

**Table 1.** Current and selected investigational bone anabolic therapies in clinical trials

| Name                                  | Active molecule                                                         | Mode of administration | Dose(s)                                                   | Indication  | References and/or ClinicalTrials.gov identifier                   | Manufacturer/Sponsor                             |
|---------------------------------------|-------------------------------------------------------------------------|------------------------|-----------------------------------------------------------|-------------|-------------------------------------------------------------------|--------------------------------------------------|
| <b>Phase III trials and beyond</b>    |                                                                         |                        |                                                           |             |                                                                   |                                                  |
| PTH (1-34) (teriparatide)             | 1-34 amino acid PTH analog                                              | SC inj                 | 20 µg daily                                               | PO, MO, CIO | (16), (18), (19)                                                  | Eli Lilly and Company                            |
| PTH (1-84)*                           | Full-length PTH analog                                                  | SC inj                 | 100 µg daily                                              | PO          | (17)                                                              | NPS Pharmaceuticals, Inc                         |
| <b>Phase II trials</b>                |                                                                         |                        |                                                           |             |                                                                   |                                                  |
| TPTD-P                                | Adhesive patch coated with teriparatide on a titanium microneedle array | Transdermal patch      | 20, 30 or 40 µg in 30 minutes wear-time                   | PO          | (28)                                                              | Zosano Pharma Inc                                |
| PTHrP(1-36)                           | PTH related peptide analog                                              | SC inj                 | 400 µg or 600 µg daily                                    | PO          | (43),<br>(NCT00853723)                                            | University of Pittsburgh                         |
| AMG 785                               | Sclerostin neutralizing monoclonal antibody                             | SC inj                 | 70, 140 and 210 mg                                        | PO          | (99)<br>(NCT00896532)                                             | Amgen Inc                                        |
| rhBMP-2/CPM                           | Bone morphogenic protein -2 in injectable calcium phosphate matrix      | intraosseous inj       | 1.0 and 2.0 mg / mL as supplementation to bisphosphonates | PO          | (NCT00752557)                                                     | Wyeth                                            |
| <b>Phase I trials</b>                 |                                                                         |                        |                                                           |             |                                                                   |                                                  |
| ZT-031 (ostabolin-C)                  | Cyclic 31-amino acid PTH analog                                         | SC inj **              | 7.5, 15, 30 or 45 µg                                      | PO          | (30)                                                              | Zelos Therapeutics and Aegis Therapeutics        |
| AMG 167                               | Sclerostin neutralizing monoclonal antibody                             | SC inj                 | 70, 140 or 210 mg daily (women) and 70 or 210 mg (men)    | PO, MO      | (NCT01101048)                                                     | Amgen Inc                                        |
| RN564                                 | Anti-DKK1 monoclonal antibody                                           | IV infusion            | Escalating doses                                          | PO          | (NCT01293487)                                                     | Pfizer Inc                                       |
| PTH134                                | Teriparatide formulation with absorption enhancer 5-CNAC                | Per os                 | 2.5 or 5 mg                                               | PO          | (NCT01224717)                                                     | Novartis Pharmaceuticals                         |
| <b>Trials terminated at Phase II</b>  |                                                                         |                        |                                                           |             |                                                                   |                                                  |
| SB-751689 (ronacaleret hydrochloride) | CaSR negative allosteric modulator (antagonizing)                       | Per os                 | 100, 200, 300 or 400 mg                                   | PO          | (NCT00471237)<br>[A follow-up observational study in (CR9112792)] | GlaxoSmithKline Inc and NPS Pharmaceuticals, Inc |
| PTH (1-34) nasal spray                | Teriparatide formulation                                                | Intranasally (spray)   | Dose-Ranging                                              | PO          | NCT00624481                                                       | Nastech Pharmaceutical Company, Inc.             |

PTH: Parathyroid hormone; SC: subcutaneous; inj: injectable; PO: postmenopausal osteoporosis; MO: Male osteoporosis; CIO: corticoid-induced osteoporosis; PTHrP: Parathyroid hormone related peptide; Inc: Incorporation; IV: Intravenous; Dkk1: Dickkopf protein 1; mg: milligram; µg: microgram; CaSR: Calcium Sensing Receptor.

\*Approved in Europe; \*\*Manufacturer (Zelos) announced an intranasal administration system to be investigated for both ostabolin-C (ZT-034) and teriparatide (ZT-031)