AT-GAA is a novel next-generation therapy for Pompe disease with improved efficacy in mice.

**Summary and Conclusions**

- Our data indicate that AT-GAA, with its higher M6P content and further stabilization by the pharmacological chaperone AT2221 at the neutral pH of blood, is more efficient in lysosomal targeting in the disease-relevant muscle than alglucosidase alfa when administered to Gaa KO mice over a 5-hour period following intravenous (IV) administration.
- Co-administration of AT2221 and GAA is more effective than alglucosidase alfa in correcting some of the disease-relevant phenotypes in Gaa KO mice, such as glycogen accumulation, neuronal proliferation, and autophagy impairment. As a result, AT-GAA has significantly improved muscle strength in disease-knockout mice compared with alglucosidase alfa.
- Taken together, the AT-GAA paradigm—the combination of AT2221/GAA—provides a new treatment strategy for Pompe disease.

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**Disclosures**

- Conflict of Interest: All authors are employees of Amicus Therapeutics, Inc. For questions, please contact Xu S at xu.su@amicus.com.

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