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He earned his undergraduate degree in biochemistry and chemistry from the State University of New York at Buffalo and his medical degree from Einstein in 1982. He completed his medical training, residency, and research fellowship at the University of California at San Francisco. He was then a clinical and research fellow in cardiovascular medicine at Johns Hopkins School of Medicine. In 2009, he was appointed chief of the division of cardiology and co-director of the Heart and Vascular Institute at Hopkins, where he also was the Michel Mirowski, M.D. Professor of Cardiology, and professor of medicine and of cellular and molecular medicine. He was mentor to dozens of postdoctoral and clinical fellows, as well as graduate and undergraduate students.

Dr. Tomaselli was elected to the American Society of Clinical Investigation in 1996 and has been a member of the Association of American Physicians since 2010. He has served on the editorial boards of a number of journals in cardiovascular science and in medicine and has been a member of study sections for the NIH, AHA, and California Tobacco Research Fund, and he was a member of international (DFG, INSERM and CIRM) grant review panels. Dr. Tomaselli was national president of the American Heart Association from 2011 to 2012. He was editor-in-chief of the Journal of Clinical Investigation from 2017 to 2018, and deputy editor until 2022.