Originally this building included a two-story slave quarters on the north side of the structure. Framing scars from earlier walls and stairways were revealed in the 1990s, which provide a glimpse into the original construction of the house, including walls, doors, windows, stairs, and the slave quarters' location. Also used as the museum's Orientation Gallery, the slave quarters serves as the starting point for all tours. The carriage house, stable, and hayloft, located on the south side of the building, now house the museum store.

The remains of the kitchen, laundry room, bathing room, and a nearly 5,000-gallon cistern are found in the basement, the location of the main service area for the house. Portions of the floor's original use, such as sinks and marble tubs, suggest the advanced technologies architect William Jay incorporated into the residence during the visit to Savannah in 1823.

The first floor of the Owens-Thomas House features a stunning entryway with marble-grained columns, marble semi-circular console tables, a brass-inlaid staircase, and Greek-key skylight. The Drawing Room features curved walls and doors, built-in sideboard, a Dining Room with a cloud-covered trompe l’oeil ceiling, and a Bedroom with a hidden display of silver, and the bedroom where Lafayette slept during his visit to Savannah in 1825.

The second floor of the house features an indoor bridge, stained glass windows, two bedrooms, and a library. All rooms in the house are furnished with fine and decorative arts that date from the 1790s-1840. Many objects were possessions of the Richardson and Owens families, and the remaining collections were mostly owned by other Savannah families of the same era and are now all part of the Telfair Museum of Art’s holdings.