CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217242Orig1s000

PRODUCT QUALITY REVIEW(S)

RECOMMENDATION

☒ Approval
☐ Not Ready for Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 217242
Assessment 1

Drug Product Name	Roflumilast Topical Foam
Dosage Forms	Foam
Strength	0.3%
Route of Administration	Topical
Rx/OTC Dispensed	Rx
Applicant	Arcutis Biotherapeutics, Inc.; Westlake Village, CA, USA
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original	Feb 16, 2023	OPQ
Amendment	Apr 10, 2023	Labeling
Amendment	Jul 20, 2023	OPMA
Amendment	Aug 3, 2023	Drug Product
Amendment	Aug 11, 2023	Drug Product
Amendment	Sep 7, 2023	Labeling
Amendment	Sep 18, 2023	Drug product, Biopharm
Amendment	Sep 28, 2023	OPMA

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Sukhamaya (Sam) Bain	Lawrence Perez
Drug Product	Hitesh Shroff	Nina Ni
Manufacturing/ Microbiology	Yan Xu	Tianhong Tim Zhou
Biopharmaceutics	Kalpana Paudel	Tapash Ghosh
Regulatory Business Process Manager	Rajani Rajan	
Application Technical Lead	Hitesh Shroff	
Laboratory (OTR)	N/A	N/A
Environmental	Hitesh Shroff	Nina Ni

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	II		(b) (4)	Active	Apr 12, 2023	LOA: Jan 29, 2021
	III			Active	N/A	LOA: Jan 3, 2023
	III			Active	N/A	LOA: Dec 14, 2022

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
NDA	22522	Daliresp (roflumilast) tablets from AstraZeneca LOA: Nov 4, 2022
IND	142047	Roflumilast topical foam from Arcutis Biotherapeutics, Inc., CA

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			
CDRH	N/A			
Clinical	N/A			
Other	N/A			

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

The applicant has provided sufficient CMC information to assure the identity, strength, purity, and quality of the proposed Zoryve (roflumilast) topical foam, 0.3%.

The Office of Pharmaceutical Manufacturing Assessment (OPMA) has made a final overall "**Approval**" recommendation for the facilities involved in this application.

The claim for the Categorical Exclusion for the Environmental Assessment is granted.

The label/labeling issues have been satisfactorily addressed.

Therefore, from the OPQ perspective, this NDA is recommended for approval with expiration dating period of 24 months.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

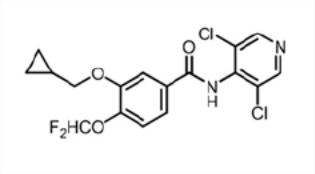
Zoryve is a non-sterile, white to off-white topical foam for the treatment of seborrheic dermatitis in adults and pediatric patients 9 years of age and older. It is supplied in a (b) (4) 60-gram pressurized white aluminum can. Each pump contains 60 g of foam. Each gram of Zoryve foam contains 3 mg of roflumilast. A thin layer of foam is applied to the affected areas on dry skin and hair once daily.

Proposed Indication(s) including Intended Patient Population	ZORYVE topical foam is a phosphodiesterase 4 inhibitor indicated for the treatment of seborrheic dermatitis in adults and pediatric patients 9 years of age and older.
Duration of Treatment	As needed
Maximum Daily Dose	N/A
Alternative Methods of Administration	N/A

B. Quality Assessment Overview

Drug Substance: Adequate

The drug substance in Zoryve foam is roflumilast. It is a white to almost white crystalline powder. It is insoluble in water. Its solubility at neutral pH is 0.8 mg/L and at pH 10 is 35.8 mg/L. The chemical name of roflumilast is 3-cyclopropylmethoxy-*N*-(3,5-dichloropyridin-4-yl)-4-(difluoromethoxy)benzamide with a molecular formula of $C_{17}H_{14}Cl_2F_2N_2O_3$, and the molecular weight of 403.21. The chemical structure of roflumilast is shown below.



The detailed CMC information the drug substance, roflumilast, is provided in DMF (b) (4) from the manufacturer, (b) (4) (b) (4). A Letter of Authorization is provided in support of this NDA. The detailed CMC information is provided in the DMF. The DMF (b) (4) was reviewed and deemed adequate by Dr. Roger Farr on April 12, 2023.

The quality of roflumilast is controlled by its specification which includes appearance, identification by infrared spectroscopy and HPLC; assay by HPLC, related substances by HPLC. etc. The API specification deemed adequate per the drug substance reviewer. (b) (4) .

Based on the available long-term stability data a retest period of (b) (4) for the drug substance, with a shelf-life storage condition of (b) (4) is granted in DMF (b) (4) (See the **Drug Substance** review)

Drug Product: Adequate

Zoryve (roflumilast) topical foam, 0.3% is indicated for the treatment of seborrheic dermatitis. It is a white to off-white non-sterile foam supplied in a 60-gram pressurized aluminum can. Each gram of Zoryve topical foam contains 3 mg of roflumilast in a foam base containing ceteareth-10 phosphate, cetearyl phosphate, cetostearyl alcohol, diethylene glycol monoethyl ether, hexylene glycol, isopropyl palmitate, methylparaben, propylparaben, purified water, sodium hydroxide, and white petrolatum. Hydrochloric acid may have been added to adjust pH. Zoryve topical foam is dispensed from an aluminum can pressurized with propellant (butane, isobutane, and propane). (b) (4)

The identity, strength, purity and quality of the drug product is controlled by its specification. The drug product specification includes the following tests: description by visual inspection, identity by HPLC and UV spectra, strength by HPLC, purity via assessment of the degradation products by HPLC and microbial enumeration, specified organism and B. Cepacian complex (BCC) per USP <61> , USP <62> and USP <60>; quality by dispersed content uniformity by HPLC, pH per USP <791>, methyl paraben and propylparaben assays by HPLC and minimum fill test per USP <755>. In addition, pump comparability and suitability tests per USP <603> and <604> are also included in the drug product specification. The in-house developed, non-compendial analytical methods were validated per ICH Q2(R1). The specification for Zoryve topical foam was reviewed by the drug product reviewer and deemed adequate.

Based on the satisfactory results of the long-term and accelerated stability data of 3 registration batches of Zoryve (roflumilast) topical foam, 0.3% 24 months of shelf-life is granted when stored upright in the proposed container closure system at 20°C to 25°C (68°F to 77°F); excursions are permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. (b) (4)

This NDA is recommended for "**Approval**" from the drug product quality perspective. (See the **Drug Product review**).

Labeling: Adequate

The PI, container/carton labels and medication guide revisions have been conveyed to the review team and will be conveyed to the applicant. This NDA is recommended for "**Approval**" from the labeling perspective. (See the **Labeling review**).

Manufacturing: Adequate

(b) (4)

(b) (4). The drug product manufacturing process and master batch record were reviewed and deemed acceptable.

The OPMA reviewer has concluded that the applicant has submitted adequate CMC information regarding Zoryve topical foam manufacturing

process and recommended this NDA for "**Approval**". (See the **Manufacturing Integrated Assessment**)

Biopharmaceutics: Adequate

The biopharmaceutics information was reviewed by the biopharmaceutics reviewer and deemed adequate. This NDA is recommended "Approval" from the biopharmaceutics perspective. The applicant has agreed to provide the (b) (4) method development report, validation report and data as they become available. (See the **Biopharmaceutics** review)

Microbiology: Adequate

Zoryve topical foam is a non-sterile multi-dose product. The drug product formulation contains (b) (4).
The antimicrobial effectiveness and preservatives, manufacturing process, microbial specification at release and stability; post-approval stability protocol, stability data and labeling were reviewed by the microbiology reviewer and deemed adequate. (See the **Microbiology** review).

Environmental Assessment: Adequate

Arcutis claimed for categorical exclusion according to 21 CFR 25.15 (a) from the requirements of the preparation of an environmental analysis per 21 CFR 25.31(b) because the estimated concentration of the substance at the point of entry into the aquatic environment will be below 1 part per billion and to the best of their knowledge no extraordinary circumstances exist. Based on the low use level and statement of no extraordinary circumstances, the claim of categorical exclusion is accepted. (See the **Drug Product** Review).

Comparability Study: N/A

Post-marketing Commitments (PMC): None

Lifecycle Management Considerations: None

C. Risk Assessment

CQAS	Initial Risk Ranking	Comments	Updated Risk Ranking after Assessment Cycle # 1	Comments
Assay	Low	In the drug product the assay of the drug substance, Roflumilast, is determined by the in-house reverse phase HPLC/UV method. This analytical method was validated per ICH Q2(R1) Guidelines.	Low – None	The long-term and accelerated stability studies of the registration and supportive batches demonstrated that there is no significant change in the assay and overall quality of the DP during the time tested.
(b) (4)	Low	The amounts of (b) (4) (b) (4) are controlled in the drug product specification.	Low to None	The amounts of (b) (4) remain within the acceptance limits at release and stability.
Pump Suitability and Integrity	Low	The pump interaction with the drug product, pressure, leakage, delivery rate and delivered amount are controlled in the drug product specification.	Low to None	Pump quality related attributes remain within the proposed specification during release and stability.

D. List of Deficiencies: None

Application Technical Lead Name and Date:

Hitesh Shroff, Ph.D.
Application Technical Lead, Branch IV
Division of New Drug Products II
November 5, 2023

56 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

CHAPTER IV: LABELING

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information: Submitted on February 16, 2023 SDN 0001

(b) (4)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights		
Proprietary and established name(s)	Inadequate	**Revise as follows:** Zoryve®(roflumilast) topical foam
Route(s) of administration	Inadequate	Delete (b) (4)
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system	Inadequate	**Revise as follows:** Topical foam: 0.3%: 3 mg of roflumilast per gram in 60-gram pressurized cans
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored".	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple- dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).	N/A	

[1] Established name = [Drug] [Route of Administration] [Dosage Form]

This section is **inadequate**.

The *drug product title in Highlights* should be revised as follows:

Zoryve® (roflumilast) topical foam

The *Dosage Forms and Strengths Heading in Highlights* should be revised as follows:

Topical foam: 0.3%: 3 mg of roflumilast per gram in 60-gram pressurized cans

1.1 FULL PRESCRIBING INFORMATION

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

(b) (4)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Inadequate	**Revise as follows:** Topical foam
Strength(s) in metric system	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (Tablets: 10 mg of drug-x hydrochloride).	N/A	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable	Inadequate	**Revise as follows:** Topical foam, 0.3%: 3 mg of roflumilast per gram of white to off-white foam in 60-gram pressurized cans
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	N/A	

This section is **inadequate**.

The *Sec. 3 Dosage Forms and Strengths* should be revised as follows:

Topical foam, 0.3%: 3 mg of roflumilast per gram of white to off-white foam in 60-gram pressurized cans

1 Page(s) of Draft Labeling has been Withheld in Full as b4 (CCI/TS) immediately following this page

QUALITY ASSESSMENT

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DESCRIPTION section		
Proprietary and established name(s)	Inadequate	Revise as shown above in red font.
Dosage form(s) and route(s) of administration	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)"	N/A	
List names of all inactive ingredients. Use USP/NF names in alphabetical order. Avoid brand names.	Adequate	
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Sterility statement (if applicable)	N/A	
Pharmacological/Therapeutic class	Adequate	
Chemical name, structural formula, molecular weight	Adequate	
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Adequate	

Section 11 (DESCRIPTION) Continued

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
For oral prescription drug products, include gluten statement (if applicable)	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity")	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

This section is **inadequate**.

The *Sec. 11 Description* should be revised as shown above in red font.

(b) (4)

[redacted]

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	Inadequate	Revise as shown above in red font.
Strength(s) in metric system	Adequate	
Available units (e.g., bottles of 100 tablets)	Adequate	

Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s)	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple- dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[X]" with x numerical citation to "OSHA Hazardous Drugs."	Adequate	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Adequate	
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*	N/A	

This section is **inadequate**.

The *Sec. 16.1 How Supplied* should be revised as shown above in red font.

(b) (4)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer	Inadequate	**Add the following marketing information:** **Marketed by:** Arcutis Biotherapeutics, Inc. Westlake Village, CA 91361 For more information, cal (b) (4) or visit http://www.zoryve.com. This information is only provided in the patient information label.

This section is **inadequate**.

Add the following marketing information:
Marketed by: Arcutis Biotherapeutics, Inc.
Westlake Village, CA 91361
For more information, call (b) (4) or visit http://www.zoryve.com.

3 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

QUALITY ASSESSMENT

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Drug Product Title, Proprietary and established name(s)	Inadequate	**Revise the drug product title as shown below:** Zoryve®(roflumilast) topical foam, 0.3%
Strength(s) in metric system	Adequate	
Route(s) of administration	Adequate	
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP.	N/A	
Net contents (e.g., tablet count, volume of liquid)	Adequate	
"Rx only" displayed on the principal display	Adequate	
NDC	Adequate	
Lot number and expiration date	Adequate	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new beyond-use-date (BUD).	Adequate	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement.	N/A	
For parenteral injectable dosage forms, include the name and quantities of all active and inactive ingredients in alphabetical order. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Linear Bar code	Adequate	
Name of manufacturer/distributor /packer	Adequate	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	Adequate	
No text on Ferrule and Cap Overseal, unless a cautionary statement is required.	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	

When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.	N/A	
And others if space is available.	N/A	

This section is **inadequate**.

Revise the Proprietary and established name as shown below:

Zoryve®(roflumilast) topical foam, 0.3%

QUALITY ASSESSMENT

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information):

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Proprietary and Established name[1]	Inadequate	**Revise as shown below:** Zoryve®(roflumilast) topical foam
Special preparation instructions (if applicable)	Adequate	
Storage and handling information (if applicable)	Adequate	
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differs from the dosage form.	N/A	
Active ingredient(s) (if applicable)	Adequate	
Alphabetical listing of inactive ingredients (if applicable)	Adequate	
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer	Adequate	

Assessment of PI, Carton and Container Labeling, Medication Guide: *ADEQUATE*
All PI, container/carton labels revisions and medication guide, shown in red, have been conveyed to the review team and will be conveyed to the applicant.

This NDA is recommended for "**Approval**" from the labeling perspective.

[1] Established name = [Drug] [Route of Administration] [Dosage Form]

ITEMS FOR ADDITIONAL ASSESSMENT: ***None***

Overall Assessment and Recommendation:

All PI, container/carton labels revisions and medication guide, shown in red, have been conveyed to the review team and will be conveyed to the applicant.

This NDA is recommended for "**Approval**" from the labeling perspective.

Assessor Name and Date:
Hitesh Shroff
OPQ, ONDP, DNDP II, Branch 4
10/30/2023

Secondary Assessor Name and Date (and Secondary Summary, as needed):

Nina Ni, Ph.D.
Branch Chief
OPQ, ONDP, DNDP II, Branch 4

22 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	217242
Assessment Cycle Number	01
Drug Product Name/ Strength	Roflumilast, 0.3%
Route of Administration	Topical foam
Applicant Name	Arcutis Biotherapeutics, Inc.
Therapeutic Classification/ OND Division	OII/DDD
Manufacturing Site	(b) (4)
Method of Sterilization	Non-sterile

Assessment Recommendation: **Adequate**

Assessment Summary:
The drug product is a non-sterile aqueous topical foam. It is filled into multi-dose cans.

List Submissions being assessed (table):

Document(s) Assessed	Date Received
Original (0001)	02/16/2023
IR Response (0007)	08/11/2023

Highlight Key Issues from Last Cycle and Their Resolution: In pre-submission meeting packages for associated IND 142047, DMA recommended providing AET data and including microbial limits testing on stability.

Remarks: This is an eCTD submission.

Concise Description of Outstanding Issues
(List bullet points with key information and update as needed): N/A

Supporting Documents: N/A

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

- **Description of drug product –** 0.3% Roflumilast foam is an aqueous, non-sterile, white to off-white topical foam indicated for the treatment of seborrheic dermatitis.

- **Drug product composition –**

Ingredient	Content % w/w	Function
Roflumilast, In-house	(b) (4)	API
(b) (4), In-house		(b) (4)
Diethylene Glycol Monoethyl Ether, NF		
Hexylene Glycol, NF		
Hydrochloric Acid, NF		
Isopropyl Palmitate, NF		
Methylparaben, NF		
Propylparaben, NF		
Purified water, USP		
Sodium Hydroxide, NF		
White Petrolatum, USP		
(b) (4)	-	
Propane/Isobutane (b) (4) -Butane (b) (4) In-house	-	

- **Description of container closure system –**

Component	Packaging	Description (Gland material code)	Manufacturer
Can	Primary	60 g (b) (4) aluminum alloy can with (b) (4)	(b) (4)
(b) (4)	Primary	(b) (4)	
	Secondary		

Assessment: The applicant has adequately described the drug product composition and the container closure system designed to maintain product sterility.

Adequate

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

7 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

BIOPHARMACEUTICS

Product Background:

NDA: NDA 217242-ORIG-1

Drug Product Name / Strength: Roflumilast foam 0.3%

Indication: Seborrheic Dermatitis

Route of Administration: Topical

Applicant Name: Arcutis Biotherapeutics, Inc.

Review Recommendation: The submission is **ADEQUATE** from Biopharmaceutics perspective with key findings summarized below:

(b) (4)

Formulation development and bridging

The final composition of roflumilast foam 0.3% is the same composition used in pivotal Phase 3 clinical studies. Therefore, no in vitro or in vivo formulation bridging study is needed.

Recommendation

From Biopharmaceutics perspective, NDA 217242 for Roflumilast foam 0.3% is adequate.

List of Submissions being reviewed:

Sequence 0001
Sequence 0011

2 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

---

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

HITESH N SHROFF
11/05/2023 01:59:06 PM