To further advance the development and implementation of glycerol-based biorefinery concepts, it is critical to analyze the glycerol conversion into high value-added products in a holistic manner, considering both production as well as the logistics aspects related to the supply chain structure. To address the optimal design and planning of the glycerol-based biorefinery supply chain, in this work, we propose a multiperiod, multistage, and multiproduct Mixed Integer Linear Programming optimization model, called GlyThink, based upon the maximization of the net present value (NPV). The proposed model is able to identify operational decisions, including locations, capacity levels, technologies, and product portfolio, as well as strategic decisions such as inventory levels, production amounts, and transportation to the final markets. Several technologies are considered for the glycerol valorization to high value-added products. Existing countries with major production and consumption of biodiesel in Europe are considered as candidates for the facility sites and demand markets, and their spatial distribution is also carefully studied. The results showed that (i) the optimal solution that provides the best NPV is obtained by establishing a multiproject supply chain for the glycerol-based integrated biorefinery, built upon four plant site locations (Germany, France, The Netherlands, and Italy); (ii) if a single-plant alternative is to be selected, Germany stands out as potentially the best location for the integrated biorefinery; (iii) government incentives might play a decisive role in the growth of a glycerol-based economy showing improved economic feasibility; and, last, (iv) the optimal product portfolio suggested is based on the production of succinic acid and lactic acid, followed by epichlorohydrin and poly-3-hydroxybutyrate (PHB).