD), y	46.9 (13.3)	46.3 (13.9)	46.3 (13.8)
Weight, mean (SD), kg	89.9 (22.2)	86.7 (21.7)	86.6 (22.1)
Body mass index, mean (SD), kg/m²	30.3 (7.0)	29.5 (6.6)	29.5 (7.0)
Female, n (%)	159 (31.0)	110 (35.1)	122 (36.3)
Race, n (%)			
White	440 (85.8)	262 (83.7)	284 (84.5)
Asian	64 (12.5)	45 (14.4)	47 (14.0)
Black or African American	5 (1.0)	2 (0.6)	1 (0.3)
Other	4 (0.8)	4 (1.3)	4 (1.2)
Age at disease onset, mean (SD), y	29.0 (14.7)	29.1 (15.3)	28.8 (15.3)
Disease duration, mean (SD), y	18.8 (12.6)	18.0 (12.4)	18.3 (13.0)
Prior systemic therapy, n (%)	300 (58.5)	174 (55.6)	198 (58.9)
Prior systemic biologic	191 (37.2)	106 (33.9)	123 (36.6)
Prior systemic non-biologic	206 (40.2)	116 (37.1)	128 (38.1)
PASI score, mean (SD)	21.1 (7.9)	21.8 (8.2)	21.3 (8.0)
sPGA score, n (%)			
3 (moderate)	401 (78.2)	241 (77.0)	265 (78.9)
4 (severe)	112 (21.8)	72 (23.0)	71 (21.1)
BSA involvement, mean (SD), %	26.9 (15.8)	28.1 (16.1)	27.0 (15.8)

[a]Patients pooled from POETYK PSO-1 and POETYK PSO-2 who were randomized to deucravacitinib in the parent trials, received continuous deucravacitinib from Day 1, and entered the POETYK LTE trial.
BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; SD, standard deviation; sPGA, static Physician Global Assessment.

Outcomes in Week 16 PASI 75 responders

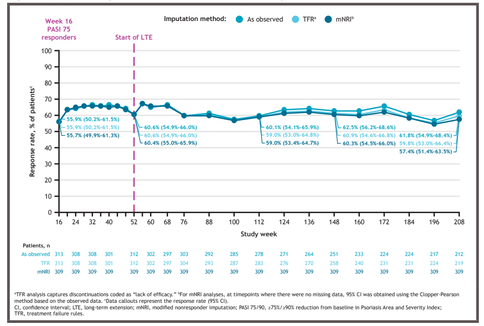
- In the cohort of Week 16 PASI 75 responders, PASI 75, PASI 90, and sPGA 0/1 response rates were maintained well from the start of the POETYK LTE trial (Week 52) to Week 208 **(Figure 3**, **Figure 4**, and **Figure 5**, respectively)
  - Results were consistent regardless of imputation method

Figure 3. PASI 75 response rates in Week 16 PASI 75 responders



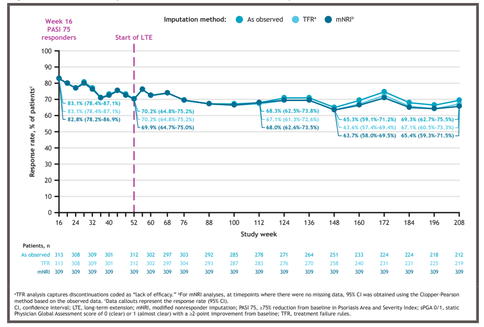
[a]TFR analysis captures discontinuations coded as "lack of efficacy." "For mNRI analyses, at timepoints where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [b]Data calculators represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 4. PASI 90 response rates in Week 16 PASI 75 responders



[a]TFR analysis captures discontinuations coded as "lack of efficacy." "For mNRI analyses, at timepoints where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [b]Data calculators represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 5. sPGA 0/1 response rates in Week 16 PASI 75 responders

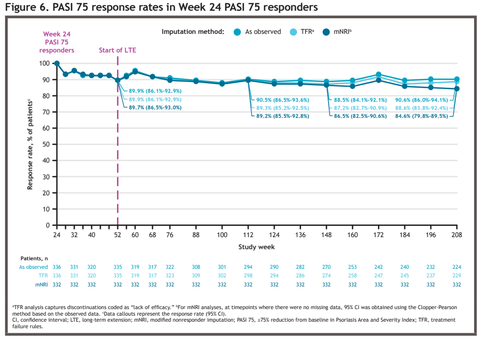


[a]TFR analysis captures discontinuations coded as "lack of efficacy." "For mNRI analyses, at timepoints where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [b]Data calculators represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TFR, treatment failure rules.

Outcomes in Week 24 PASI 75 responders

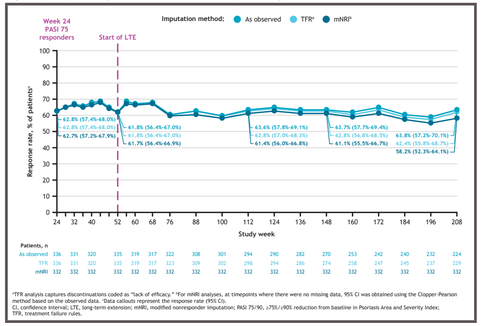
- In the cohort of Week 24 PASI 75 responders, PASI 75, PASI 90, and sPGA 0/1 response rates were maintained well from the start of the POETYK LTE trial to Week 208 **(Figure 6**, **Figure 7**, and **Figure 8**, respectively)
  - Results were consistent regardless of imputation method

Figure 6. PASI 75 response rates in Week 24 PASI 75 responders



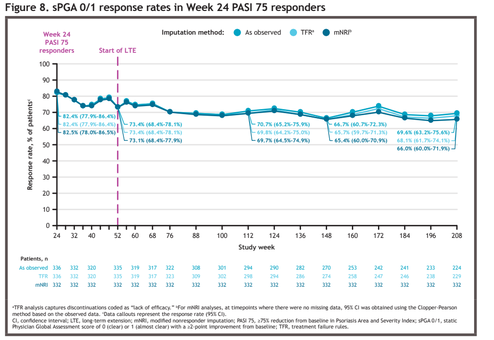
[a]TFR analysis captures discontinuations coded as "lack of efficacy." "For mNRI analyses, at timepoints where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [b]Data calculators represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 7. PASI 90 response rates in Week 24 PASI 75 responders



[a]TFR analysis captures discontinuations coded as "lack of efficacy." "For mNRI analyses, at timepoints where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [b]Data calculators represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 8. sPGA 0/1 response rates in Week 24 PASI 75 responders



[a]TFR analysis captures discontinuations coded as "lack of efficacy." "For mNRI analyses, at timepoints where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [b]Data calculators represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TFR, treatment failure rules.

Conclusions

- Clinical efficacy was maintained through 4 years (208 weeks) with continuous deucravacitinib treatment with minimal loss of response in patients who achieved PASI 75 at Week 16 or Week 24 in the parent trials and had enrolled in the POETYK LTE trial
- These findings further support the use of once-daily oral deucravacitinib as an effective long-term treatment for patients with moderate to severe plaque psoriasis in patients who respond well at Week 16 or at Week 24

References

1. Burke JR, et al. *Sci Transl Med*. 2019;11:eaaw1736.
2. Sotyktu [package insert]. Princeton, NJ, USA: Bristol Myers Squibb; September 2022.
3. Sotyktu [EU summary of product characteristics]. Dublin, Ireland: Bristol Myers Squibb EEIG; December 2023.
4. Sotyktu [package insert]. Tokyo, Japan: Bristol Myers Squibb K.K.; September 2022.
5. Sotyktu [product monograph]. Montreal, QC, Canada: Bristol Myers Squibb Canada Co.; November 2022.
6. Sotyktu [product information]. Mulgrave, VIC, Australia: Bristol Myers Squibb Australia Pty. Ltd.; December 2022.
7. Wrobleski ST, et al. *J Med Chem*. 2019;62:8973-8995.
8. Armstrong AW, et al. *J Am Acad Dermatol*. 2023;88:29-39.
9. Strober B, et al. *J Am Acad Dermatol*. 2023;88:40-51.
10. Lebwohl M, et al. *Br J Dermatol*. 2024;190:668-679.
11. Armstrong A, et al. Presented at the 32nd EADV Congress; 11-14 October 2023; Berlin, Germany.
12. Reich K, et al. *Br J Dermatol*. 2021;185:1146-1159.
13. Papp K, et al. *Br J Dermatol*. 2021;185:1135-1145.

Acknowledgments

- This study was sponsored by Bristol Myers Squibb
- Writing and editorial assistance was provided by Kimberly MacKenzie, PhD, of Peloton Advantage, LLC, an OPEN Health company, funded by Bristol Myers Squibb

Disclosures

- **BS:** Consultant with honoraria: AbbVie, Acelyrin, Alamar, Almirall, Alumis, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Capital One, Celltrion, CorEvitas Psoriasis Registry, Dermavant, Imagenebio, Janssen/J&J Innovative Medicine, Kangpu Biopharmaceuticals, Leo Pharma, Lilly, Maruho, Meiji Seika Pharma, Monte Carlo, Novartis, Pfizer, Protagonist, Rapt Therapeutics, Regeneron, Sanofi, SG Cohen, Sun Pharma, Takeda, UCB, Union Therapeutics, Ventyx Biosciences, and vTv Therapeutics; Speaker: AbbVie, Arcutis, Dermavant, Incyte, Janssen/J&J Innovative Medicine, Lilly, Regeneron, and Sanofi; Co-scientific director (consulting fee) and investigator: CorEvitas Psoriasis Registry; Editor-in-chief with honorarium: *Journal of Psoriasis and Psoriatic Arthritis*; Stock options: Connect Biopharma and Mindera Health
- **SI:** Grants and/or personal fees: AbbVie, Alexion pharma, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eisai, Janssen, GSK, Kaken, Kyowa Kirin, Leo Pharma, Lilly, Maruho, Novartis, Sun Pharma, Taiho Yakuhin, Torii Yakuhin, and UCB
- **CP:** Grants and consultant: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Janssen, Leo Pharma, Lilly, Merck, Mylan, Novartis, Pfizer, Sandoz, and UCB
- **MG:** Advisory board, principal investigator, and consulting and lecture fees: AbbVie, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim International GmbH, Lilly, Janssen, Novartis, Sanofi Genzyme, Sun Pharma, and UCB; Advisory board, primary investigator, and lecture fees: Galderma SA, Leo Pharma, Pfizer, and Regeneron; Advisory board, primary investigator and consultant fees: Aslan; Primary investigator and consultant fees: Akros Pharma and Kyowa Kirin; Primary investigator: Aristea, AnaptysBio, Bristol Myers Squibb, Cohenus Biosciences, Dermira, GSK, Incyte, Medimmune, Meiji Seika, Merck, MoonLake Immunotherapeutics, and Nimbus Therapeutics; Advisory board: Asana Biosciences
- **LS:** Consultant, paid investigator, advisory board and/or speaker: AbbVie, Amgen, Anacor, Ascend, Astellas, AstraZeneca, Blaze Bioscience, Boehringer Ingelheim, Botanix, Bristol Myers Squibb/Celgene, Connect Biopharma, Dermira, Enkang, Equillium, Evelo Biosciences, Galderma, Genentech, Genesis Care, GSK, Hexima, Incyte, InflaRx GmbH, Invion, Janssen, Kiniksa, Kobbo Labs, Leo Pharma, LG Chem, Lilly, Lipidio Pharma, Mayne, Medimmune, Merck, Merck-Serono, Nektar Therapeutics, Novartis, Olix, Otsuka, Pfizer, Phosphagenics, Photon MD, Principia, Regeneron, Ribon, Samumed, Sanofi Genzyme, SHR Pharmacy, Sun Pharma, Takeda, UCB, and Zai Lab
- **SJS:** Nothing to disclose
- **TP:** Advisory board and consulting fees: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb/Celgene, Galderma, Incyte, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi Genzyme, Sun Pharma, and UCB
- **MJC and SB:** Employees and shareholders: Bristol Myers Squibb
- **KH:** Consultant: Bristol Myers Squibb via Syneos Health
- **MA:** Advisory boards: AbbVie, Amgen, Boehringer Ingelheim, Janssen Biotech, and Leo Pharma; Consulting fees: AbbVie, Amgen, Janssen Biotech, Leo Pharma, Lilly, Novartis, Sun Pharma, and UCB; Honoraria: AbbVie, Amgen, Boehringer Ingelheim, Janssen Biotech, Leo Pharma, Lilly, Novartis, Sun Pharma, and UCB; Investigator: AbbVie, Amgen, Boehringer Ingelheim, Janssen Biotech, Leo Pharma, Lilly, Merck, Novartis, Sun Pharma, and UCB; Research grants: AbbVie, Amgen, Boehringer Ingelheim, Janssen Biotech, Leo Pharma, Merck, and Sun Pharma; Speaker: AbbVie, Amgen, Janssen Biotech, Leo Pharma, Sun Pharma, and UCB
- **LSG:** Consultant, advisory board member, and/or speaker: AbbVie, Amgen, Arcutis, Aslan, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Galderma, Incyte, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB
- **AFA:** Grants (funds to institution): AbbVie, Amgen, Arcutis, Castle Biosciences, Dermavant, Galderma, and Leo Pharma; Advisory board/Consulting: AbbVie, Allergan, Almirall, Alphyn, Amgen, Apogee, Arcutis, Avita Medical Bausch Health, Beiersdorf, Bristol Myers Squibb, Canfield, Cara Therapeutics, Castle Biosciences, Cutera, Dermavant, EPI Health, Galderma, Incyte, Janssen, Leo Pharma, Lilly, L'Oreal, Ortho, Pfizer, Sanofi-Regeneron, Swiss American, UCB, VisualDx, and Vyne; Speaker: Bristol Myers Squibb, Janssen/J&J, L'Oreal, Regeneron, and Sanofi Genzyme
- **DT:** Research support and principal investigator (clinical trial funds to institution): AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Galderma, Janssen-Cilag, Leo Pharma, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB; Consultant: AbbVie, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Leo Pharma, Novartis, Pfizer, and UCB; Lecturer: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Roche-Posay, Sanofi, Target RWE, and UCB; Scientific advisory board: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen-Cilag, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi, and UCB
- **ML:** Research funds on behalf of Mount Sinai: AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant, Incyte, Janssen, Lilly, Ortho Dermatologics, Regeneron, and UCB; Consultant: Almirall, AltruBio, AnaptysBio, Arcutis, Avotres, Boehringer Ingelheim, Brickell Biotech, Bristol Myers Squibb, Castle Biosciences, Celltrion, CorEvitas Psoriasis Registry, Dermavant, EPI Health, Evommune, Forte Biosciences, Galderma, Genentech, Incyte, Leo Pharma, Meiji Seika Pharma, Mindera Health, Pfizer, Seanergy, Strata, Trevi, and Verrica
- **NTI:** Funding as a speaker, consultant, advisor, or investigator: Bristol Myers Squibb, Castle Biosciences, Dermavant Sciences, DermTech, Galderma, Leo Pharma, Lilly, Ortho Dermatologics, Pfizer, RBC Consultants, Verrica, WebMD
- **MCC:** Consultant (with honoraria): AbbVie, Bristol Myers Squibb, Dermavant, Incyte, Lilly, and Verrica; Speaker (with honoraria): AbbVie, Amgen, Bristol Myers Squibb, Dermavant, Evelo Biosciences, Incyte, Journey Medical, Leo Pharma, Lilly, Ortho, Pfizer, Regeneron, and Verrica

Email: bstrober30@me.com