Supplemental Table 4. Limitations to the timeline analyses

Date of first final protocol is the earliest date available to perform any analysis.	Uncertainty regarding the amount of time spent into planning the clinical development program before finalizing the first protocol. The planning around the first-in-man clinical study is unknown. Therefore, the time elapsed before a decision was taken to finalize the first clinical study protocol remains speculative.
Country-specific effects were not investigated.	The choice of countries can influence the initiation of a study, as the regulatory and ethical approvals may differ and, in part, depend on the date of submission by the sponsor. In a multinational clinical study, numerous factors can influence the recruitment (FSI dates and overall recruitment), including translations, validation of patient-reported outcomes and country-specific amendments (where required). In the European Union Clinical Trial Registry, the individual approval dates of each member state could have been accessed. However, there were numerous non-EU countries; hence, a full analysis was not possible.
The impact of protocol amendments on timelines was not assessed.	It was not possible to estimate the individual effect of a protocol amendment on the recruitment timelines. Protocol amendments are implemented for several reasons, including revisions to the inclusion and exclusion criteria of subject recruitment as new data becomes available from other clinical studies in the clinical development of the substance, or in the same medication class. A protocol amendment may accelerate the completion of the study; however, it may also result in the prolongation of recruitment (eg, if a safety signal has been detected in the CDP leading to a revision in the exclusion criteria). Furthermore, there is uncertainty with respect to the countries which required a local protocol amendment.
Change in clinical development sponsor or the impact of co-development in clinical development, or the impact of a different marketing authorization holder to the clinical development sponsor.	The initial sponsor may have merged with or been acquired by another pharmaceutical company. This could explain project drag and the interruptions in the F/TAF, FTC+RFV+TAF and eluxadoline CDPs, where the sponsor named on the CSRs changed over the course of the CDP.[16]
The impact of the experience of clinical development and each study team was not assessed.	This information was not available. It would require the names *Curriculum Vitae* of the study team members to be available and incorporated into this analysis.
The impact of hiring additional expertise (eg, external vendors) on the timelines could not be analyzed.	The information on vendors was normally redacted.