CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761082Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	November 3, 2021
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko (filgrastim-xxxx[a]) injection, 300 mcg/mL and 480 mcg/1.6 mL; 300 mcg/0.5 mL and 480 mcg/0.8 mL
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Kashiv BioSciences, LLC (Kashiv)
PNR ID #:	2021-1044724153
DMEPA 2 Safety Evaluator:	Celeste Karpow, PharmD, MPH
DMEPA 2 Team Leader:	Hina Mehta, PharmD
DMEPA 2 Associate Director for Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD

[a] The nonproprietary name suffix for this BLA has not yet been determined; therefore, the placeholder, filgrastim-xxxx, is used throughout this review to refer to the nonproprietary name and suffix for this product.

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Releuko, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A, respectively. Kashiv did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Kashiv previously submitted the proposed proprietary name, (b) (4) *** on October 7, 2016. However, the Division of Medication Error Prevention and Analysis (DMEPA) found the name, (b) (4) *** unacceptable due to orthographic similarities and shared product characteristics with the proprietary name, (b) (4) under IND 115333 on March 8, 2017.

Kashiv then submitted the name, Releuko, for review on July 6, 2017 under IND 115333 and on July 10, 2017 under BLA 761082. DMEPA found the name to be acceptable on September 18, 2017; however, the application received a complete response from the Agency. Kashiv resubmitted the name, Releuko, for review on December 11, 2018 under BLA 761082. DMEPA found the name to be acceptable on March 1, 2019; however, the application again received a complete response from the Agency. Kashiv resubmitted the name, Releuko, for review on July 2, 2020 under BLA 761082. DMEPA found the name to be acceptable on September 18, 2020; however, the application again received a complete response from the Agency. Kashiv submitted the name, Releuko, under BLA 761082 for review on February 2, 2021. DMEPA found the name to be acceptable on April 23, 2021; however, the application again received a complete response from the Agency.

Thus, Kashiv submitted the name, Releuko, for review on August 27, 2021. We note that the product characteristics remain the same since our previous review.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 27, 2021.

- Intended Pronunciation: reh loo' koe
- Nonproprietary Name: filgrastim-xxxx
- Indication of Use:
    - Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever
    - Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
    - Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)

- Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

- Route of Administration: subcutaneous or intravenous
- Dosage Form: injection
- Strength:
  - Vials: 300 mcg/mL and 480 mcg/1.6 mL &
  - Prefilled syringes: 300 mcg/0.5 mL and 480 mcg/0.8 mL
- Dose and Frequency:

Indication	Usual Dosage	Frequency of Administration
Myelosuppressive Chemotherapy or Induction and/or Consolidation Chemotherapy	5 mcg/kg/day	Once daily subcutaneous injection or by short (15 to 30 minutes) intravenous infusion
Bone Marrow Transplantation	10 mcg/kg/day	Once daily as an intravenous infusion lasting no longer than 24 hours
Congenital Neutropenia	6 mcg/kg/day	Subcutaneous injection twice per day
Idiopathic or Cyclic Neutropenia	5 mcg/kg/day	Subcutaneous injection daily

- How Supplied:
  - 300 mcg/mL and 480 mcg/1.6 mL single-dose vials supplied in cartons of 10 vials
  - 300 mcg/0.5 mL and 480 mcg/0.8 mL prefilled syringes supplied in cartons of 10 prefilled syringes
- Storage: Store Releuko at 2°C to 8°C (36°F to 46°F) in the pack to protect from light. Do not leave Releuko in direct sunlight. Do not freeze Releuko. Avoid shaking. Transport via a pneumatic tube has not been studied.
- Reference Listed Drug/Reference Product: Neupogen, BLA 103353

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Releuko.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Releuko would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) and the Division of Non-Malignant Hematology (DNH) concurred with the findings of OPDP's assessment for Releuko.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Releuko.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[b].

2.2.2 Components of the Proposed Proprietary Name

Kashiv indicated in their submission that the proposed proprietary name, Releuko, is derived from Leukocytes. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On September 13, 2021, the Division of Non-Malignant Hematology (DNH) did not forward any comments or concerns relating to Releuko at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

One hundred eleven practitioners participated in DMEPA's prescription studies for Releuko.

In the computerized provider order entry (CPOE) study, one participant entered an incorrect sequence of letters, 'ill' instead of 'rel', when searching for the study name, which generated a pick list that did not contain the proposed study name Releuko. After 15 seconds passed, the participant then incorrectly selected the name 'Illicium Anisatum Whole Extract', suggesting that the participant selected a random name in order to proceed with the simulation study. Thus, in this case, the study response is unlikely to be representative of a plausible CPOE based risk. We evaluate this name in Appendix F.

The remaining responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[c] identified 59 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified 5 names not previously analyzed. These names are included in Table 1 below.

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[b] USAN stem search conducted on September 13, 2021.

[c] POCA search conducted on September 13, 2021 in version 4.4.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and FDA Name Simulation Study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity

Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	4
Low similarity name pair: combined match percentage score ≤54%	2

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 6 names contained in Table 1 determined none of the names will pose a risk for confusion with Releuko as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA 2 communicated our findings to the Division of Non-Malignant Hematology (DNH). At that time we also requested additional information or concerns that could inform our review. On November 2, 2021, the Division of Non-Malignant Hematology (DNH) stated no additional concerns with the proposed proprietary name, Releuko.

3 CONCLUSION

The proposed proprietary name, Releuko, is acceptable.

If you have any questions or need clarifications, please contact Linda Wu, OSE project manager, at 240-402-5120.

3.1 COMMENTS TO KASHIV BIOSCIENCES, LLC

We have completed our review of the proposed proprietary name, Releuko, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your submission, received on August 27, 2021, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [d]

[d] National Coordinating Council for Medication Error Reporting and Prevention. https://www.nccmerp.org/about-medication-errors Last accessed 10/05/2020.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.

- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[e]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign

[e] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

   Four separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions, verbal pronunciation of the drug name or during computerized provider order entry. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

   In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

   When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

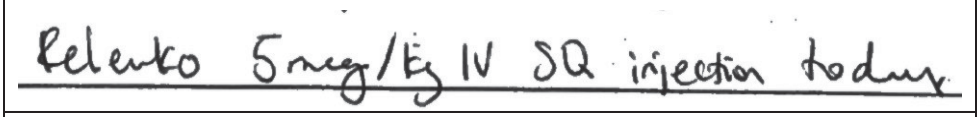
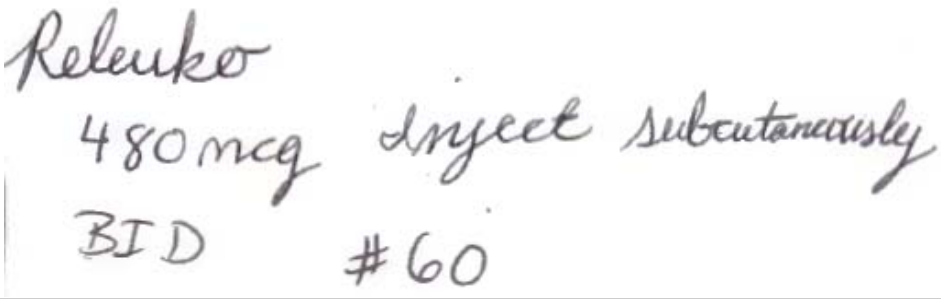
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Releuko Study (Conducted on September 10, 2021)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  Outpatient Prescription:  	Releuko Inject 480 mcg subcutaneously twice daily. Dispense #60
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Releuko	

FDA Prescription Simulation Responses (Aggregate Report)

261 People Received Study

111 People Responded

Study Name: Releuko

Total	**29**	**34**	**24**	**24**	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
ILLICIUM ANISATUM WHOLE EXTRACT	0	1	0	0	1
MELUCO	0	0	1	0	1
REKEVKO	0	0	0	1	1
RELEKO	0	0	0	1	1
RELENKO	1	0	0	19	20
RELEUKO	28	33	2	2	65
RELEVKO	0	0	0	1	1
RELOUCO	0	0	1	0	1
RELUCCO	0	0	2	0	2
RELUCO	0	0	14	0	14
RELUKO	0	0	3	0	3
RYLUCO	0	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name:** Releuko **Established name:** filgrastim-xxxx **Dosage form:** injection **Strength(s):** 300 mcg/mL and 480 mcg/1.6 mL; 300 mcg/0.5 mL and 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg once daily, 6 mcg/kg twice daily, or 10 mcg/kg once daily.	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
	N/A		

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
	N/A	

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Releuko **Established name:** filgrastim-xxxx **Dosage form:** injection **Strength(s):** 300 mcg/mL and 480 mcg/1.6 mL; 300 mcg/0.5 mL and 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg once daily, 6 mcg/kg twice daily, or 10 mcg/kg once daily.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	(b) (4) ***	57	This name pair has sufficient orthographic and phonetic differences.
2.	Reltone	56	This name pair has sufficient orthographic and phonetic differences.
3.	(b) (4) ***	50	This name pair has sufficient orthographic and phonetic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%)

No.	Name	POCA Score (%)
1.	Illicium Anisatum Whole Extract	15

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described**.**

No.	Name	POCA Score (%)	Failure preventions
1.	(b) (4) ***	58	(b) (4)
2.	Revolt	55	Veterinary product.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[f].

No.	Name	POCA Score (%)
	N/A	

[f] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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/

CELESTE A KARPOW
11/03/2021 11:19:28 AM

HINA S MEHTA
11/03/2021 12:37:01 PM

CHI-MING TU
11/03/2021 04:00:49 PM

NONPROPRIETARY NAME SUFFIX REVIEW

Division of Mitigation Assessment and Medication Error Surveillance (DMAMES)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	October 7, 2021
Responsible OND Division:	Division of Non-Malignant Hematology (DNH)
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko (filgrastim-ayow) Injection Vials: 300 mcg/mL, 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL, 480 mcg/0.8 mL
Product Type:	Single Ingredient Product and Biologic-Device Combination Product
Applicant/Sponsor Name:	Kashiv BioSciences LLC (Kashiv)
FDA Received Date:	August 27, 2021
OSE Nexus NPNS ID #:	2021-53
DMAMES Primary Reviewer:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 2 Division Director:	Danielle Harris, PharmD

1 PURPOSE OF REVIEW

This review is to reassess the proposed four-letter suffix, -ayow, for BLA 761082, which was found conditionally acceptable on February 29, 2018[a], March 7, 2019[b], August 12, 2020[c], and May 6, 2021[d] for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761082.

1.1 Regulatory History

On July 10, 2017, Adello Biologics LLC (previous Applicant) submitted a list of suffixes, in their order of preference, to be used in the nonproprietary name of their product. Adello also provided for our consideration findings from their evaluation method and process used to select each proposed suffix[e]. We note that Adello submitted a total of three proposed suffixes.

- FDA found Adello's four-letter suffix, -ayow, conditionally acceptable for BLA 761082 on January 29, 2018[a].
- BLA 761082 received a Complete Response (CR) letter on May 10, 2018.
- Kashiv submitted a Class 2 Resubmission on December 11, 2018.
- FDA found the four-letter suffix -ayow conditionally acceptable upon re-evaluation on March 7, 2019[b].
- BLA 761082 received a Complete Response (CR) letter on June 11, 2019.
- Kashiv submitted a Class 2 Resubmission on June 24, 2020.
- FDA found the four-letter suffix -ayow conditionally acceptable upon re-evaluation on August 12,2020[c].
- BLA 761082 received a Complete Response (CR) letter on December 22, 2020.
- Kashiv submitted a Class 2 Resubmission on February 2, 2021.

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[a] Garrison, N. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 29 JAN 2018. RCM No.: 2017-1376.

[b] Mena-Grillasca, C. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 07 MAR 2019. RCM No.: 2017-1376-1

[c] Mena-Grillasca, C. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 12 AUG 2020. RCM No.: 2017-1376-2.

[d] Mena-Grillasca, C. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 06 May 2021, RCM No. 2017-1376-3.

[e] Request for Proprietary Name Review – Suffix Evaluation. 2017 Jul 10. Available at ¥¥cdsesub1¥evsprod¥bla761082¥0001¥m1¥us¥request-for-proprietary-name-suffix.pdf

- FDA found the four-letter suffix -ayow conditionally acceptable upon re-evaluation on May 6, 2021[d].
- BLA 761082 received a Complete Response (CR) letter on August 2, 2021.
- Kashiv submitted a Class 2 Resubmission on August 27, 2021.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

filgrastim-ayow

We reassessed the previously proposed four-letter suffix, -ayow, using the principles described in the applicable guidance.[f]

We determined that the proposed suffix -ayow, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMAMES' ANALYSIS

These findings were shared with OPDP. On October 5, 2021, OPDP did not identify any concerns that would render this suffix unacceptable. DMAMES also communicated our findings to the Division of Non-Malignant Hematology (DNH) on October 7, 2021.

4 CONCLUSION

We find the suffix -ayow acceptable and recommend the nonproprietary name filgrastim-ayow is used throughout the labels and labeling.

[f] See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

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CARLOS M MENA-GRILLASCA
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DANIELLE M HARRIS
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SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	May 6, 2021
Responsible OND Division:	Division of Non-Malignant Hematology (DNH)
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko (filgrastim-ayow) Injection Vials: 300 mcg/mL, 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL, 480 mcg/0.8 mL
Product Type:	Single Ingredient Product and Biologic-Device Combination Product
Applicant/Sponsor Name:	Kashiv BioSciences LLC (Kashiv)
FDA Received Date:	February 2, 2021
OSE RCM #:	2017-1376-3
DMEPA Primary Reviewer:	Carlos M Mena-Grillasca, BS Pharm
DMEPA Deputy Director:	Danielle Harris, PharmD

1 PURPOSE OF REVIEW

This review is to reassess the proposed four-letter suffix, -ayow, for BLA 761082, which was found conditionally acceptable on February 29, 2018[a], March 7, 2019[b], and August 12, 2020[c] for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761082.

1.1 Regulatory History

On July 10, 2017, Adello Biologics LLC (previous Applicant) submitted a list of suffixes, in their order of preference, to be used in the nonproprietary name of their product. Adello also provided for our consideration findings from their evaluation method and process used to select each proposed suffix[d]. We note that Adello submitted a total of three proposed suffixes.

- FDA found Adello's four-letter suffix, -ayow, conditionally acceptable for BLA 761082 on January 29, 2018[a].
- BLA 761082 received a Complete Response (CR) letter on May 10, 2018.
- Kashiv submitted a Class 2 Resubmission on December 11, 2018.
- FDA found the four-letter suffix -ayow conditionally acceptable upon re-evaluation on March 7, 2019[b].
- BLA 761082 received a Complete Response (CR) letter on June 11, 2019.
- Kashiv submitted a Class 2 Resubmission on June 24, 2020.
- FDA found the four-letter suffix -ayow conditionally acceptable upon re-evaluation on August 12,2020[c].
- BLA 761082 received a Complete Response (CR) letter on December 22, 2020.
- Kashiv submitted a Class 2 Resubmission on February 2, 2021.

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[a] Garrison, N. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 29 JAN 2018. RCM No.: 2017-1376.

[b] Mena-Grillasca, C. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 07 MAR 2019. RCM No.: 2017-1376-1

[c] Mena-Grillasca, C. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 12 AUG 2020. RCM No.: 2017-1376-2.

[d] Request for Proprietary Name Review – Suffix Evaluation. 2017 Jul 10. Available at ¥¥cdsesub1¥evsprod¥bla761082¥0001¥m1¥us¥request-for-proprietary-name-suffix.pdf

2 ASSESSMENT OF THE NONPROPRIETARY NAME

filgrastim-ayow

We reassessed the previously proposed four-letter suffix, -ayow, using the principles described in the applicable guidance.[e]

We determined that the proposed suffix -ayow, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA'S ANALYSIS

These findings were shared with OPDP. On April 27, 2021, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA also communicated our findings to the Division of Non-Malignant Hematology (DNH) on May 6, 2021.

4 CONCLUSION

We find the suffix -ayow acceptable and recommend the nonproprietary name filgrastim-ayow is used throughout the labels and labeling.

[e] See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

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/s/

CARLOS M MENA-GRILLASCA
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DANIELLE M HARRIS
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PROPRIETARY NAME MEMORANDUM

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*****This document contains proprietary information that cannot be released to the public*****

Date of This Review:	April 23, 2021
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko (filgrastim-ayow) injection Vials: 300 mcg/mL and 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL and 480 mcg/0.8 mL
Product Type:	Single Ingredient Product and Drug-Device Combination Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Kashiv BioSciences (Kashiv)
PNR ID #:	2021-1044723874
DMEPA Safety Evaluator:	Stephanie DeGraw, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Releuko, which was previously found conditionally acceptable by DMEPA under BLA 761082 (see Regulatory History below). Kashiv submitted the name, Releuko, under BLA 761082 for review on February 2, 2021. We note that all product characteristics remain the same.

1.1 REGULATORY HISTORY

Kashiv previously submitted the proposed proprietary name, (b) (4) *** on October 7, 2016. However, the Division of Medication Error Prevention and Analysis (DMEPA) found the name, (b) (4) *** unacceptable due to orthographic similarities and shared product characteristics with the proprietary name, (b) (4) under IND 115333 on March 8, 2017.[a]

Kashiv then submitted the name, Releuko, for review on July 6, 2017 under IND 115333 and on July 10, 2017 under BLA 761082. DMEPA found the name to be acceptable on September 18, 2017[b]; however, the application received a complete response from the Agency. Kashiv resubmitted the name, Releuko, for review on December 11, 2018 under BLA 761082. DMEPA found the name to be acceptable on March 1, 2019[c]; however, the application again received a complete response from the Agency. Kashiv resubmitted the name, Releuko, for review on July 2, 2020 under BLA 761082. DMEPA found the name to be acceptable on September 18, 2020[d]; however, the application again received a complete response from the Agency.

Thus, Kashiv submitted the name, Releuko, under BLA 761082 for review on February 2, 2021.

2 METHODS AND DISCUSSION

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Releuko would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Non-Malignant Hematology (DNH) concurred with the findings of OPDP's assessment for Releuko.

2.2 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, we evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. Our reassessment did not change our conclusion regarding the previously identified names of concern. Additionally, we searched the United States Adopted Name (USAN) stem list to

[a] Garrison, N. Proprietary Name Review for (b) (4) (IND 115333). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 MAR 8. Panorama No. 2016-10674485.

[b] Garrison, N. Proprietary Name Review for Releuko (IND 115333 and BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 SEP 18. Panorama Nos. 2017-16225798 and 2017-16275200.

[c] DeGraw, S. Proprietary Name Review for Releuko (BLA 761082) Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 MAR 01. Panorama No. 2018-27909849.

[d] DeGraw, S. Proprietary Name Review for Releuko (BLA 761082) Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 SEP 18. Panorama No. 2020-41062979.

determine if the proposed proprietary name contains any USAN stems as of the last USAN updates. The April 2, 2021 search of USAN stems did not find any USAN stems in the proposed proprietary name, Releuko.

2.3 COMMUNICATION OF DMEPA'S ANALYSIS AT MIDPOINT OF REVIEW

We communicated our findings to the Division of Non-Malignant Hematology (DNH). At that time, we also requested additional information or concerns that could inform our review. On April 23, 2021, the Division of Non-Malignant Hematology (DNH) stated no additional concerns with the proposed proprietary name, Releuko.

3 CONCLUSION

Our re-assessment did not identify any names that represent a potential source of drug name confusion. Therefore, we maintain that the proposed proprietary name, Releuko, is acceptable.

If you have any questions or need clarifications, please contact Linda Wu, OSE project manager, at 240-402-5120.

3.1 COMMENTS TO KASHIV BIOSCIENCES

We have completed our review of the proposed proprietary name, Releuko, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your submission, received on February 2, 2021, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCE

1. **USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)**

   USAN Stems List contains all the recognized USAN stems.

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/s/

STEPHANIE L DEGRAW
04/29/2021 04:46:33 PM

HINA S MEHTA
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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	September 18, 2020
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko (filgrastim-ayow)[a] injection Vials: 300 mcg/mL and 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL and 480 mcg/0.8 mL
Product Type:	Single Ingredient and Drug-Device Combination Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Kashiv BioSciences (Kashiv)
Panorama #:	2020-41062979
DMEPA Safety Evaluator:	Stephanie DeGraw, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD

[a] BLA 761082 has been developed as a proposed biosimilar to US-licensed Neupogen (filgrastim). The nonproprietary name (b) (4) has been found conditionally acceptable for this BLA on August 13, 2020.

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Releuko, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Kashiv did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, (b) (4) *** on October 7, 2016. However, the Division of Medication Error Prevention and Analysis (DMEPA) found the name, (b) (4) *** unacceptable due to orthographic similarities and shared product characteristics with the proprietary name, (b) (4) under IND 115333 on March 8, 2017.[b]

The Applicant then submitted the name, Releuko, for review on July 6, 2017 under IND 115333 and on July 10, 2017 under BLA 761082. DMEPA found the name to be acceptable on September 18, 2017[c]; however, the application received a complete response from the Agency. The Applicant resubmitted the name, Releuko, for review on December 11, 2018 under BLA 761082. DMEPA found the name to be acceptable on March 1, 2019[d]; however, the application again received a complete response from the Agency.

Kashiv resubmitted the name, Releuko, for review on July 2, 2020.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on July 2, 2020.

- Intended Pronunciation: reh loo' koe
- Nonproprietary Name: filgrastim-ayow
- Indication of Use:
    - Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever
    - Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
    - Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)
    - Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

[b] Garrison, N. Proprietary Name Review for (b) (4) (IND 115333). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 MAR 8. Panorama No. 2016-10674485.
[c] Garrison, N. Proprietary Name Review for Releuko (IND 115333 and BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 SEP 18. Panorama Nos. 2017-16225798 and 2017-16275200.
[d] DeGraw, S. Proprietary Name Review for Releuko (BLA 761082) Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 MAR 01. Panorama No. 2018-27909849.

- Route of Administration: Subcutaneous and Intravenous
- Dosage Form: injection
- Strength:
    - 300 mcg/mL and 480 mcg/1.6 mL single-dose vials
    - 300 mcg/0.5mL and 480 mcg/0.8mL prefilled syringes
- Dose and Frequency:

Indication	Usual Dosage	Frequency of Administration
Myelosuppressive Chemotherapy or Induction and/or Consolidation Chemotherapy	5 mcg/kg/day	Once daily subcutaneous injection or by short (15 to 30 minutes) intravenous infusion
Bone Marrow Transplantation	10 mcg/kg/day	Once daily as an intravenous infusion lasting no longer than 24 hours
Congenital Neutropenia	6 mcg/kg/day	Subcutaneous injection twice per day
Idiopathic or Cyclic Neutropenia	5 mcg/kg/day	Subcutaneous injection daily

- How Supplied:
    - 300 mcg/mL and 480 mcg/1.6 mL single-dose vials supplied in cartons of 10 vials
    - 300 mcg/0.5 mL and 480 mcg/0.8 mL prefilled syringes supplied in cartons of 10 prefilled syringes
- Storage: Store Releuko at 2°C to 8°C (36°F to 46°F) in the pack to protect from light. Do not leave Releuko in direct sunlight. Do not freeze Releuko. Avoid shaking. Transport via a pneumatic tube has not been studied.
- Reference Listed Drug/Reference Product: Neupogen, BLA 103353

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Releuko.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Releuko would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Nonmalignant Hematology (DNH) concurred with the findings of OPDP's assessment for Releuko.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Releuko.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[e].

2.2.2 Components of the Proposed Proprietary Name

Kashiv indicated in their submission that the proposed name, Releuko, is derived from leukocytes. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, July 29, 2020, e-mail, the Division of Nonmalignant Hematology (DNH) did not forward any comments or concerns relating to Releuko at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Eighty-five (85) practitioners participated in DMEPA's prescription studies for Releuko. The responses did not overlap with any currently marketed products. However, 7 participants in the outpatient study misinterpreted Releuko for "Relenko," which is a close variation to the marketed product Relenza (NDA 021036). Despite the close hit in the FDA name simulation study, we find that the name pair, Releuko and Relenza, have minimal potential of confusion for the following reasons:

Orthographically, the suffixes ('za' *versus* 'ko') differ due to the upstroke letter k in the sixth position of Releuko. Phonetically, the second and third syllables of this name pair have notable differences when spoken ('len-za' *versus* 'loo-koe'). Releuko and Relenza differ in terms of strength (300 mcg/mL and 480 mcg/1.6 mL vials; 300 mcg/0.5 mL and 480 mcg/0.8 mL prefilled syringes *versus* 5 mg), dosage form (injection *versus* powder), and route of administration (subcutaneous and intravenous *versus* inhalation). The route of administration would need to be specified for Releuko and does not overlap between the products. Furthermore, the dose of Releuko is weight-based whereas the dose of Relenza is two inhalations (or 10 mg). Therefore, in the absence of overlapping product characteristics, we do not think that the name pair is vulnerable to name confusion. This name pair is evaluated in Appendix E.

See Appendix B for the full results from the prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[f] identified 54 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name reviews. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics

[e] USAN stem search conducted on August 11, 2020.
[f] POCA search conducted on August 11, 2020 in version 4.4.

have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified 6 names not previously analyzed. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and FDA Prescription Simulation Study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity

Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	6
Low similarity name pair: combined match percentage score ≤54%	0

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 7 names contained in Table 1 determined none of the names will pose a risk for confusion with Releuko as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Nonmalignant Hematology (DNH) via e-mail on August 31, 2020. At that time, we also requested additional information or concerns that could inform our review. DNH stated no additional concerns with the proposed proprietary name, Releuko.

3 CONCLUSION

The proposed proprietary name, Releuko, is acceptable.

If you have any questions or need clarifications, please contact Linda Park, OSE project manager, at 240-402-5120.

3.1 COMMENTS TO KASHIV BIOSCIENCES

We have completed our review of the proposed proprietary name, Releuko, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your submission, received on July 2, 2020, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:
    a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [g]

[g] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[h]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

[h] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

   Four separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions, verbal pronunciation of the drug name or during computerized provider order entry. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

   In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

   When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

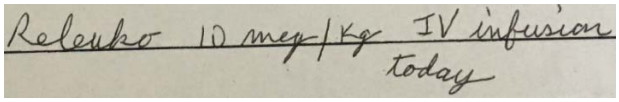
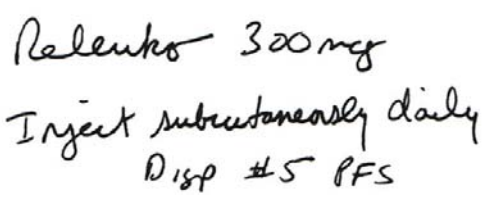
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: **Prescription Simulation Samples and Results**

Figure 1. Releuko Study (Conducted on July 24, 2020)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Releuko 300 mcg Inject subcutaneously daily Dispense 5 prefilled syringes
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Releuko	

FDA Prescription Simulation Responses (Aggregate Report)

207 People Received Study
85 People Responded

Study Name: Releuko

Total	17	23	17	28	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
RALUCO	0	0	1	0	1
RELENKO	7	0	0	0	7
RELEUKO	9	23	0	26	58
RELEUKO 10/MG KG	0	0	0	1	1
RELEUKO IV INFUSION	0	0	0	1	1
RELEUKS	1	0	0	0	1
RELICO	0	0	1	0	1
RELUCCO	0	0	1	0	1
RELUCKO	0	0	2	0	2
RELUCO	0	0	5	0	5
RELUFO	0	0	1	0	1
RELUKO	0	0	4	0	4
REYLUCCO	0	0	1	0	1
RILUCO	0	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name:** Releuko **Established name:** filgrastim-ayow **Dosage form:** injection **Strength(s):** • **Vial:** 300 mcg/mL and 480 mcg/mL • **PFS:** 300 mcg/0.5 mL and 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg once daily, 6 mcg/kg twice daily, or 10 mcg/kg once daily.	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	(b) (4) ***	74	(b) (4)

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
2.	Relief	58

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Releuko **Established name:** filgrastim-ayow **Dosage form:** injection **Strength(s):** • **Vial:** 300 mcg/mL and 480 mcg/mL • **PFS:** 300 mcg/0.5 mL and 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg once daily, 6 mcg/kg twice daily, or 10 mcg/kg once daily.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
3.	Relenza	56	Orthographically, this name pair has different suffixes ('za' vs. 'ko'). Additionally, Releuko contains an upstroke letter in the 6th position, which is absent from Relenza. Phonetically, the 2nd syllable ('len' vs. 'loo') and 3rd syllable ('za' vs. 'ko') of this name pair have notable differences when spoken. Although the both products may be administered once or twice daily, the products differ in terms of strength (300 mcg/mL or 480 mcg/mL or 300 mcg/0.5 mL or 480 mcg/0.8 mL vs. 5 mg), dose (5 mcg/kg, 6 mcg/kg, or 10 mcg/kg vs. two inhalations or 10 mg), dosage form (injection vs. powder), and route of administration (subcutaneous or intravenous vs. oral inhalation); thus, the product characteristic differences provide additional differentiation if included on a prescription.
4.	Rezurock***	58	This name pair has sufficient orthographic and phonetic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%) – N/A

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
5.	(b) (4) ***	59	(b) (4)
6.	(b) (4) ***	57	(b) (4)

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[i].

No.	Name	POCA Score (%)
7.	Koselugo	56

[i] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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/s/

STEPHANIE L DEGRAW
09/18/2020 09:33:25 AM

HINA S MEHTA
09/18/2020 01:25:19 PM

NONPROPRIETARY NAME SUFFIX REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	August 12, 2020
Responsible OND Division:	Division of Non-Malignant Hematology (DNH)
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko (filgrastim-ayow) Injection Vials: 300 mcg/mL, 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL, 480 mcg/0.8 mL
Product Type:	Single Ingredient Product and Biologic-Device Combination Product
Applicant/Sponsor Name:	Kashiv BioSciences LLC (Kashiv)
FDA Received Date:	June 24, 2020
OSE RCM #:	2017-1376-2
DMEPA Primary Reviewer:	Carlos M Mena-Grillasca, BS Pharm
DMEPA Deputy Director:	Danielle Harris, PharmD

1 PURPOSE OF MEMO

This memorandum is to reassess the proposed four-letter suffix, -ayow, for BLA 761082, which was found conditionally acceptable on February 29, 2018[a] and March 7, 2019[b], for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761082.

1.1 Regulatory History

On July 10, 2017, Adello Biologics LLC (previous Applicant) submitted a list of suffixes, in their order of preference, to be used in the nonproprietary name of their product. Adello also provided for our consideration findings from their evaluation method and process used to select each proposed suffix[c]. We note that Adello submitted a total of three proposed suffixes.

- FDA found Adello's four-letter suffix, -ayow, conditionally acceptable for BLA 761082 on January 29, 2018[a].
- BLA 761082 received a Complete Response (CR) letter on May 10, 2018.
- Kashiv submitted a Class 2 Resubmission on December 11, 2018.
- FDA found the four-letter suffix -ayow conditionally acceptable upon re-evaluation on March 7, 2019[b]
- BLA 761082 received a Complete Response (CR) letter on June 11, 2019
- Kashiv submitted a Class 2 Resubmission on June 24, 2020.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

filgrastim-ayow

We reassessed the previously proposed four-letter suffix, -ayow, using the principles described in the applicable guidance.[d]

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[a] Garrison, N. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 29 JAN 2018. RCM No.: 2017-1376.

[b] Mena-Grillasca, C. Nonproprietary Name Suffix Review (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 07 MAR 2019. RCM No.: 2017-1376-1

[c] Request for Proprietary Name Review – Suffix Evaluation. 2017 Jul 10. Available at ¥¥cdsesub1¥evsprod¥bla761082¥0001¥m1¥us¥request-for-proprietary-name-suffix.pdf

[d] See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

We determined that the proposed suffix -ayow, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA'S ANALYSIS

These findings were shared with OPDP. Per an email correspondence dated August 10, 2020, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA also communicated our findings to the Division of Non-Malignant Hematology (DNH) via e-mail on August 12, 2020.

4 CONCLUSION

We find the suffix -ayow acceptable and recommend the nonproprietary name filgrastim-ayow is used throughout the labels and labeling.

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/s/

CARLOS M MENA-GRILLASCA
08/12/2020 09:44:34 PM

DANIELLE M HARRIS
08/13/2020 10:48:36 AM

MEMORANDUM

NONPROPRIETARY NAME SUFFIX

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	March 7, 2019
Responsible OND Division:	Division of Hematology Products (DHP)
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko (filgrastim-ayow) Injection Vials: 300 mcg/mL, 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL, 480 mcg/0.8 mL
Product Type:	Single Ingredient Product and Biologic-Device Combination Product
Applicant/Sponsor Name:	Kashiv BioSciences LLC (Kashiv)
FDA Received Date:	December 11, 2018
OSE RCM #:	2017-1376-1
DMEPA Primary Reviewer:	Carlos M Mena-Grillasca, BS Pharm
DMEPA Deputy Director:	Danielle Harris, PharmD, BCPS

1 PURPOSE OF MEMO

This memorandum is to reassess the proposed four-letter suffix, -ayow, for BLA 761082, which was found conditionally acceptable on January 29, 2018[a], for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761082.

1.1 Regulatory History

On July 10, 2017, Adello Biologics LLC (previous Applicant) submitted a list of suffixes, in their order of preference, to be used in the nonproprietary name of their product. Adello also provided for our consideration findings from their evaluation method and process used to select each proposed suffix[b]. We note that Adello submitted a total of three proposed suffixes.

FDA found Adello's first proposed four-letter suffix, -ayow, conditionally acceptable for BLA 761082 on January 29, 2018[a]. However, BLA 761082 received a Complete Response (CR) letter on May 10, 2018. Thus, Adello submitted a Class 2 Resubmission on December 11, 2018. Subsequent to the Class 2 resubmission, all rights to application BLA 761082 and related responsibilities were transferred from Adello Biologics LLC to Kashiv BioSciences LLC[c].

2 ASSESSMENT OF THE NONPROPRIETARY NAME

filgrastim-ayow

We reassessed the previously proposed four-letter suffix, -ayow, using the principles described in the applicable guidance.[d]

We determined that the proposed suffix -ayow, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA'S ANALYSIS

These findings were shared with OPDP. Per email correspondence dated March 6, 2019, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA also communicated our findings to the Division of Hematology Products (DHP) via e-mail on March 7, 2019.

4 CONCLUSION

We find the suffix -ayow acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to filgrastim-ayow. DMEPA will communicate our findings to the Applicant via letter.

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[a] Garrison, N. Nonproprietary Name Suffix Memorandum for filgrastim-ayow (BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 29 JAN 2018. RCM No.: 2017-1376.

[b] Request for Proprietary Name Review – Suffix Evaluation. 2017 Jul 10. Available at \\cdsesub1\evsprod\bla761082\0001\m1\us\request-for-proprietary-name-suffix.pdf

[c] Change in Ownership – Cover Letter. 2019 Feb 19. Available at \\cdsesub1\evsprod\bla761082\0039\m1\us\12-cover-letters\cover-letter-0039.pdf

[d] See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

4.1 Recommendations for Kashiv BioSciences LLC

We find the nonproprietary name, filgrastim-ayow, conditionally acceptable for your proposed product. Should your 351(k) BLA be approved during this review cycle, filgrastim-ayow will be the proper name designated in the license. You should revise your proposed labels and labeling accordingly and submit the revised labels and labeling to your BLA for our review prior to approval. However, please be advised that if your application receives a complete response, the acceptability of your proposed suffix will be re-evaluated when you respond to the deficiencies. If we find your suffix unacceptable upon our re-evaluation, we would inform you of our finding.

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/

CARLOS M MENA-GRILLASCA
03/08/2019 10:24:56 AM

DANIELLE M HARRIS
03/08/2019 01:02:31 PM

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	March 1, 2019
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko ("filgrastim-xxxx")[a] injection Vials: 300 mcg/mL, 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL, 480 mcg/0.8 mL
Product Type:	Single Ingredient and Drug-Device Combination Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Adello Biologics, LLC (Adello)
Panorama #:	2018-27909849
DMEPA Safety Evaluator:	Stephanie DeGraw, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD

[a] BLA 761082 has been developed as a proposed biosimilar to US-licensed Neupogen (filgrastim). Since the nonproprietary name for this BLA has not yet been determined, the nonproprietary name placeholder, filgrastim-xxxx, is used throughout this review.

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Releuko, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Adello did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, (b) (4) *** on October 7, 2016. However, the Division of Medication Error Prevention and Analysis (DMEPA) found the name, (b) (4) *** unacceptable due to orthographic similarities and shared product characteristics with the proprietary name, (b) (4) under IND 115333 on March 8, 2017.[b]

The Applicant then submitted the name, Releuko, for review on July 6, 2017 under IND 115333 and on July 10, 2017 under BLA 761082. DMEPA found the name to be acceptable on September 18, 2017[c]; however, the application received a complete response from the Agency.

Adello resubmitted the name, Releuko, for review on December 11, 2018.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on December 11, 2018.

- Intended Pronunciation: reh loo' koe
- Active Ingredient: "filgrastim-xxxx"
- Indication of Use:
  - Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever
  - Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
  - Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)
  - Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia
- Route of Administration: Subcutaneous and Intravenous
- Dosage Form: injection

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[b] Garrison, N. Proprietary Name Review for (b) (4) (IND 115333). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 MAR 8. Panorama No. 2016-10674485.

[c] Garrison, N. Proprietary Name Review for Releuko (IND 115333 and BLA 761082). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 SEP 18. Panorama Nos. 2017-16225798 and 2017-16275200

- Strength: 300 mcg/mL single dose vial (supplied as 300 mcg/mL and 480 mcg/1.6 mL) and 600 mcg/mL prefilled syringe (supplied as 300 mcg/0.5mL and 480 mcg/0.8mL)
- Dose and Frequency:

Indication	Usual Dosage	Frequency of Administration	Dosing Interval
Myelosuppressive Chemotherapy or Induction and/or Consolidation Chemotherapy	5 mcg/kg/day	Once daily subcutaneous injection or by continuous intravenous infusion	Every 24 hours
Bone Marrow Transplantation	10 mcg/kg/day	Once daily as an intravenous infusion lasting no longer than 24 hours	Every 24 hours
Autologous Peripheral Progenitor Cell Collection	10 mcg/kg/day	Once daily as a subcutaneous injection administered for at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis	Every 24 hours
Congenital Neutropenia	6 mcg/kg/day	Subcutaneous injection twice per day	Every 12 hours
Idiopathic or Cyclic Neutropenia	5 mcg/kg/day	Subcutaneous injection daily	Every 24 hours
Myelosuppressive doses of radiation	10 mcg/kg/day	Subcutaneous injection daily	Every 24 hours

- How Supplied:
    - 300 mcg/mL and 480 mcg/1.6 mL single-dose vials in a carton of 10 vials with a vial tray
    - 300 mcg/0.5 mL and 480 mcg/0.8 mL prefilled syringes in blister packs
- Storage: Store Releuko at 2°C to 8°C (36°F to 46°F) in the pack to protect from light. Do not leave Releuko in direct sunlight. Do Not freeze Releuko. Avoid shaking. Transport via a pneumatic tube has not been studied.
- Reference Listed Drug/Reference Product: Neupogen, BLA 103353

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Releuko.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Releuko would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Hematology Products (DHP) concurred with the findings of OPDP's assessment for Releuko.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Releuko.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[d].

2.2.2 Components of the Proposed Proprietary Name

Adello indicated in their submission that the proposed name, Releuko, is derived from leukocytes. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, December 28, 2018 e-mail, the Division of Hematology Products (DHP) did not forward any comments or concerns relating to Releuko at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety-seven (97) practitioners participated in DMEPA's prescription studies for Releuko. The responses did not overlap with any currently marketed products. However, 22 participants in the outpatient study and 2 participants in the inpatient study misinterpreted Releuko for "Relenko," which is a close variation to the marketed product Relenza (NDA 021036). Despite the close hit in the FDA name simulation study, we find that the name pair, Releuko and Relenza, have minimal potential of confusion for the following reasons:

Orthographically, the suffixes ('za' vs. 'ko') differ due to the upstroke letter k in the sixth position of Releuko. Phonetically, the second and third syllables of this name pair have notable differences when spoken ('len-za' vs. 'loo-koe'). Releuko and Relenza differ in terms of strength (300 mcg/mL and 480 mcg/1.6 mL vials; 300 mcg/0.5 mL and 480 mcg/0.8 mL prefilled syringes *versus* 5 mg) and route of administration (subcutaneous and intravenous *versus* inhalation). The route of administration would need to be specified for Releuko and does not overlap between the products. Furthermore, the dose of Releuko is weight-based whereas the dose of Relenza is two inhalations

[d] USAN stem search conducted on January 23, 2019.

(or 10 mg). Therefore, in the absence of overlapping product characteristics, we do not think that the name pair is vulnerable to name confusion (see Appendix E for evaluation of the name pair).

Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[e] identified 49 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified four names not previously analyzed. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and FDA Prescription Simulation Study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity

Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	5
Low similarity name pair: combined match percentage score ≤54%	0

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the five names contained in Table 1 determined none of the names will pose a risk for confusion with Releuko as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Hematology Products (DHP) via e-mail on February 21, 2019. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Hematology Products (DHP) on February 21, 2019, they stated no additional concerns with the proposed proprietary name, Releuko.

[e] POCA search conducted on January 23, 2019 in version 4.3.

3 CONCLUSION

The proposed proprietary name, Releuko, is acceptable.

If you have any questions or need clarifications, please contact Neil Vora, OSE project manager, at 240-402-4845.

3.1 COMMENTS TO ADELLO BIOLOGICS, LLC

We have completed our review of the proposed proprietary name, Releuko, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your submission, received on December 11, 2018, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [f]

[f] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[g]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

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[g] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

   Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

   In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned, and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

   When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

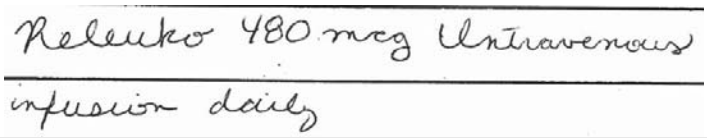
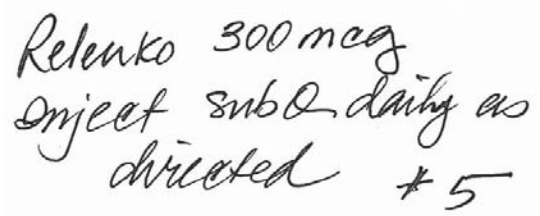
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: **Prescription Simulation Samples and Results**

Figure 1. Releuko Study (Conducted on February 1, 2019)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Releuko 300 mcg Inject subcutaneously daily as directed Dispense 5
Outpatient Prescription:  	

FDA Prescription Simulation Responses (Aggregate Report)

303 People Received Study
97 People Responded

Study Name: Releuko

Total	25	51	21	97
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
RALOCO	0	1	0	1
RALUCO	0	25	0	25
RALUKO	0	9	0	9
RALUKO 300 MG	0	1	0	1
RALUQO	0	1	0	1
RELENKO	22	0	2	24
RELEOKOH	0	1	0	1
RELEUDO	0	0	1	1
RELEUKO	2	0	15	34
RELEUKO IV	0	0	1	1
RELEVKO	0	0	1	1
RELOKO	0	1	0	1
RELUCO	0	6	0	6
RELUKO	1	2	0	3
REULEUKO	0	0	1	1

ROLUCCO	0	1	0	1
ROLUCO	0	1	0	1
ROLUKO	0	1	0	1
RYLUCO	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%) --- N/A

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Reliefor	59

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Releuko **Established name:** "filgrastim-xxxx" **Dosage form:** injection **Strength(s):** • **Vial:** 300 mcg/mL, 480 mcg/mL • **Prefilled syringe:** 300 mcg/0.5 mL, 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg/day or 10 mcg/kg/day. The frequency of administration and dosing interval vary depending on the indication.	POCA Score (%)	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
2.	(b) (4) ***	58	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Releuko **Established name:** "filgrastim-xxxx" **Dosage form:** injection **Strength(s):** • **Vial:** 300 mcg/mL, 480 mcg/mL • **Prefilled syringe:** 300 mcg/0.5 mL, 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg/day or 10 mcg/kg/day. The frequency of administration and dosing interval vary depending on the indication.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
3.	Relenza	56	Orthographically, this name pair has different suffixes ('za' vs. 'ko'). Additionally, Releuko contains an upstroke letter in the sixth position, which is absent from Relenza. Phonetically, the second syllable ('len' vs. 'loo') and third syllable ('za' vs. 'ko') of this name pair have notable differences when spoken. The following differences in product characteristics may also help to mitigate the risk of errors: • Strength: Releuko is available as 300 mcg/mL or 480 mcg/mL or 300 mcg/0.5 mL or 480 mcg/0.8 mL which would need to be specified, whereas Relenza is available in a single strength (5 mg) which may not be specified on an order. • Dose: the dose of Releuko is weight-based whereas the dose of Relenza is two inhalations (or 10 mg). • Route of Administration: Releuko is administered subcutaneously or intravenously which would need to be specified, whereas Relenza is administered via inhalation. Therefore, in this scenario, due to the above-mentioned factors and the phonetic and orthographic differences, we find this name pair acceptable.

No.	**Proposed name:** Releuko **Established name:** "filgrastim-xxxx" **Dosage form:** injection **Strength(s):** • **Vial:** 300 mcg/mL, 480 mcg/mL • **Prefilled syringe:** 300 mcg/0.5 mL, 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg/day or 10 mcg/kg/day. The frequency of administration and dosing interval vary depending on the indication.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
4.	Xtrelus	55	This name pair has sufficient orthographic and phonetic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%) --- N/A

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described**.**

No.	Name	POCA Score (%)	Failure preventions
5.	(b) (4)***	59	Proposed proprietary name for (b) (4) was withdrawn by the Sponsor.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[h]. --- N/A

[h] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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/s/

STEPHANIE L DEGRAW
03/01/2019 04:23:24 PM

HINA S MEHTA
03/01/2019 04:46:31 PM

MEMORANDUM
NONPROPRIETARY NAME SUFFIX

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	January 29, 2018
Requesting Office or Division:	Division of Hematology Products (DHP)
Application Type and Number:	BLA 761082
Product Name and Strength:	Releuko (filgrastim-ayow) Injection Vials: 300 mcg/mL, 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL, 480 mcg/0.8 mL
Total Product Strength:	Vials: 300 mcg/mL Prefilled syringes: 600 mcg/mL
Product Type:	Single Ingredient Product and Drug-device Combination Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Adello Biologics, LLC
Panorama #:	2017-1376
DMEPA Primary Reviewer:	Nicole Garrison, PharmD, BCPS
OMEPRM Associate Director:	Kellie Taylor, PharmD, MPH

1 PURPOSE OF MEMO

This memorandum summarizes our evaluation of the suffixes proposed by Adello for the nonproprietary name and communicates our recommendation for the nonproprietary name.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

On July 10, 2017, Adello submitted a list of suffixes, in their order of preference, to be used in the nonproprietary name of their product. The Applicant also provided for our consideration findings from their evaluation method and process used to select each proposed suffix for their product. We note that the Applicant submitted a total of three proposed suffixes.

We reviewed Adello's proposed suffixes in the order of preference listed by the Applicant, along with the supporting data they submitted, against the criteria described in the final guidance.[a]

1. filgrastim-ayow

Adello's first proposed suffix -ayow, is comprised of some letters that represent common medical abbreviations (ay is an abbreviation for acrocyanotic; ow is an abbreviation for once weekly, open wound, outer wall, and overweight). We considered whether the inclusion of the letters (ay and ow) with the suffix could be misleading or a source of confusion and errors, but we could not identify a plausible risk based on the expected use of this product or, based upon known causes of medication errors.

We also determined that –ayow is not too similar to any other products' suffix designation, that the suffix is devoid of meaning, and does not make any misrepresentations with respect to safety or efficacy of this product. Therefore, we find the proposed suffix -ayow acceptable for this product.

These findings was shared with OPDP. In email correspondence dated January 11, 2018, OPDP did not identify any concerns that would render this proposed suffix unacceptable.

3. CONCLUSIONS

We find that Releuko's proposed suffix –ayow acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to filgrastim-ayow.

3.1 COMMENTS TO THE APPLICANT

We find the nonproprietary name, filgrastim-ayow, conditionally acceptable for your proposed product. Should your 351(k) BLA be approved during this review cycle, filgrastim-ayow will be the proper name designated in the license and you should revise your proposed labels and labeling accordingly. However, please be advised that if your application receives a complete response, the acceptability of your proposed suffix will be re-evaluated when you respond to the

[a] See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

deficiencies. If we find your proposal unacceptable upon our re-evaluation, we would inform you of our finding.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

NICOLE B GARRISON
01/29/2018

KELLIE A TAYLOR
01/30/2018

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	September 18, 2017
Application Type and Number:	IND 115333 and BLA 761082
Product Name and Strength:	Releuko ("Theragrastim"*) Injection Vials: 300 mcg/mL, 480 mcg/1.6 mL Prefilled syringes: 300 mcg/0.5 mL, 480 mcg/0.8 mL
Total Product Strength:	Vials: 300 mcg/mL Prefilled syringes: 600 mcg/mL
Product Type:	Single-Ingredient and Drug-device combination Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Adello Biologics, LLC
Panorama #:	2017-16225798 and 2017-16275200
DMEPA Safety Evaluator:	Nicole Garrison, PharmD, BCPS
DMEPA Team Leader:	Hina Mehta, PharmD

* For purposes of this review, we generally refer to Adello Biologics' proposed product by Adello Biologics' descriptor "Theragrastim." FDA has not yet designated a nonproprietary name for Adello Biologics' proposed biosimilar product that includes a distinguishing suffix (see Draft Guidance on Nonproprietary Naming of Biological Products).

Contents

Reference ID: 4943671

1 INTRODUCTION

This review evaluates the proposed proprietary name, Releuko, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, (b) (4) *** on October 7, 2016. However, the Division of Medication Error Prevention and Analysis (DMEPA) found the name, (b) (4) *** unacceptable due to orthographic similarities and shared product characteristics with the proprietary name, (b) (4) in OSE Review #2016-10674485, dated March 8, 2017.

Thus, the Applicant submitted the name, Releuko, for review on July 6, 2017 under the IND and July 10, 2017 under the BLA.

1.2 PRODUCT INFORMATION

The following product information is provided in the July 6, 2017 and July 10, 2017 proprietary name submission.

- Intended Pronunciation: reh loo' koe
- Active Ingredient: "Theragrastim"*
- Indication of Use:
  - Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever
  - Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
  - Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)
  - Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia
  - Increase survival in patients acutely exposed to myelosuppressive doses of radiation. (Hematopoietic Syndrome of Acute Radiation Syndrome)

* For purposes of this review, we generally refer to Adello Biologics' proposed product by Adello Biologics' descriptor "Theragrastim." FDA has not yet designated a nonproprietary name for Adello Biologics' proposed biosimilar product that includes a distinguishing suffix (see Draft Guidance on Nonproprietary Naming of Biological Products).

- Route of Administration: Subcutaneous and Intravenous
- Dosage Form: Injection
- Strength: 300 mcg/mL single dose vial (supplied as 300 mcg/mL and 480 mcg/1.6 mL) and 600 mcg/mL prefilled syringe (supplied as 300 mcg/0.5mL and 480 mcg/0.8mL)
- Dose and Frequency:

Indication	Usual Dosage	Frequency of Administration	Dosing Interval
Myelosuppressive Chemotherapy or Induction and/or Consolidation Chemotherapy	5 mcg/kg/day	Once daily subcutaneous injection or by continuous IV infusion	Every 24 hours
Bone Marrow Transplantation	10 mcg/kg/day	Once daily as an IV infusion lasting no longer than 24 hours	Every 24 hours
Autologous Peripheral Progenitor Cell Collection	10 mcg/kg/day	Once daily as a subcutaneous injection administered for at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis	Every 24 hours
Congenital Neutropenia	6 mcg/kg/day	Subcutaneous injection twice per day	Every 12 hours
Idiopathic or Cyclic Neutropenia	5 mcg/kg/day	Subcutaneous injection daily	Every 24 hours
Myelosuppressive doses of radiation	10 mcg/kg/day	Subcutaneous injection daily	Every 24 hours

- How Supplied:
    - 300 mcg/mL and 480 mcg/1.6 mL single-dose vials in a carton of 10 vials with a vial tray
    - 300 mcg/0.5 mL and 480 mcg/0.8 mL prefilled syringes in blister packs
- Storage: Store Releuko at 2°C to 8°C (36°F to 46°F) in the pack to protect from light. Do not leave Releuko in direct sunlight. Do Not freeze Releuko. Avoid shaking. Transport via a pneumatic tube has not been studied.
- Reference Listed Drug: Neupogen, BLA 103353

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Hematology Products, (DHP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name[a].

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Releuko, is derived from leukocytes. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, July 26, 2017 e-mail, the Division of Hematology Products (DHP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Seventy-four (74) practitioners participated in DMEPA's prescription studies. In the inpatient study, seven participants misinterpreted Releuko for "Relenko," which is a close variation to the marketed product Relenza (NDA 021036). In the outpatient study, two participants misinterpreted Releuko for "Relurko," which is a close variation to the formerly marketed product, Reluri. Despite the close hit in the FDA Rx Study, we think that the name pairs, Releuko and Relenza or Releuko and Reluri, have minimal potential of confusion for the following reasons:

Releuko vs. Relenza

Orthographically, the suffixes ('za' vs. 'ko') differ due to the upstroke letter k in the sixth position of Releuko. The third syllables of this name pair have notable differences when spoken ('za' vs. 'ko'). Releuko and Relenza differ in terms of strength (300 mcg/mL or 480 mcg/mL or 300 mcg/0.5 mL or 480 mcg/0.8 mL vs. 5 mg) and route of administration (subcutaneous and intravenous vs. inhalation). Therefore, in the absence of overlapping product characteristics, we do not think that the name pair is vulnerable to name confusion (see Appendix E for evaluation of the name pair).

Releuko and Reluri

Orthographically, the suffixes ('i' vs. 'ko') differ due to the upstroke letter k in the sixth position of Releuko. The third syllables of this name pair have notable differences when spoken ('i' vs.

[a] USAN stem search conducted on August 16, 2017.

'ko'). Additionally, this product was formerly marketed and currently discontinued with no generic equivalents. This name pair is evaluated in Appendix G.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[b] identified 45 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%**.** These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and FDA Prescription Simulation Study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	43
Low similarity name pair: combined match percentage score ≤54%	1

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 45 names contained in Table 1 determined 45 names will not pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Hematology Products (DHP) via e-mail on September 11, 2017. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the September 14, 2017, they stated no additional concerns with the proposed proprietary name, Releuko.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Wana Manitpisitkul, OSE project manager, at 240-402-4156.

3.1 COMMENTS TO THE APPLICANT

[b] POCA search conducted on August 7, 2017 in version 4.1.

We have completed our review of the proposed proprietary name, Releuko, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your July 10, 2017 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. ***USAN Stems (http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page)***

   USAN Stems List contains all the recognized USAN stems.

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

3. ***Electronic Drug Registration and Listing System (eDRLS) database***

The electronic Drug Registration and Listing System (eDRLS) was established to supports the FDA's Center for Drug Evaluation and Research (CDER) goal to establish a common Structured Product Labeling (SPL) repository for all facilities that manufacture regulated drugs. The system is a reliable, up-to-date inventory of FDA-regulated, drugs and establishments that produce drugs and their associated information.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [c]

[c] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[d]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g.,

[d] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

   When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?

Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg

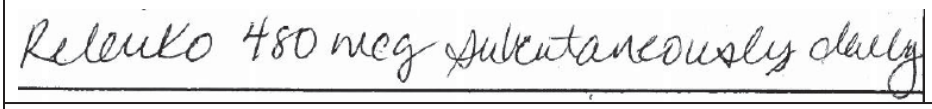
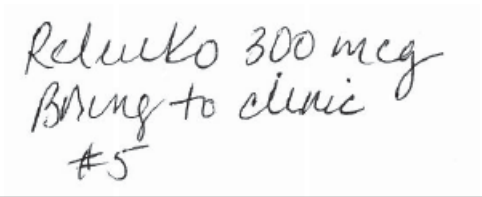
<table>
<tr><td>Step 2</td><td colspan="2">Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <u>with</u> overlapping or similar strengths or doses.</td></tr>
<tr><td></td><td>Orthographic Checklist (Y/N to each question)
Do the names begin with different first letters?
Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.
Are the lengths of the names dissimilar* when scripted?
*FDA considers the length of names different if the names differ by two or more letters.
Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names?
Is there different number or placement of cross-stroke or dotted letters present in the names?
Do the infixes of the name appear dissimilar when scripted?
Do the suffixes of the names appear dissimilar when scripted?</td><td>Phonetic Checklist (Y/N to each question)
Do the names have different number of syllables?
Do the names have different syllabic stresses?
Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Across a range of dialects, are the names consistently pronounced differently?</td></tr>
</table>

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Releuko Study (Conducted on July 24, 2017)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  Outpatient Prescription:  	Releuko 300 mcg Bring to clinic Dispense #5

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

291 People Received Study

74 People Responded

Study Name: Releuko

Total	33	20	21	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
GRALUCO	0	1	0	1
HORLUKO	0	1	0	1
ORLUCCO	0	1	0	1
ORLUCO	0	4	0	4
ORLUKO	0	1	0	1
RALUCO	0	1	0	1
RELENKO	0	0	7	7
RELEUKO	24	0	14	38

RELUCKO	3	1	0	4
RELUCO	0	2	0	2
RELUIKO	4	0	0	4
RELURKO	2	0	0	2
RILUKO	0	1	0	1
ROLUCKO	0	1	0	1
ROLUCO	0	3	0	3
ROLUKO	0	1	0	1
ROULOUCO	0	1	0	1
WATOLOCOL	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name: Releuko** **Established name: "Theragrastim*"** **Dosage form: Injection** **Strength(s):** • **Vial:** 300 mcg/mL, 480 mcg/mL • **Prefilled syringe:** 300 mcg/0.5 mL, 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg/day or 10 mcg/kg/day. The frequency of administration and dosing interval vary depending on the indication.	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Releuko***	100	Subject of this review.

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Proleukin	63
2.	Relador	62
3.	(b) (4)***	62
4.	Relcof C	60
5.	Prelu-2	59
6.	Rea Lo 39	59
7.	Urelle	56
8.	Rebetol	55
9.	Relovox	55

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name: Releuko** **Established name: "Theragrastim*"** **Dosage form: Injection** **Strength(s):** • **Vial:** 300 mcg/mL, 480 mcg/mL • **Prefilled syringe:** 300 mcg/0.5 mL, 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg/day or 10 mcg/kg/day. The frequency of administration and dosing interval vary depending on the indication.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Rilutek	68	This name pair has different suffixes ('ko' vs. 'tek'). Releuko contains a upstroke letter in the sixth position and Rilutek contains two upstroke letters in the fifth and seventh positions. The third syllables of this name pair have notable differences when spoken ('ko' vs. 'tek'). Strength: 300 mcg/mL or 480 mcg/mL or 300 mcg/0.5 mL or 480 mcg/0.8 mL vs. 50 mg Route of Administration: subcutaneous and intravenous vs. oral
2.	(b) (4)***	66	(b) (4)
3.	Rulox	62	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name: Releuko** **Established name: "Theragrastim*"** **Dosage form: Injection** **Strength(s):** • **Vial:** 300 mcg/mL, 480 mcg/mL • **Prefilled syringe:** 300 mcg/0.5 mL, 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg/day or 10 mcg/kg/day. The frequency of administration and dosing interval vary depending on the indication.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
4.	Rea-Lo	59	This name pair has different infixes ('a' vs. 'leu'). Rea-Lo has 5 letters, whereas Releuko has 7 letters, giving it a shorter length when scripted. Rea-Lo has one upstroke letter and Releuko has 2 upstroke letters. Additionally, Rea-Lo has a modifier which is absent from Releuko. The second syllables of this name pair have notable differences when spoken ('a' vs. 'leu'). Dose: 5 mcg/kg/day or 10 mcg/kg/day vs. apply to affected skin twice per day or as directed by your physician. Route of Administration: subcutaneous and intravenous vs. topical Dosage Form: injection vs. cream
5.	Relistor	58	This name pair has different suffixes ('tor' vs. 'ko'). The second ('is' vs. 'leu') and third ('tor' vs. 'ko') syllables of this name pair have notable differences when spoken. Strength: 300 mcg/mL or 480 mcg/mL or 300 mcg/0.5 mL or 480 mcg/0.8 mL vs.12 mg/0.6 mL or 150 mg or 8 mg/0.4 mL
6.	Rela	58	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name: Releuko** **Established name: "Theragrastim*"** **Dosage form: Injection** **Strength(s):** • **Vial:** 300 mcg/mL, 480 mcg/mL • **Prefilled syringe:** 300 mcg/0.5 mL, 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg/day or 10 mcg/kg/day. The frequency of administration and dosing interval vary depending on the indication.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
7.	Xarelto	58	This name pair has sufficient orthographic and phonetic differences.
8.	Zileuton	58	This name pair has sufficient orthographic and phonetic differences.
9.	Relenza	56	This name pair has different suffixes ('za' vs. 'ko'). Releuko contains an upstroke letter in the sixth position, which is absent from Relenza. The third syllables of this name pair have notable differences when spoken ('za' vs. 'ko'). Strength: 300 mcg/mL or 480 mcg/mL or 300 mcg/0.5 mL or 480 mcg/0.8 mL vs. 5 mg Route of Administration: subcutaneous and intravenous vs. inhalation.
10.	Riluzole	56	This name pair has different suffixes ('ole' vs. 'ko'). Releuko contains an upstroke letter in the sixth position, whereas Riluzole contains an upstroke letter in the seventh position. The third syllables of this name pair have notable differences when spoken ('ole' vs. 'ko'). Strength: 300 mcg/mL or 480 mcg/mL or 300 mcg/0.5 mL or 480 mcg/0.8 mL vs. 50 mg Route of Administration: subcutaneous and intravenous vs. oral

No.	**Proposed name: Releuko** **Established name: "Theragrastim*"** **Dosage form: Injection** **Strength(s):** • **Vial:** 300 mcg/mL, 480 mcg/mL • **Prefilled syringe:** 300 mcg/0.5 mL, 480 mcg/0.8 mL **Usual Dose:** 5 mcg/kg/day or 10 mcg/kg/day. The frequency of administration and dosing interval vary depending on the indication.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
11.	Relafen	55	This name pair has different infixes ('a' vs. 'leu') and suffixes ('fen' vs. 'ko'). Releuko contains an upstroke letter in the sixth position, whereas Relafen contains an upstroke letter in the fifth position. The second ('a' vs. 'leu') and third ('fen' vs. 'ko') syllables of this name pair have notable differences when spoken. Strength: 300 mcg/mL or 480 mcg/mL or 300 mcg/0.5 mL or 480 mcg/0.8 mL vs. 500 mg or 750 mg Route of Administration: subcutaneous and intravenous vs. oral

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%)

No.	Name	POCA Score (%)
1.	Kurvelo	52

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described**.**

No.	Name	POCA Score (%)	Failure preventions
1.	(b) (4) ***	66	(b) (4)
2.	Reluri	64	This name was identified in RxNorm database. Per RedBook, the brand name is listed as discontinued, with no generic equivalents available.
3.	Lorelco	64	This product was identified in Drugs at FDA, however is discontinued withdrawn FR effective 6/4/04. There are no generic equivalents available.
4.	Orelox	64	This is an international product marketed in Germany, Brazil, France, Italy, Mexico, South Africa, and Turkey.
5.	Relifor	62	This product is for veterinary use only.
6.	Rulox #1	62	This name was identified in RxNorm database. Per RedBook, the brand name is listed as discontinued, with no generic equivalents available.
7.	Rulox #2	62	This name was identified in RxNorm database. Per RedBook, the brand name is listed as discontinued, with no generic equivalents available.
8.	Relera	60	This name was identified in RxNorm database. Per RedBook, the brand name is listed as discontinued, with no generic equivalents available.
9.	Ralgro	58	This product is for veterinary use only.
10.	(b) (4) ***	56	Proposed proprietary name, (b) (4) *** found unacceptable by DMEPA (OSE# 2016-10674485 dated 3/8/17). The Sponsor submitted a new name, Releuko, which is the subject of this review.
11.	Redux	56	This name was identified in RxNorm database. Per RedBook, the brand name is listed as discontinued, with no generic equivalents available.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[e].

No.	Name	POCA Score (%)
1.	(b) (4) ***	64

[e] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

No.	Name	POCA Score (%)
2.	Cellucon	61
3.	Urolet	60
4.	Elocon	58
5.	Prulet	56
6.	Trilog	56
7.	Xeloda	56
8.	Saleto	55
9.	Saleto-200	55
10.	Saleto-400	55
11.	Saleto-600	55
12.	Saleto-800	55

Appendix I: Names identified in the eDRLS database not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name
	N/A

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

NICOLE B GARRISON
09/18/2017

HINA S MEHTA
09/18/2017