Villa Mondragone is the largest of the ancient twelve Villas Tusculanum built in the fifteenth century as summer residence of the papal nobility and economic powers. In 1567 the cardinal Marco Sittico Altemps acquired the fund and promoted the works for the construction of the new factory, commissioning the project to Martino Longhi il Vecchio. In 1574 a first building was completed on the ruins of an ancient roman villa of the second century A.D. The name "Mondragone" refers to the heraldic dragon which occupies the central position in the coat of arms of the Boncompagni family (family name of Pope Gregorius XIII and great friend of the Altemps).

At the ending quarter of the sixteenth century, the Altemps made built another building that was called Retirata of Mondragone. In 1613 Cardinal Scipione Caffarelli Borghese, bought Villa Mondragone and after he started imposing and significant works of enlargement of the Villa under the direction of the Flemish architect Jan Van Santen, better known as Giovanni Vasanzio; probably there were also involved Carlo Maderno and Jacopo Mola di Coldrerio.

An engraving by Matteo Greuter of 1629 shows the massive construction completed and very like at the present age. The original constructions of the Altemps, the Casino and the Retirata, were welded into a single building block on the west side, while at the east, the building was placed side by side by the new Garden of weathervane concluded by monumental Ninfeo upstream, and by the Portico (called the Vasanzio) downstream.

In the middle of Terrazzone, that closed the plant toward the valley, and it framed everything with four pinnacles, there is the magnificent Dragon fountain. At that time, even the majestic Portale delle Armi, access to the vast field of residential villas of the so called Status Borghesianum, was already built. In 1626 the new Pope Urban VII moved the papal summer residence Castel Gandolfo marking the start of a gradual decline of the entire complex of Villas of Tusculanum and in particular of Mondragone. In 1865 the Villa was used by the Jesuits for an important educational institution: the Noble College of Mondragone whose activity gained and maintained international fame lasted until 1935. In 1981 the Villa was sold by the Company of Jesus at the University of Rome Tor Vergata in order to be used, after initial interventions of restoration, such seat for important national and international conferences.