

THE AMYLOIDOSIS FORUM: Five Years of Progress for the Public-Private Partnership to Advance Drug Development for Amyloidosis



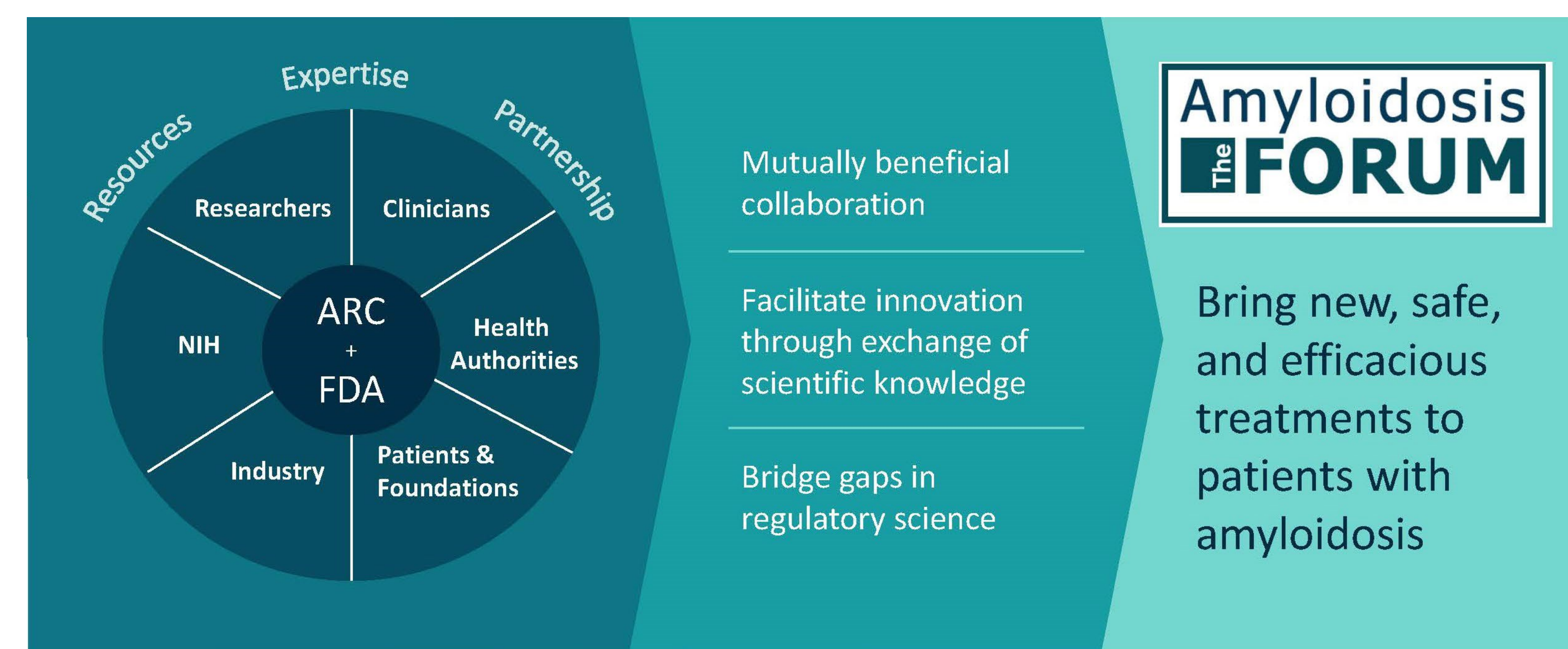
K. HSU¹, J. SIGNOROVITCH², P. JOHNSON¹, J. ZIGTERMAN¹, M.S. MAURER³, A. DISPENZIERI⁴, V. SANCHORAWALA⁵, S. DORBALA⁶, S. CAIRNS-SMITH¹, P. DUNNMON⁷, R. ADIGUN⁸, I. LOUSADA¹

¹Amyloidosis Research Consortium, Newton, MA, USA; ²Analysis Group, Boston, MA, USA; ³Clinical Cardiovascular Research Laboratory for the Elderly, Columbia University Medical Center, New York, NY, USA; ⁴Mayo Clinic Division of Hematology, Rochester, MN, USA; ⁵Amyloidosis Center, Boston University Chobanian & Avedisian School of Medicine and Boston Medical Center, Boston, MA, USA; ⁶Departments of Cardiovascular Medicine and Nuclear Radiology, Brigham and Women's Hospital, Boston, MA, USA; ⁷Janssen Research and Development, Raritan, NJ, USA; ⁸United States Food and Drug Administration, Silver Spring, MD, USA

THE AMYLOIDOSIS FORUM: A PPP BETWEEN THE AMYLOIDOSIS RESEARCH CONSORTIUM (ARC) AND THE UNITED STATES FOOD & DRUG ADMINISTRATION (FDA)

- Developing treatments for multisystemic rare diseases like light chain (AL) and transthyretin (ATTR) amyloidosis pose unique challenges given the limited patient population and heterogeneity of the disease.
- While the treatment landscape for AL and ATTR amyloidosis has rapidly evolved over the past 5 years, many challenges remain for drug developers.
- **Formed in 2019, the initial goal of the Forum was to bridging regulatory scientific gaps in drug development for AL amyloidosis, with the scope broadening to include ATTR amyloidosis in 2022.**
- The Amyloidosis Forum fosters collaboration between academia, industry, patients, and health authorities to accelerate the development of new treatments and diagnostics for AL and ATTR amyloidosis (Figure 1).
- The Amyloidosis Forum uses a range of approaches to solicit stakeholder input and identify priorities for these collaborative approaches, including organizing public meetings and formation of cross-stakeholder working groups to advance key topics and disseminate findings through peer-reviewed publications.

Figure 1: The Amyloidosis Forum Structure



RESULTS

2019-2023

- The Amyloidosis Forum has convened a series of meetings (Table 1) and working groups to focus on challenges facing drug development in AL amyloidosis, novel endpoints for clinical trials in AL amyloidosis (Figure 2), the potential for imaging to serve as endpoints in clinical trials for AL amyloidosis, and challenge facing drug development and access in ATTR amyloidosis.

2024 and Beyond

- The Amyloidosis Forum will launch prioritized cross-stakeholder working groups focused on bridging the regulatory science gaps through **Federated Analytics, Standardization of Imaging, Prognostic Factors**, and building the **Foundational Evidence for Endpoints. Public Dissemination of Activities and Key Outcomes**

Public Dissemination of Activities and Key Outcomes

- Proceedings from 5 public meetings (available at www.amyloidosisforum.org) and working group activities have resulted in numerous peer-reviewed publications and conference presentations.

References

1 The Inaugural Amyloidosis Forum Panelists., Lousada, I. The Amyloidosis Forum: a public private partnership to advance drug development in AL amyloidosis. *Orphanet J Rare Dis* 15, 268 (2020). 2 Maurer et al. Proposed Cardiac End Points for Clinical Trials in Immunoglobulin Light Chain Amyloidosis: Report from the Amyloidosis Forum Cardiac Working Group. *Circ Heart Fail.* 2022; 15:e009038. 3 Mauermann et al. Peripheral Nervous, Hepatic, and Gastrointestinal Endpoints for AL Amyloidosis, Clinical Trial: Report from the Amyloidosis Forum Multi-organ System Working Group. *Adv Ther* 40, 4695-4710 (2023). 4 Rizio et al. Health-Related Quality of Life Instruments for Clinical Trial in AL Amyloidosis: Report from the Amyloidosis Forum HRQOL Working Group. *Patient Related Outcome Measures*, 14, 153-169. 2023. 5 Signorovitch et al. Pathway for Development and Validation of Multi-domain Endpoints for Amyloid Light Chain (AL) Amyloidosis. *Ther Innov Regul Sci* (2024). 6 Leung et al. Renal Response Criteria for Clinical Trials in Amyloid Light Chain Amyloidosis. *Kidney Int Rep* (2024), in press. 7 Dispenzieri et al. Evaluation of NT-proBNP as surrogate endpoint in AL amyloidosis: development of a platform for federated, multi-institution meta-analysis of randomized trials. XVIII Meeting of the International Society of Amyloidosis, 2022 8 Maurer et al. Advancing Transthyretin Amyloidosis Drug Development in an Evolving Treatment Landscape: Amyloidosis Forum Meeting Proceedings. *Adv Ther* in press (2024).

Figure 2: Developing Novel Endpoints in AL Amyloidosis

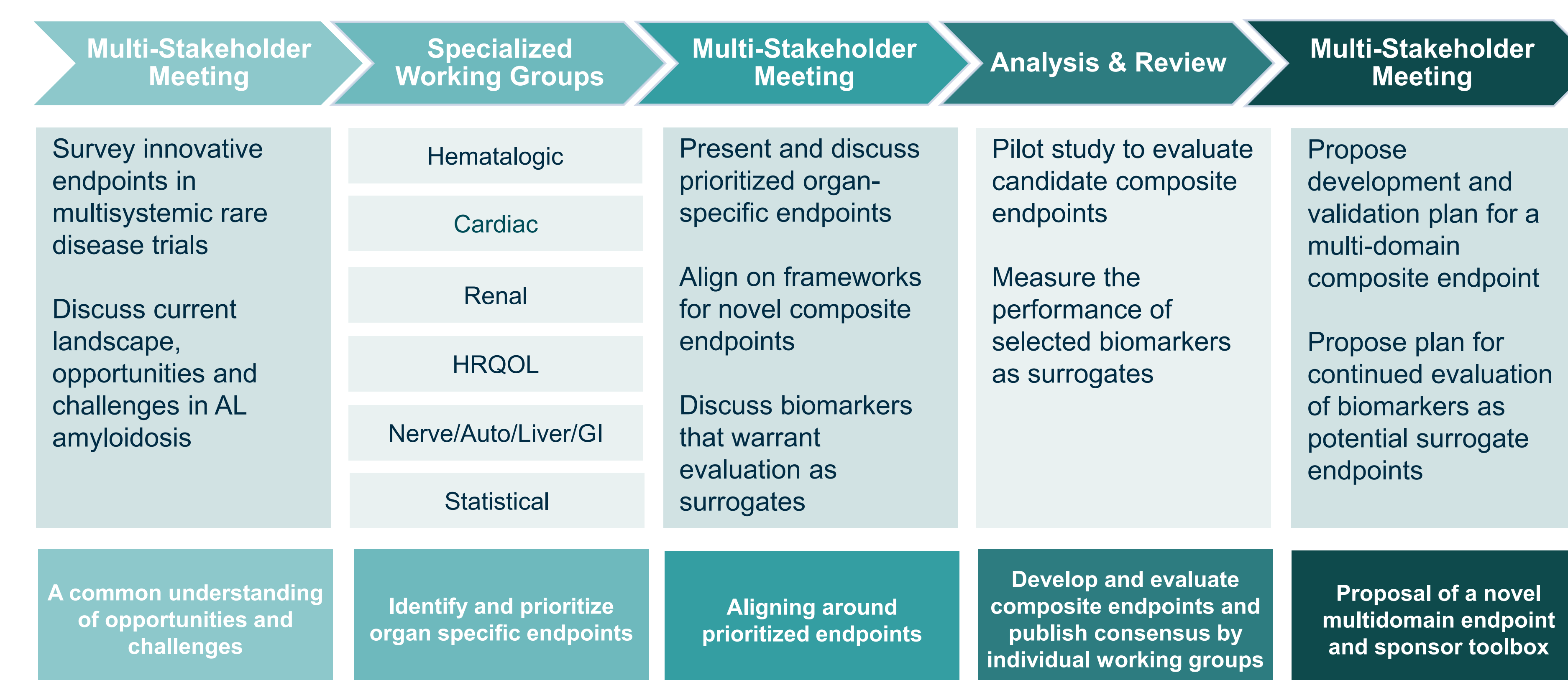
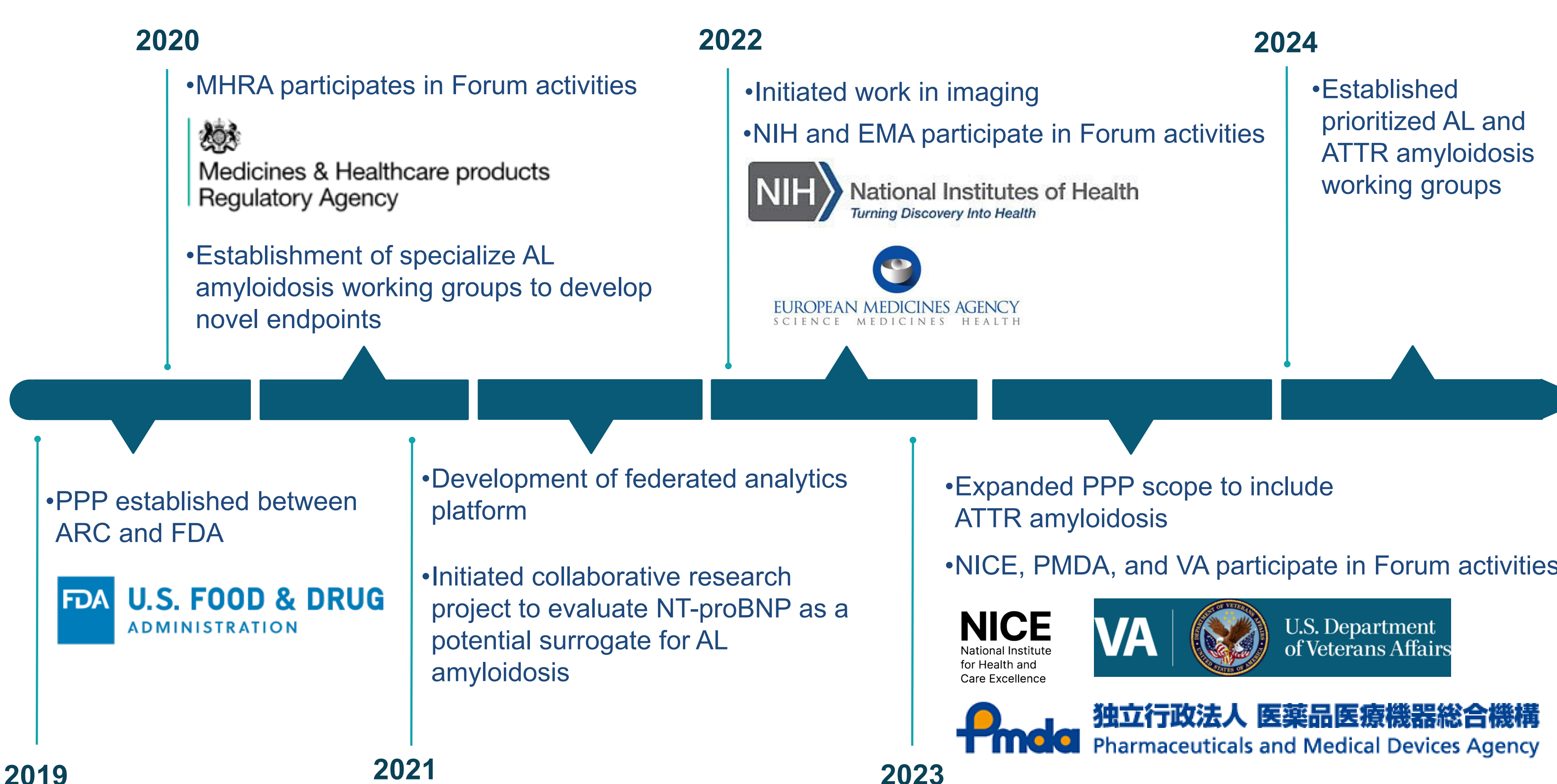


Figure 3: 2024 Amyloidosis Forum Progress (2019 – 2024)



CONCLUSIONS

- Since inception 5 years ago, the Amyloidosis Forum has identified opportunities for the development of novel clinical endpoints and analysis methodologies in AL amyloidosis, the standardization of imaging techniques, and future-facing working groups to consider methods to address ongoing challenges for therapeutic and diagnostic development in AL and ATTR amyloidosis.
- **The Amyloidosis Forum provides a unique opportunity for mutually beneficial collaboration across a diverse group of stakeholders by facilitating innovation through exchange of scientific knowledge in amyloidosis.**
- The Amyloidosis Forum seeks to expand participation and further advance drug development through the establishment of community-informed working groups. Contact amyloidosisforum@arci.org to participate.

Table 1: Amyloidosis Forum Meetings

Meeting	Participants	Key Outcomes
2019: Advancing Drug Development in AL Amyloidosis: Understanding AL Amyloidosis	• 27 Speakers • 2 Health Authorities (EMA & FDA) • 3 Countries	Prioritized topics in AL amyloidosis: ¹ • novel trial designs and endpoints • role of imaging to assess burden of disease and response to therapy, • disease-specific patient reported outcome measures • natural history studies
2020: Novel Endpoint and Analyses in Multisystem Rare Disease Clinical Trials and the Current Landscape in AL Amyloidosis	• 16 Speakers • 2 Health Authorities (FDA, & MHRA) • 3 Countries	Launched-specialized working groups in the following areas: • Organ systems • HRQOL • Statistical methods
2021: Considerations for Novel Endpoint Development in AL Amyloidosis	• 48 Speakers • 2 Health Authorities (FDA & MHRA) • 3 Countries	• Prioritized-organ-specific endpoints ²⁻⁶ • Development of Federated Analytics platform and collaborative project to evaluate the potential of NT-proBNP as a surrogate endpoint ⁷
2022: Potential Pathways for Development of Imaging Endpoints for Clinical Trials in AL and ATTR Amyloidosis	• 39 Speakers • 4 Health Authorities (EMA, FDA, MHRA, NIH) • 6 Countries	Defined importance of establishing rigor, reproducibility, and accuracy of imaging modalities to assessing cardiac structural and functional changes and amyloid load
2023: Advancing Drug Development in ATTR in an Evolving Treatment Landscape	• 58 Speakers • 5 Health Authorities (EMA, FDA, MHRA, NICE, PMDA, & VA) • 6 Countries	Prioritized topics in ATTR amyloidosis: • Leveraging contemporary real-world data to design clinical trials in ATTR amyloidosis ⁸ • Generating evidence from clinical trials that address clinically relevant questions