Legacy Healthcare Updates on Regulatory Focus for Cinainu in Europe, US and Japan

March 28, 2025, Epalinges, Switzerland

Legacy Healthcare expands its efforts to advance regulatory discussions with National Health Authorities in Europe, U.S. Food and Drug Administration (FDA) and Japan Pharmaceuticals and Medical Devices Agency (PMDA). This in part reflects the company's decision to withdrawal its marketing authorization application (MAA) for Cinainu following the outcome of the centralized assessment procedure with the European Medicines Agency (EMA).

Cinainu has demonstrated positive efficacy and safety results in its pivotal Phase 2/3 trial (RAAINBOW) on children and adolescents with moderate to severe alopecia areata conducted under an EMA-approved Paediatric Investigation Plan (PIP). The study met its primary endpoint in the predefined Full Analysis Set (FAS), and in 2023, the EMA's Paediatric Committee (PDCO) issued a positive opinion confirming full compliance of the development program with the agreed PIP.

During the centralized assessment procedure, the Committee for Medicinal Products for Human Use (CHMP) adopted a position that diverged from the scientific and procedural framework established through the EMA-agreed PIP and endorsed by the PDCO. Key elements of the development strategy—including the primary analysis population (FAS) and non-clinical requirements—were not accepted by the CHMP, despite having been formally agreed earlier in the regulatory process. The FAS, which had been explicitly accepted by the PDCO and formed the basis for the study's primary efficacy outcome, aligns with established ICH and EMA guideline criteria for use as primary analysis population. The rationale provided by the CHMP for not accepting the FAS was based on considerations that are not reflected in ICH or EMA guidelines and, in the Company's view, lack scientific justification.

The CHMP's stance on non-clinical data was equally unexpected. Cinainu is composed of botanical extracts from onion, lemon, guarana, and cacao—plants with a long history of safe human use. In addition, over 600 patients were exposed to the product in clinical trials and 100 million daily doses commercialized as cosmetic-status lotion, with no reported safety concern. As part of the PIP approval process, involving the PDCO and other EMA committee and working groups, it was concluded that no additional non-clinical studies were required. The CHMP's subsequent request for long-term toxicity and carcinogenicity studies therefore stands in clear contradiction with the earlier scientific conclusions formally endorsed by EMA.

This divergence resulted in a CHMP opinion issued on November 14, 2024, which does not reflect the development plan agreed with EMA or the data generated in accordance with it.

In addition, although the CHMP raised concerns related to Cinainu's herbal composition, the Herbal Medicinal Products Committee (HMPC)—EMA's designated expert body for herbal medicinal products—was not consulted, despite its foreseen role in such assessments. Further limitations in the evaluation process were observed during the re-examination phase, where key regulatory documents, including the PIP and PDCO opinions, were not shared with the ad-hoc expert group.

In light of these circumstances, Legacy Healthcare concluded that the conditions for a consistent and coherent regulatory assessment were no longer in place. The Company therefore made the strategic decision to withdraw its MAA and formally requested the retraction of the CHMP opinion and related public documentation.

"Cinainu's development was conducted in full alignment with the regulatory guidance established through the EMA-agreed Paediatric Investigation Plan. We stand by the clinically meaningful efficacy demonstrated in the RAAINBOW study and remain fully committed to advancing Cinainu toward market approval, particularly in the United States," said Saad Harti, CEO of Legacy Healthcare.

The Company is making public both the Withdrawal Letter and Follow-Up Letter submitted to EMA, which outline in detail the rationale for this decision and provide additional context on the regulatory process.

In addition to starting National Health Authorities consultations in Europe, the company continues its interaction with FDA in the US and PMDA in Japan pursuing approval for Cinainu.

About Cinainu

Cinainu is a topical drug candidate composed of four botanical extracts (onion, citrus, guarana, cocoa) with a well-established safety profile, designed to treat children and adolescents suffering from moderate to severe alopecia areata. Over 100 million daily doses have been commercially used worldwide in non-prescription settings, and over 600 patients have been exposed to Cinainu in different clinical trials, up to 12 months, with no reported safety concern.

About Legacy Healthcare

Legacy Healthcare is a Swiss-based biopharmaceutical company focused on leveraging the pleiotropic activity and safety profile of plants known safe for human use to develop prescription botanical drugs that address serious medical conditions. The company's first product candidate, Cinainu, has demonstrated strong safety and efficacy in a phase 2/3 study involving patients suffering from alopecia areata, a chronic autoimmune condition with highly damaging psycho-social issues that impact all who suffer from it, especially children.

For more information about Legacy Healthcare please visit www.legacyhealthcare.ch

For inquiries: contact@legacyhealthcare.ch

26 February 2025

To : EMA Executive Director
CHMP Chair
European Medicines Agency
Domenico Scarlattilaan 6
1083 HS Amsterdam, The Netherlands

Ref: CINAINU cutaneous solution
Centralized Marketing Authorization Application - Withdrawal
Submission sequence number: 0011
Reference number: EMEA/H/C/0004155/0000

Dear EMA Executive Director, Dear CHMP Chair,

Legacy Healthcare (France) SAS, the Applicant, hereby notifies the EMA of the withdrawal of the Marketing Authorization Application (MAA) of CINAINU cutaneous solution. CINAINU is composed of extracts from four plants (onion, lemon, guarana, cocoa) and was proposed for the treatment of moderate to severe alopecia areata in children and adolescents.

On November 14, 2024, the CHMP issued a negative opinion on Cinainu MAA. The CHMP clinical and non-clinical grounds for refusal are in direct contradiction with the EMA-approved Paediatric Investigation Plan (PIP) for Cinainu and the positive opinion from the EMA Paediatric Committee (PDCO) confirming compliance with the agreed PIP. Furthermore, despite the CHMP raising quality-related concerns, the Committee on Herbal Medicinal Products (HMPC), EMA's designated expert body for herbal medicinal products, was never consulted during the CHMP assessment procedure.

Additionally, new analysis and associated data submitted during re-examination were not evaluated on the basis of an unadopted procedural advice, and the ad-hoc expert group convened for CINAINU was not provided with essential regulatory documents, including the PIP, PDCO opinion, and key quality dossier elements (eCTD Modules 2.3 & 3). Thus, the Applicant has made the decision to withdraw the application and requests at this point of time from EMA the retraction of CHMP opinion and forthcoming EPAR.

We consent for this letter to be published on EMA website.

Yours sincerely,

[redacted]

Saad Harti, CEO

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March 20, 2025

To : EMA Executive Director
CHMP Chair
EMA Secretariat
European Medicines Agency
Domenico Scarlattilaan 6
1083 HS Amsterdam, The Netherlands

cc : Andrea Taft – Product Lead
CINAINU-4155@ema.europa.eu

Ref: CINAINU cutaneous solution – Withdrawal European Public Assessment Report (WEPAR)
Submission sequence number: 0013
Reference number: EMEA/H/C/0004155/0000

Dear EMA Executive Director, Dear CHMP Chair, Dear EMA Secretariat,

Legacy Healthcare (France) SAS (the Company) acknowledges EMA's request to propose deletions of commercially confidential information (CCI) and personal data in the CHMP withdrawal European public assessment report (W-EPAR) of Cinainu. The Company also notes EMA's indication that, should the requested redactions not be submitted by 10:00 AM on March 21, 2025, EMA will proceed unilaterally with redactions and publish the W-EPAR without the Company's input.

The Company strongly objects to this ultimatum for the following reasons:

1. Absence of a legal deadline for W-EPAR publication

Article 11 of Regulation (EC) 726/2004 does not impose any specific time limit for the publication of a W-EPAR. While EMA procedural advice suggests publication within three months of a withdrawal letter, this remains an advice rather than a binding requirement. The urgency imposed by EMA in this instance is therefore unjustified and unwarranted, especially given the current retraction request.

2. Protection of commercially confidential information

Article 11 of Regulation (EC) 726/2004 explicitly requires the deletion of all CCI from the W-EPAR. Should EMA proceed with the publication of the W-EPAR without the Company's input, particularly in relation to undisputable CCI, or in a manner that unjustifiably harms the Company's economic interests, Legacy Healthcare reserves all legal rights to seek indemnification for any resulting damages.

3. Information undermining Company's economic interest already communicated

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In addition to the undisputable CCI contained in the quality and manufacturing sections of the W-EPAR, Legacy Healthcare has already formally communicated in its letters dated February 26, 2025 and March 10, 2025 that the entire W-EPAR, along with the CHMP opinion issued on November 14, 2024, is based on procedurally flawed and scientifically inconsistent assessments. As such, not retracting these documents would cause additional serious economic harm to the Company, in addition of being inconsistent with EMA policy 001[1,2] which requires that a W-EPAR which does not conform to requirements shall be prevented from release by EMA.

Given these serious concerns, Legacy Healthcare formally reiterates its request for the immediate retraction of both the CHMP opinion and the forthcoming W-EPAR.

In light of the above, CCI and personal data redactions can only be considered once EMA has issued a decision on the retraction request and with respect to the specific documents ultimately designated for publication.

We appreciate your attention to this urgent matter.

Yours sincerely,

Saad Harti
CEO

Attachment:

- ema tracking table

[1] The European Medicines Agency's Integrated Quality Management System - POLICY/0001 - EMEA/MB/355781/2007Rev.1
[2] EMA Quality Management Policy - EMA/228979/2024