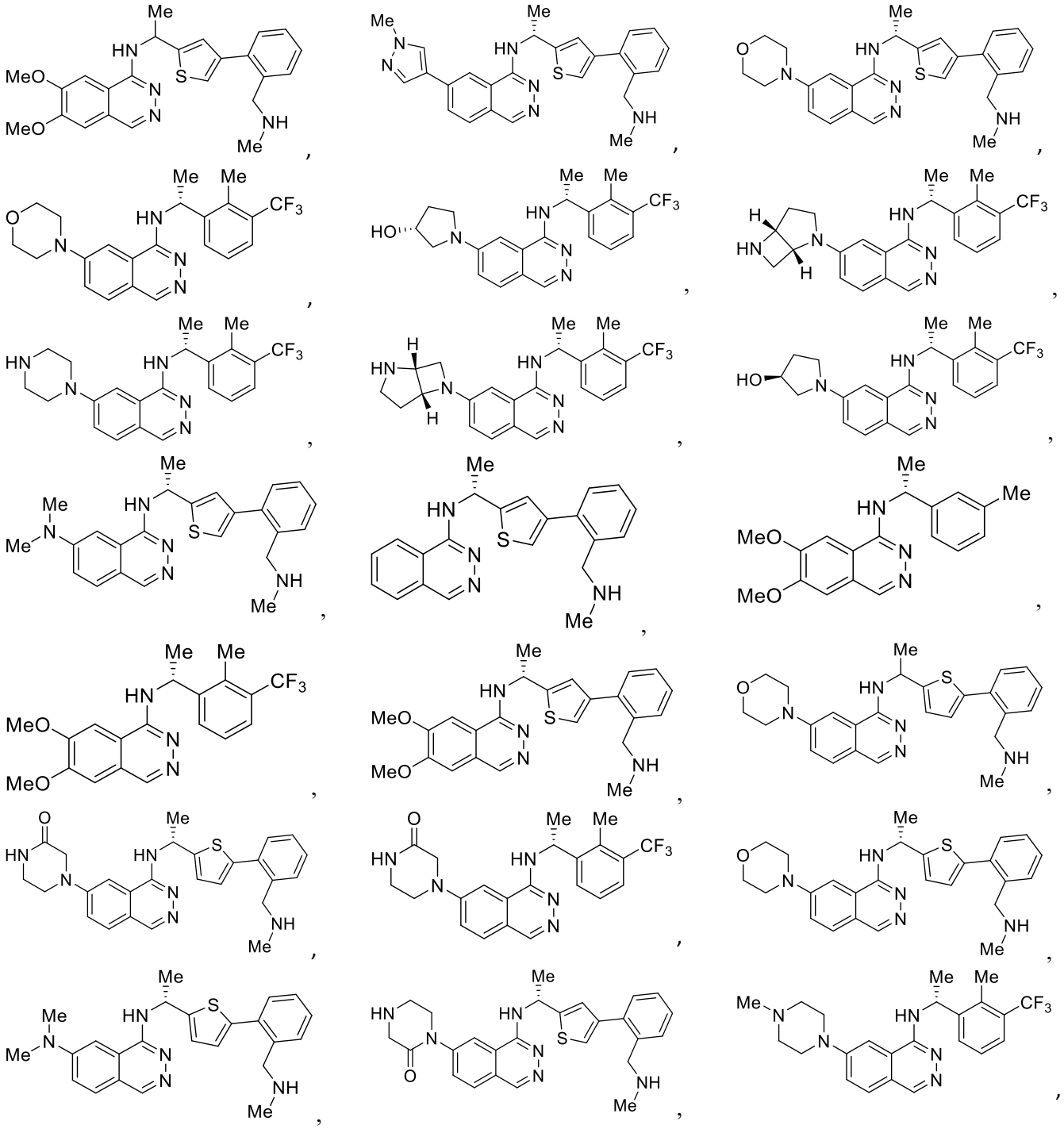
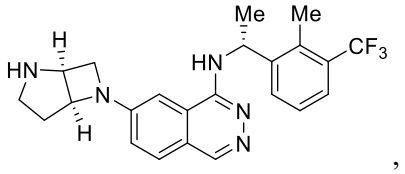
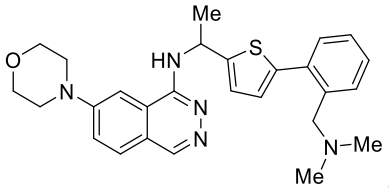
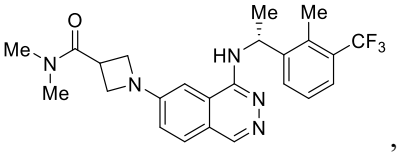
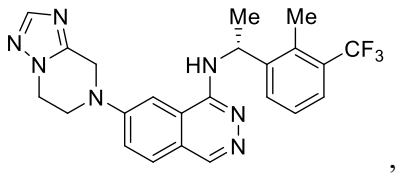
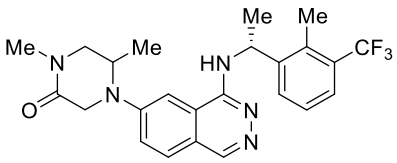
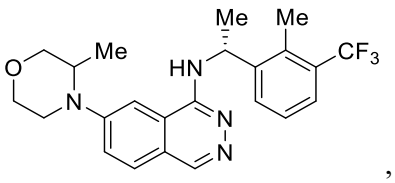
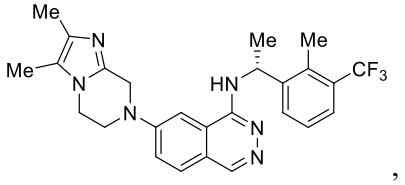
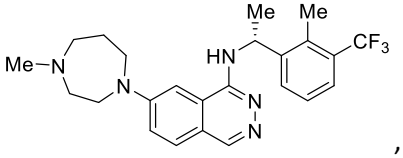
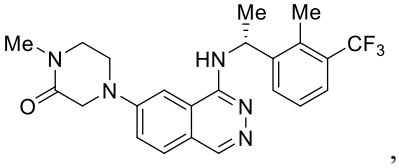
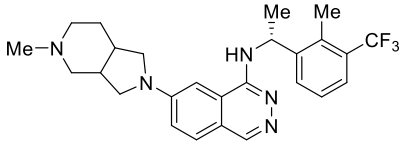
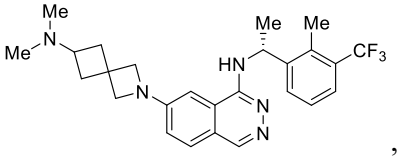
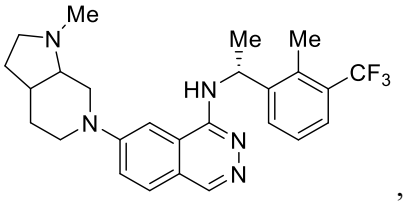
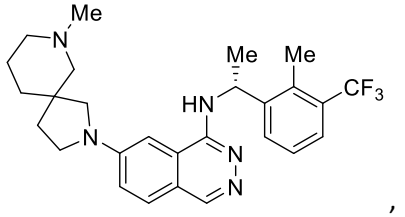
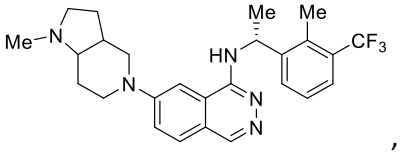
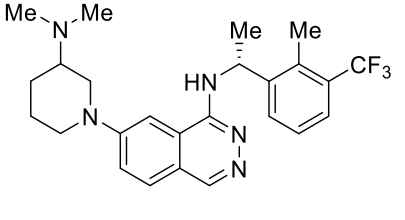
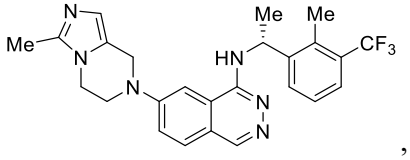
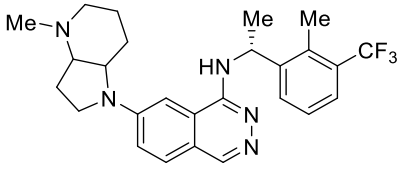
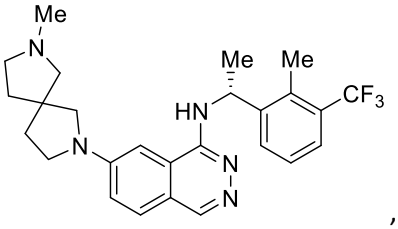
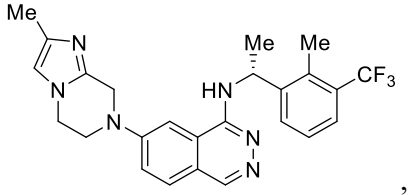
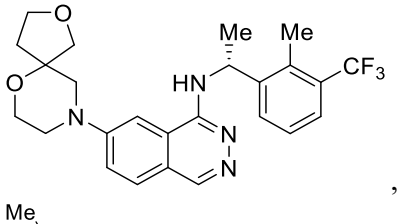
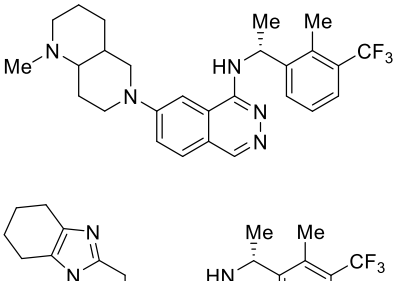
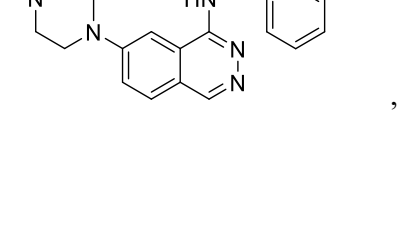
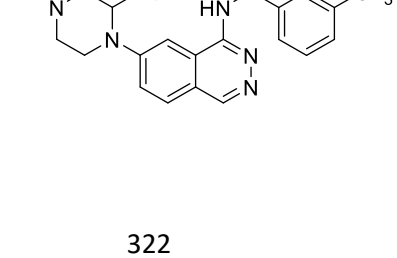
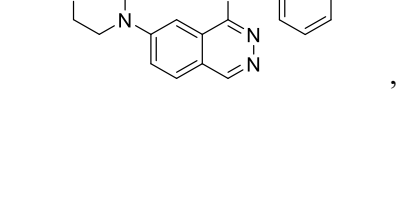
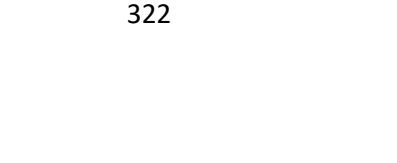
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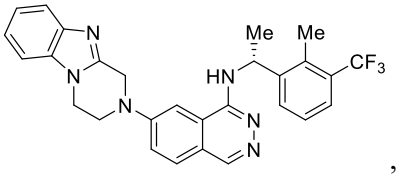
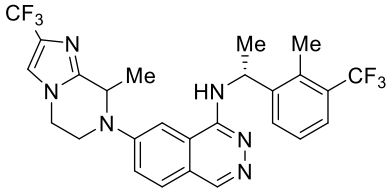
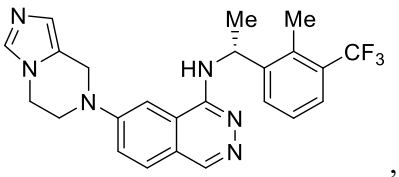
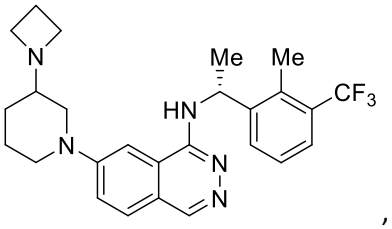
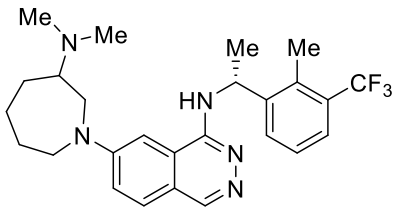
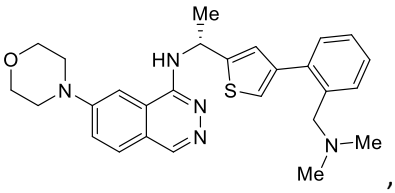
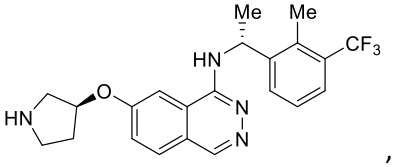
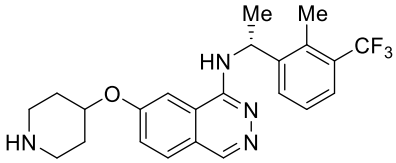
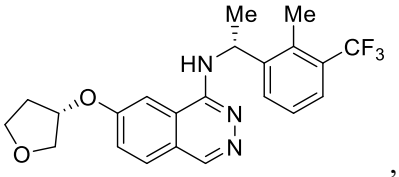
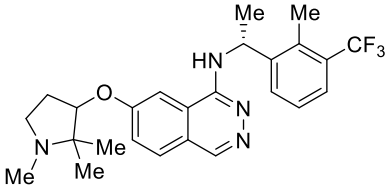
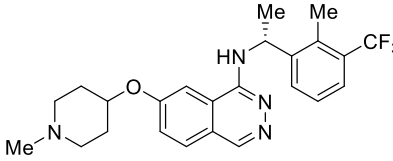
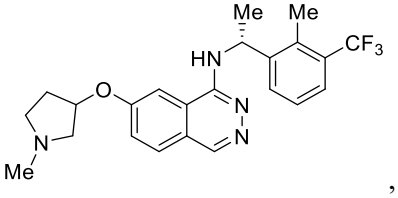
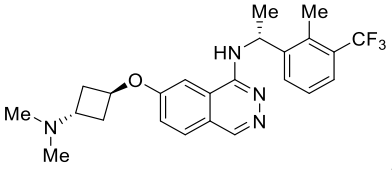
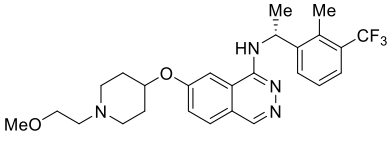
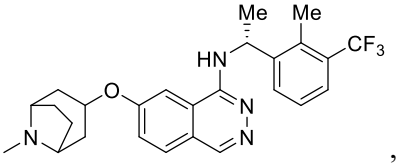
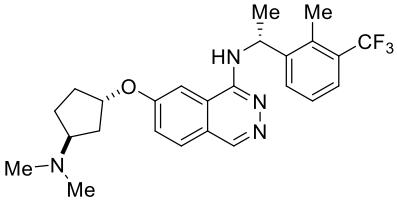
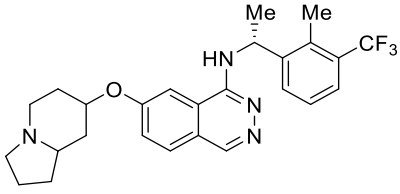
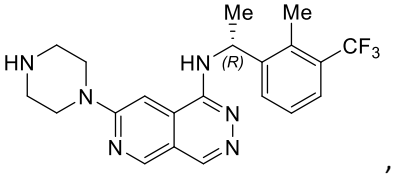
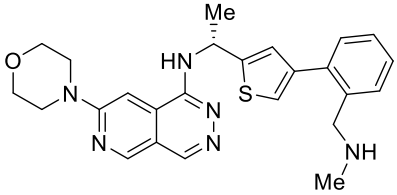
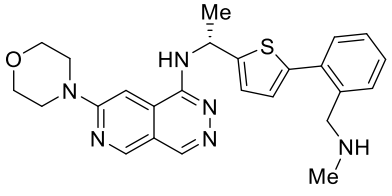
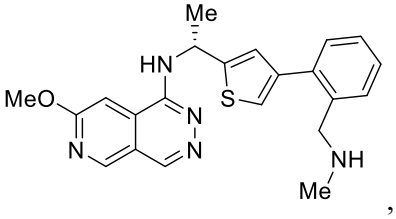
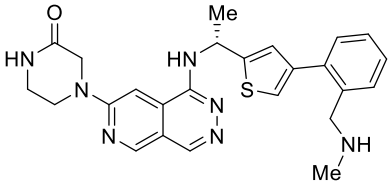
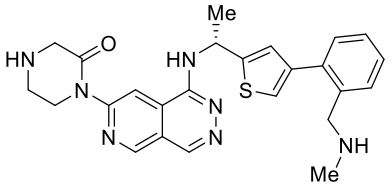
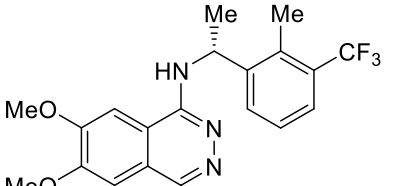
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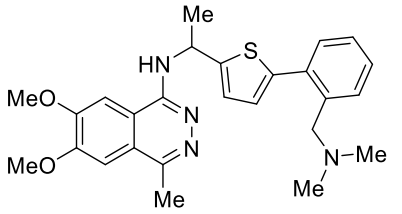
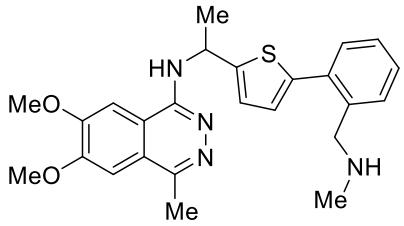
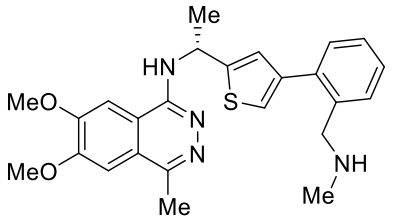
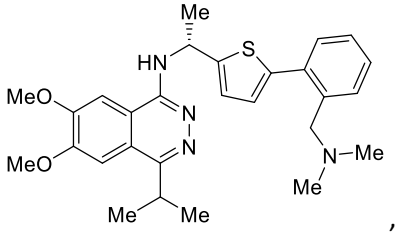
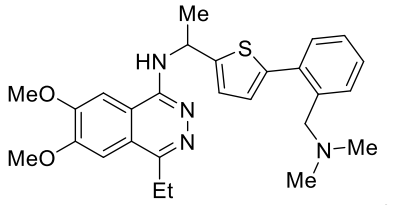
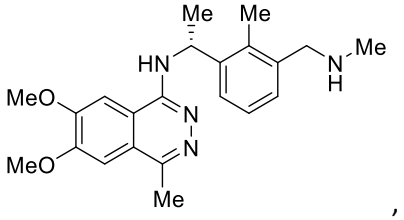
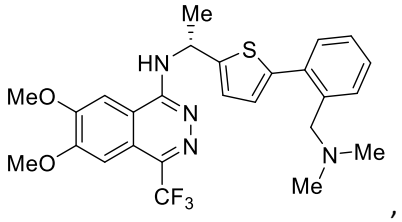
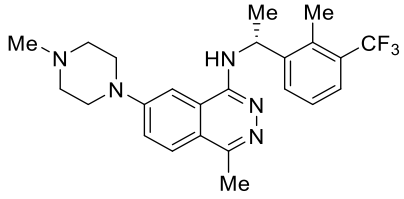
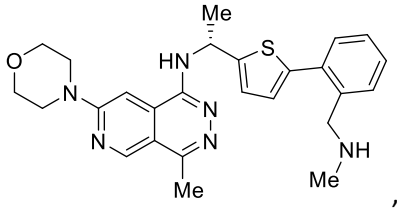
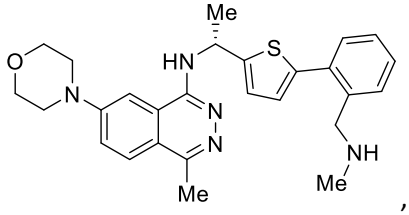
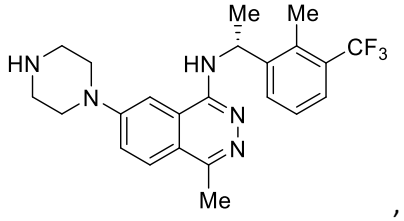
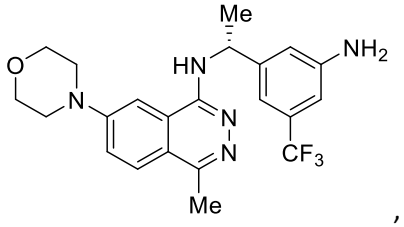
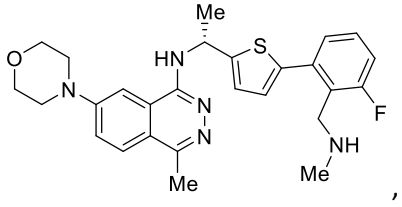
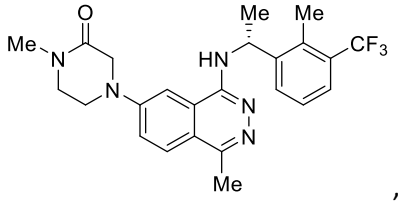
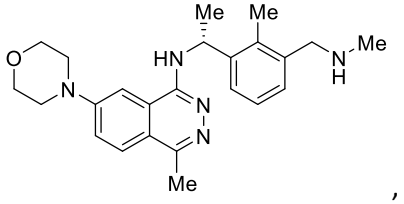
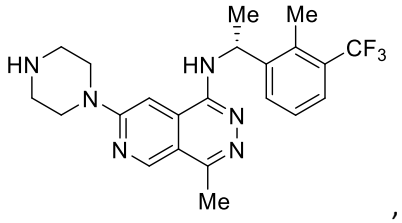
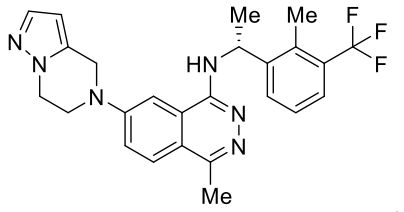
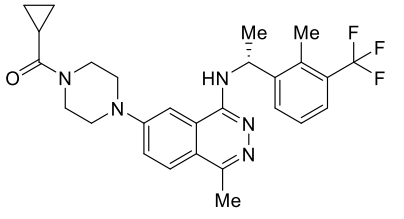
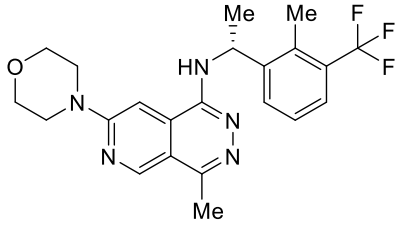
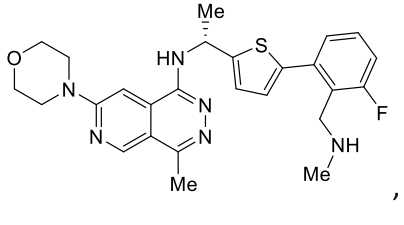
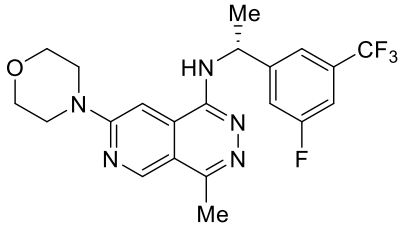
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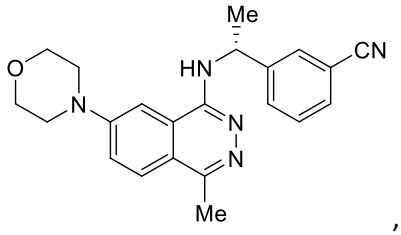
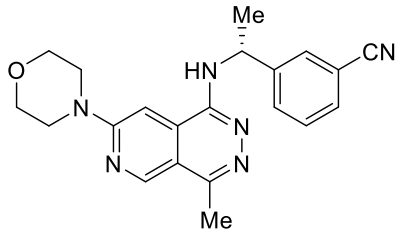
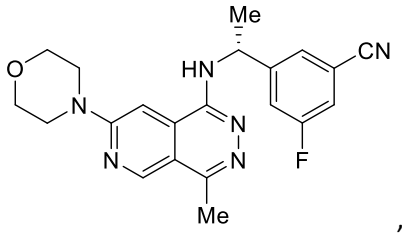
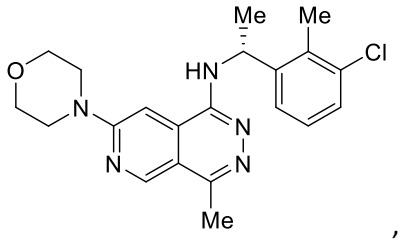
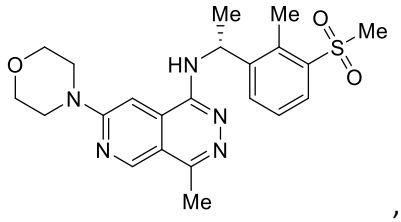
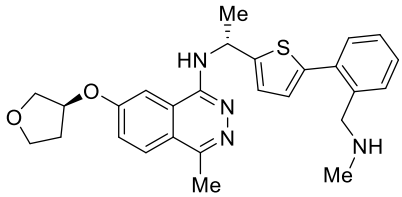
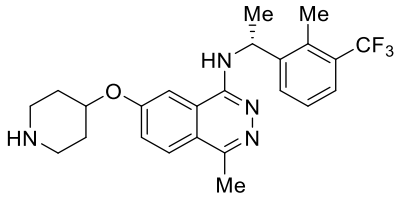
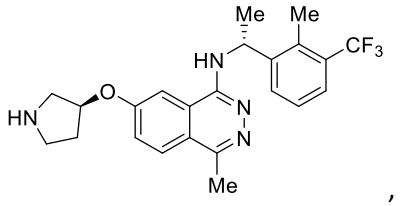
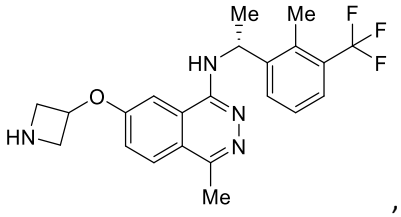
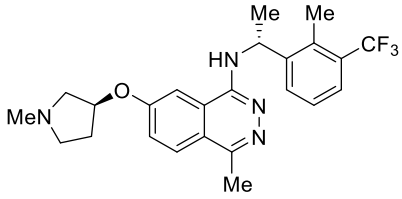
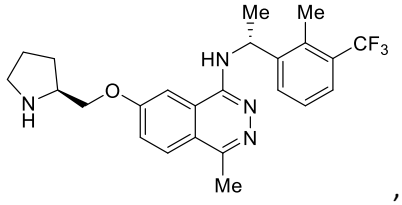
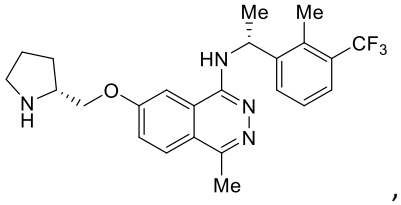
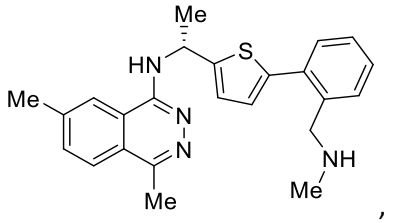
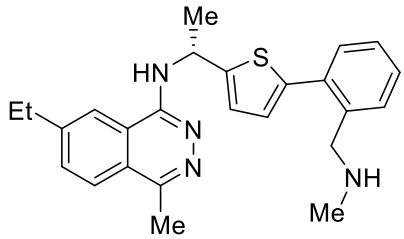
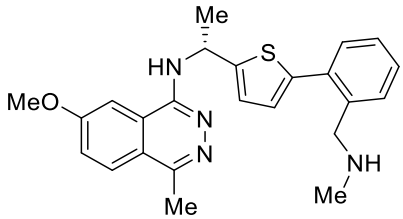
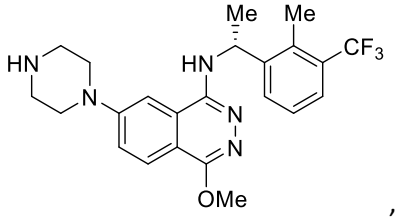
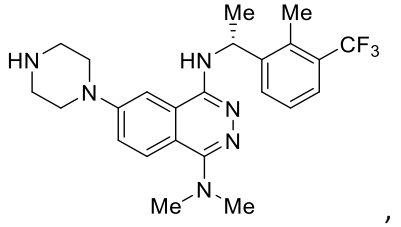
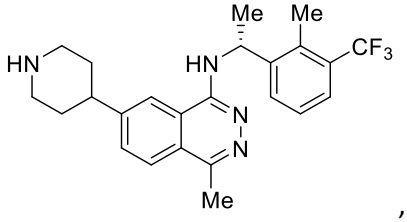
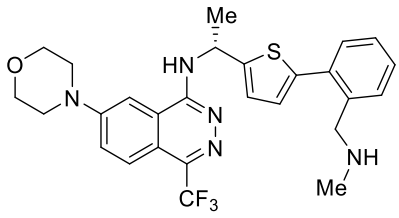
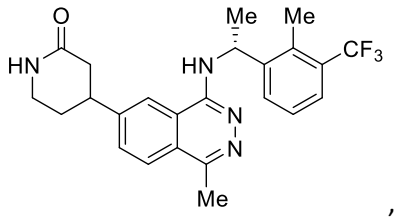
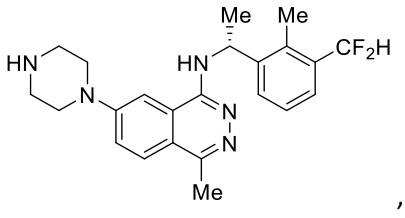
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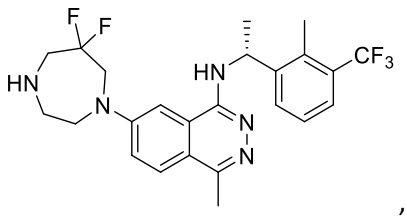
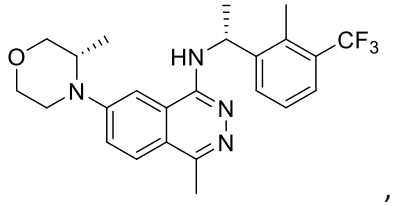
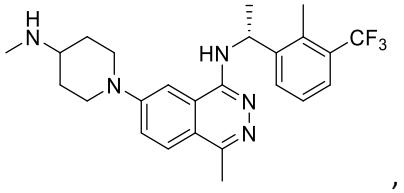
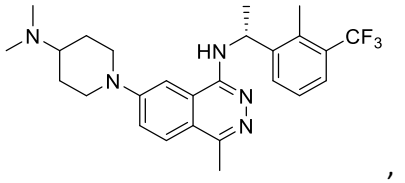
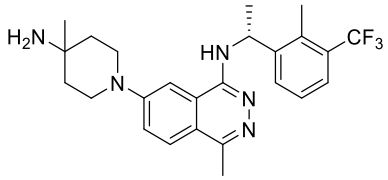
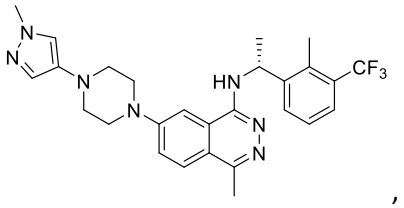
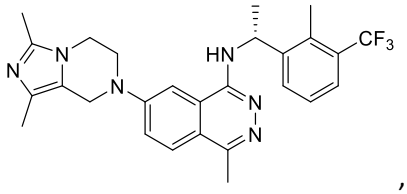
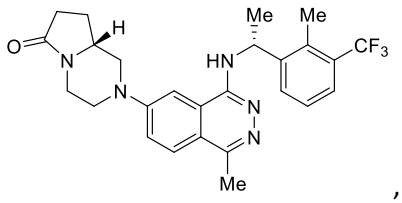
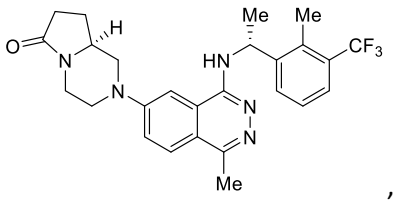
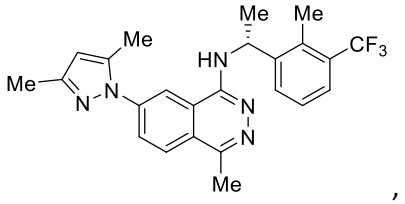
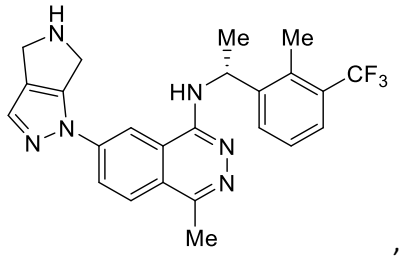
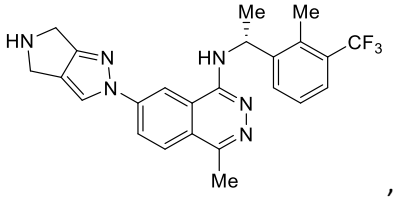
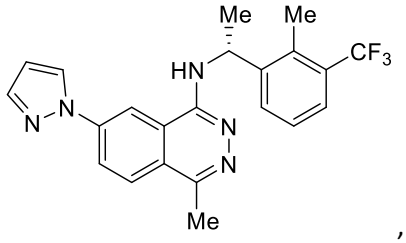
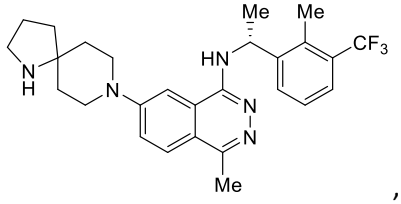
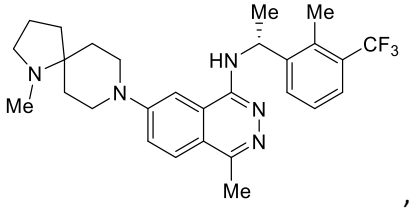
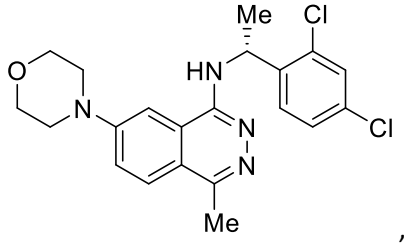
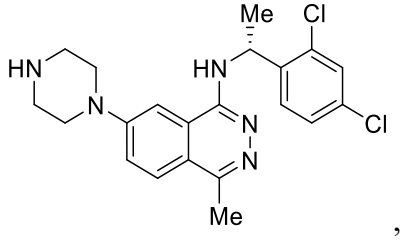
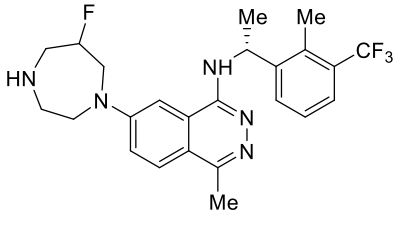

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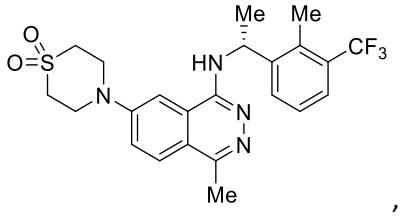
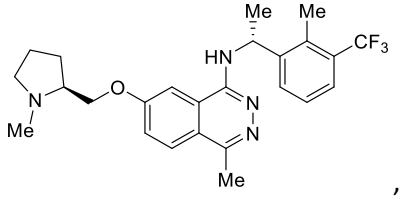
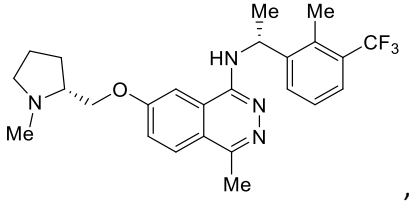
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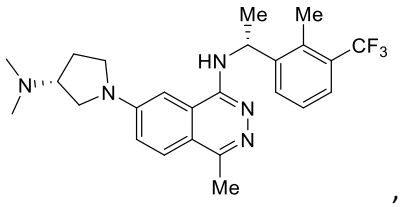
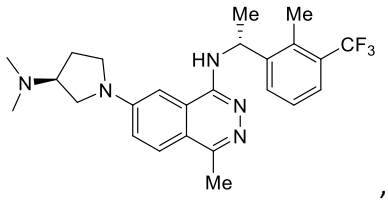
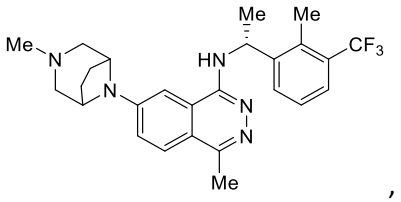
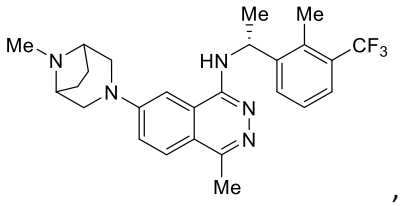
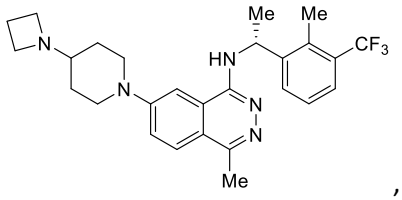
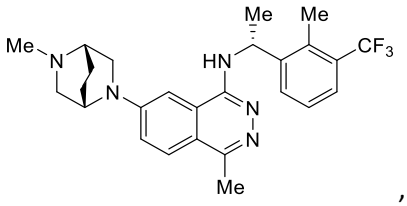
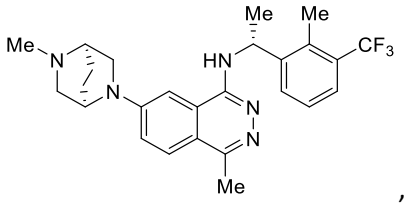
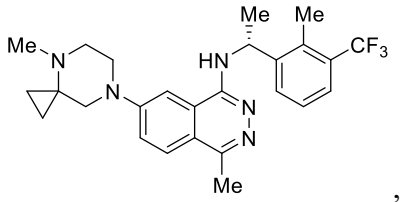
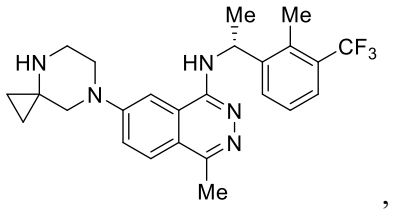
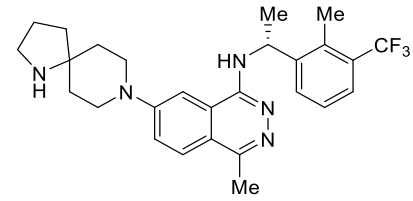
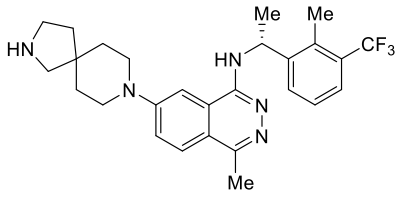
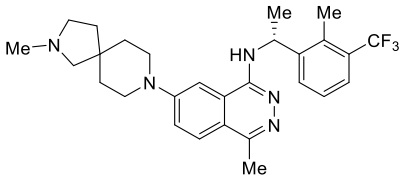
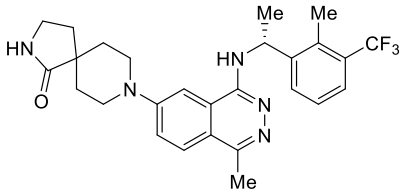
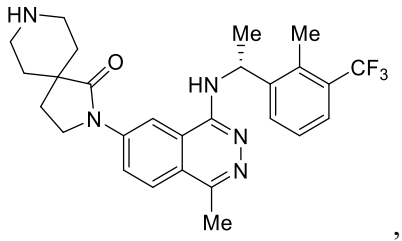
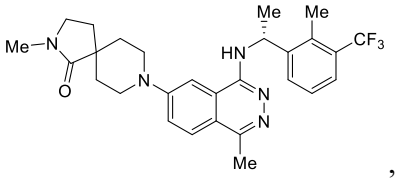
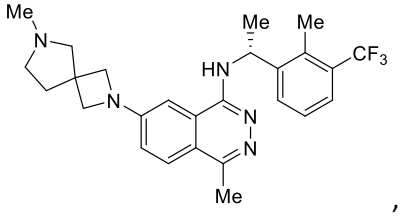
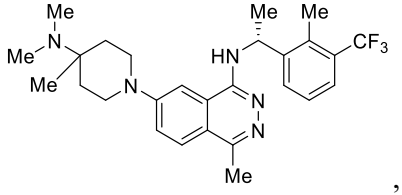
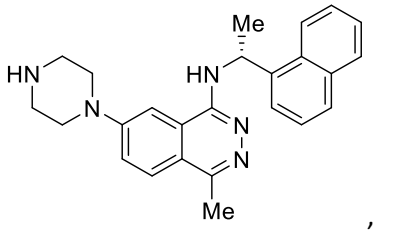
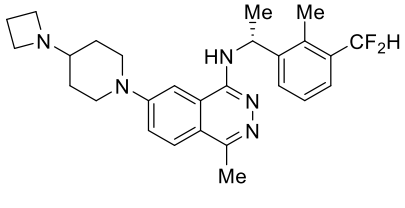
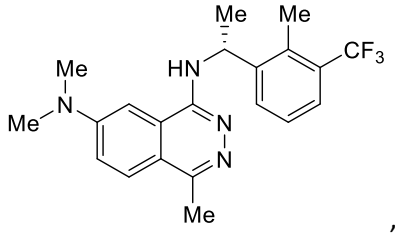
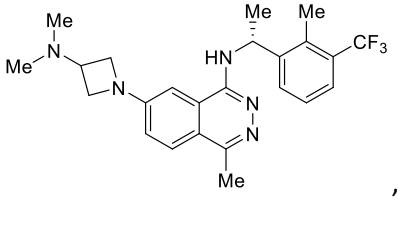
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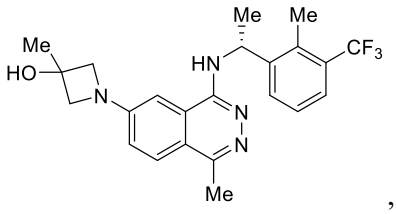
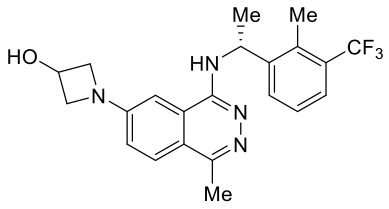
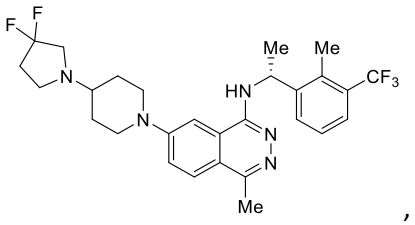
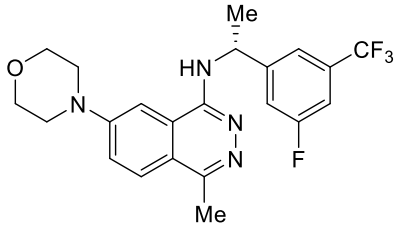
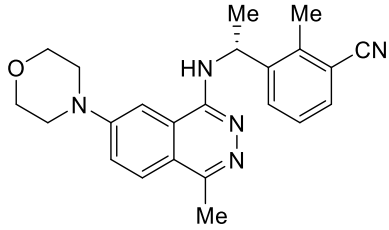
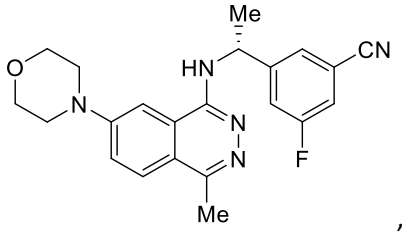
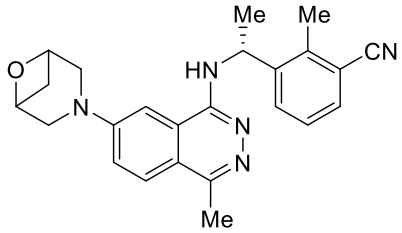
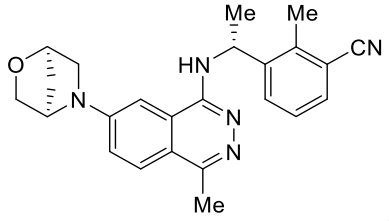
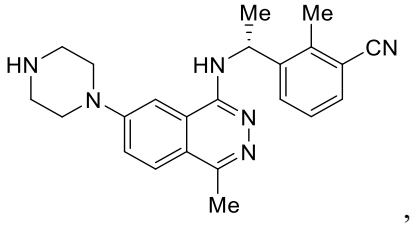
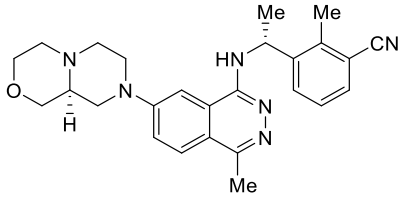
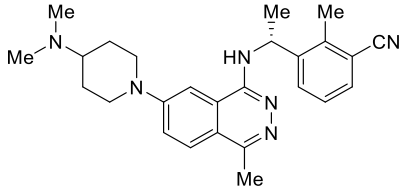
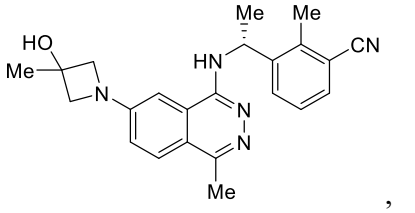
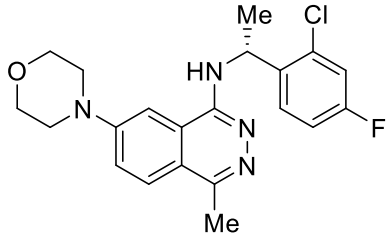
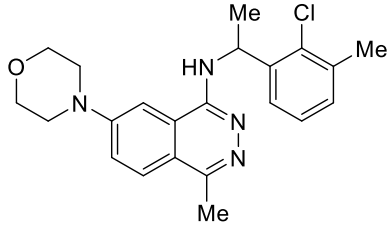
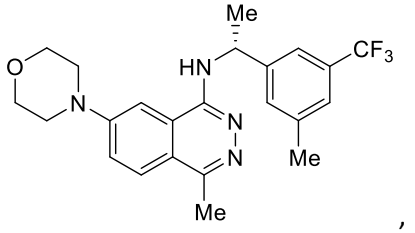
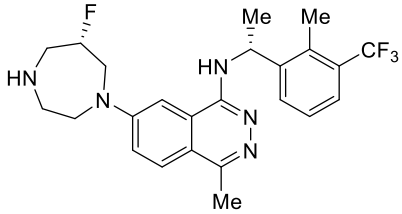
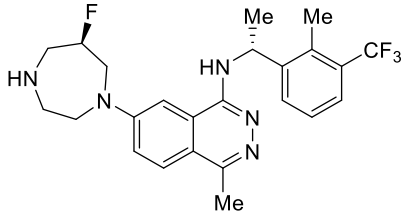
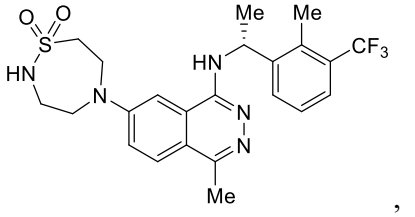
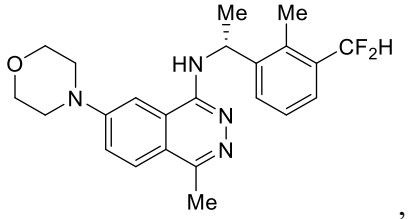
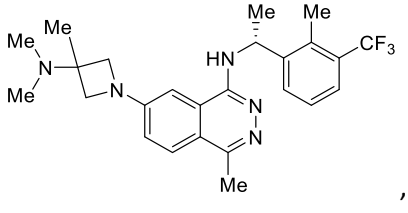
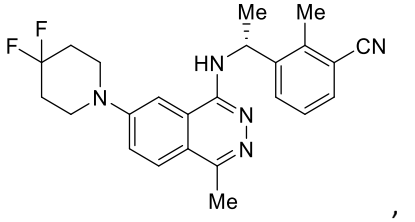
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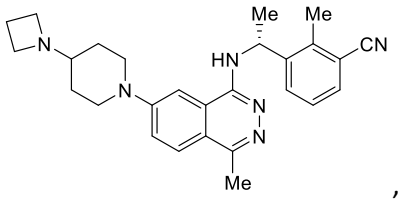
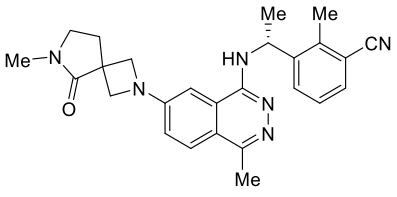
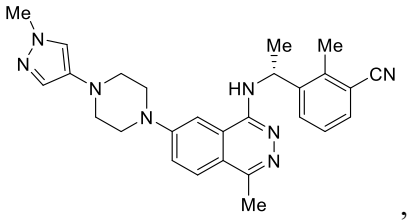
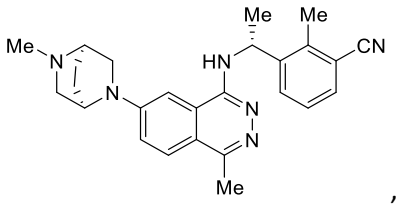
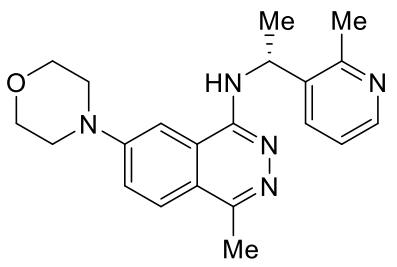
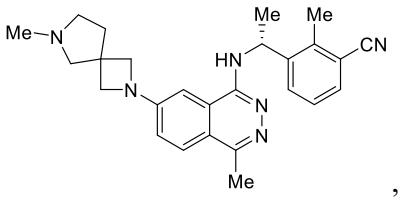
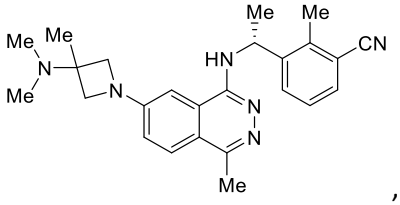
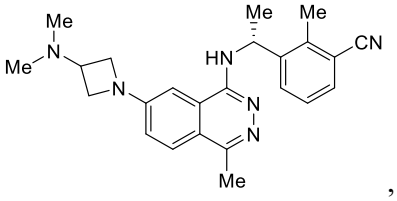
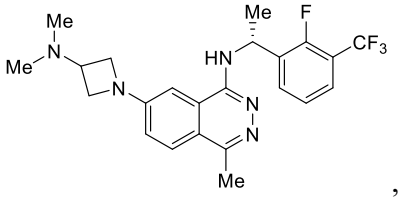
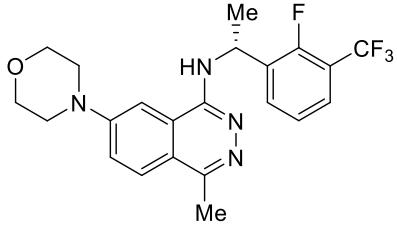
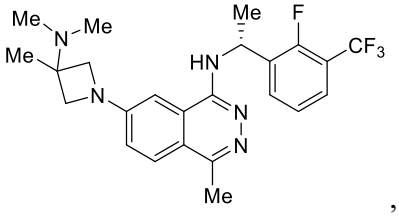
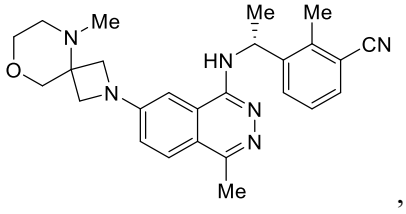
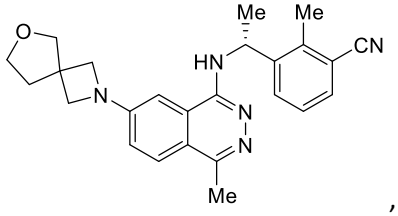
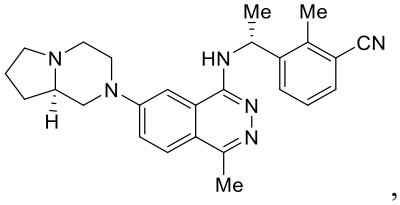
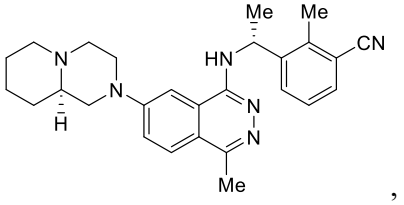
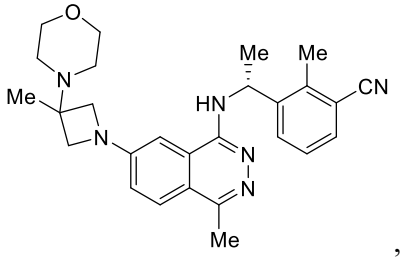
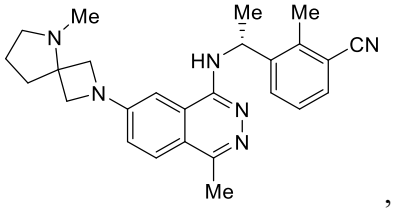
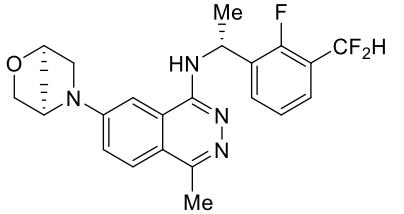
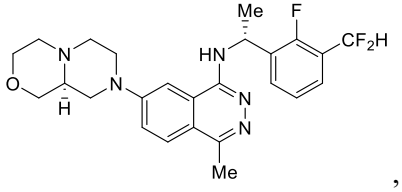
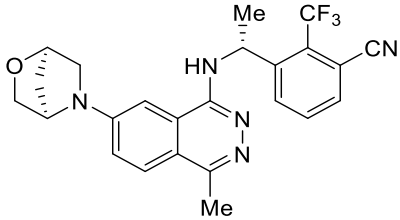
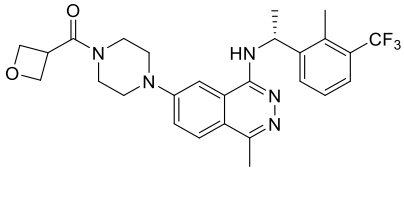

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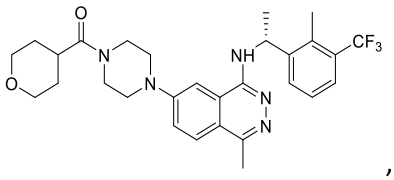
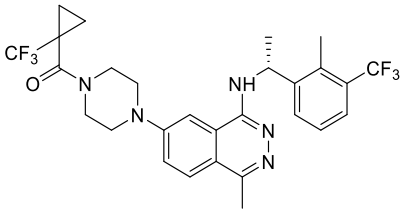
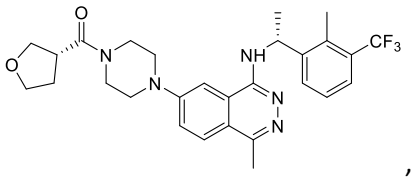
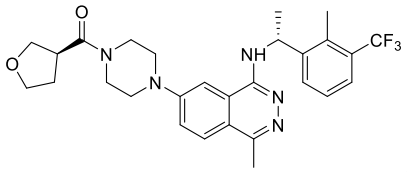
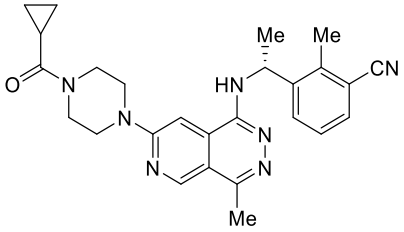
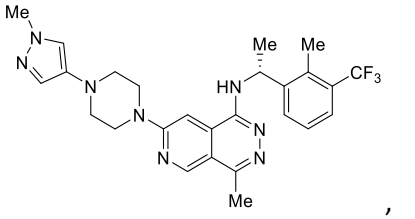
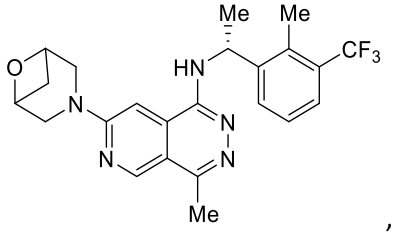
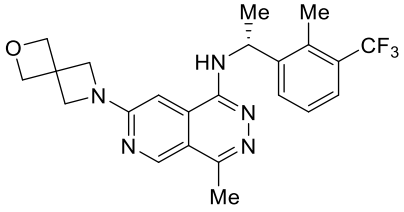
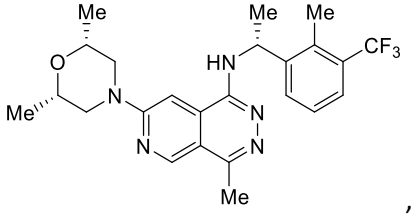
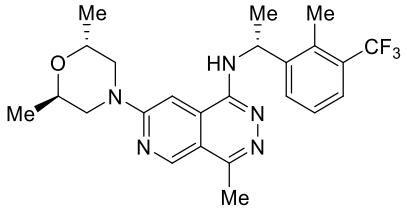
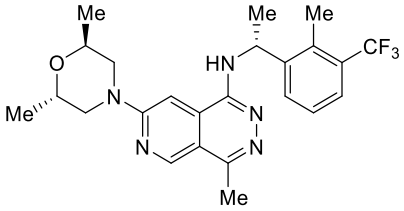
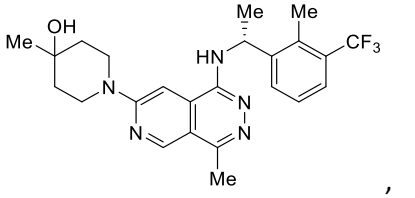
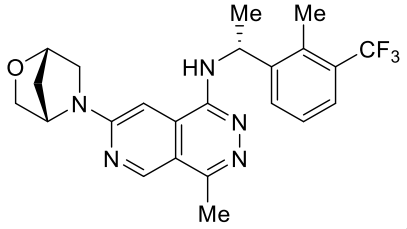
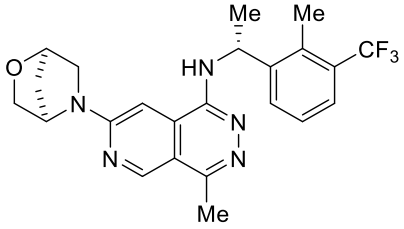
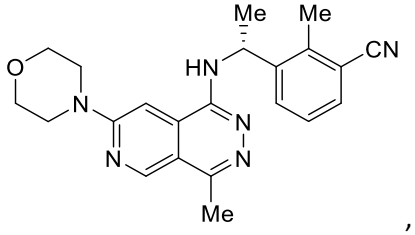
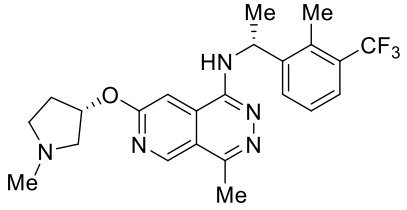
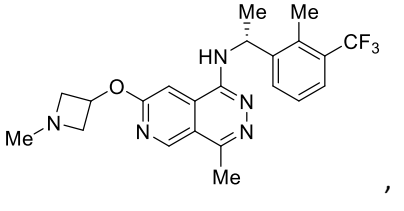
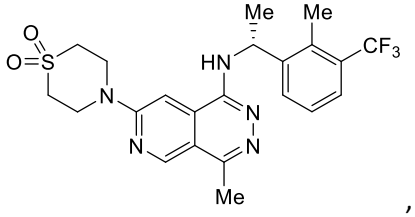
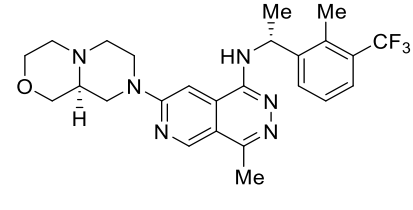
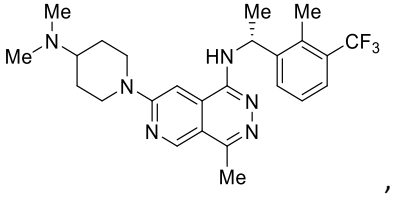
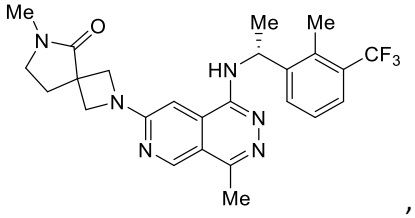

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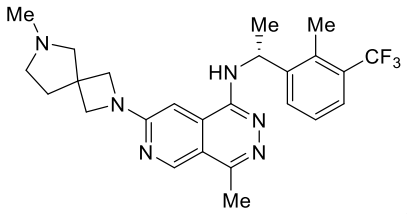
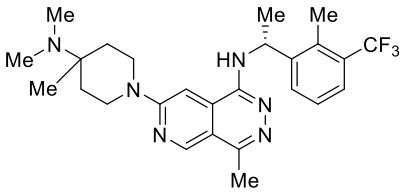
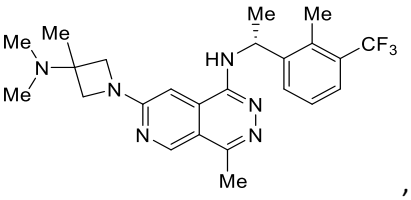
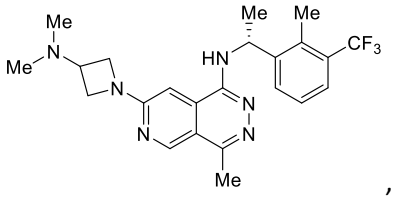
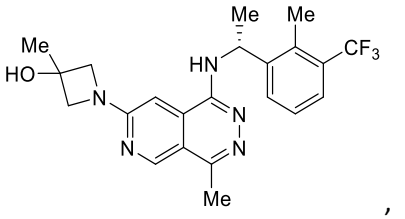
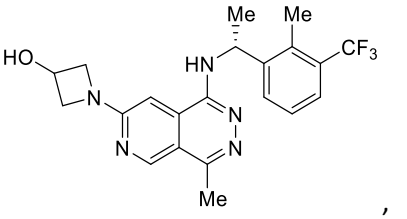
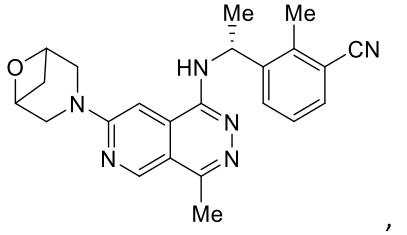
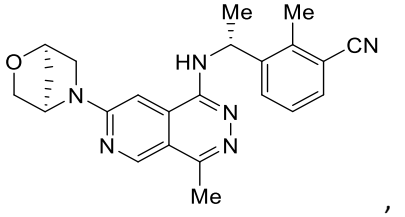
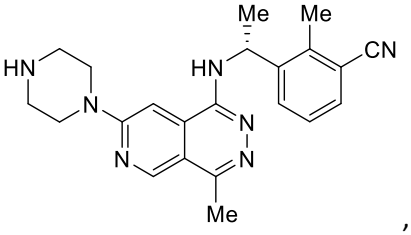
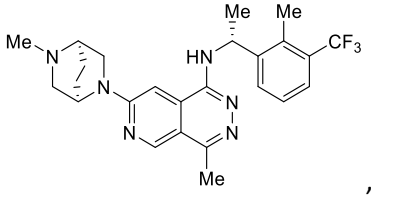
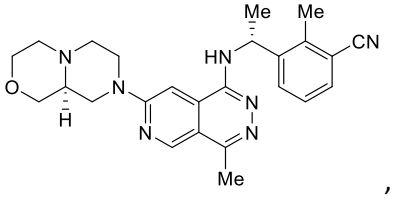
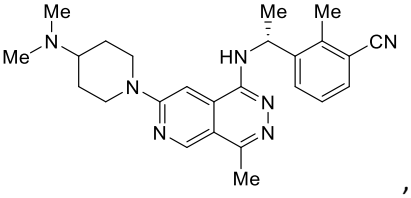
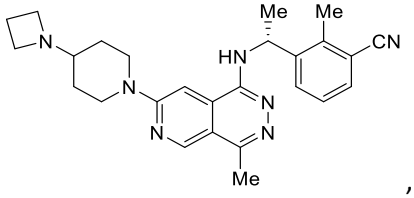
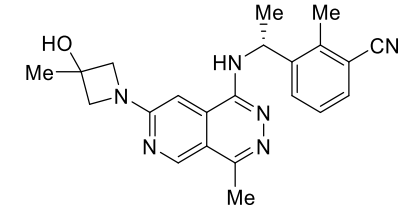
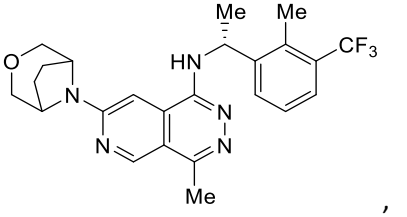
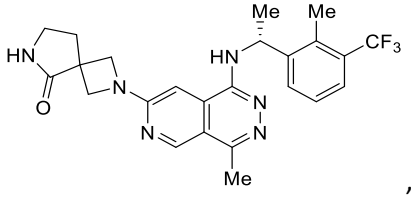
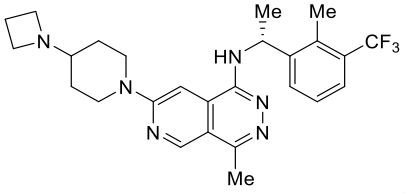
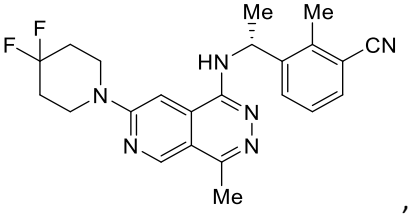
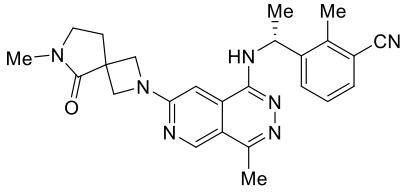
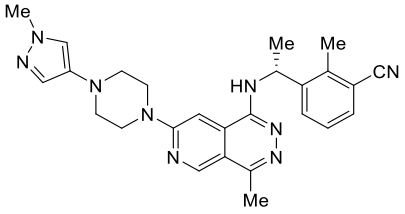
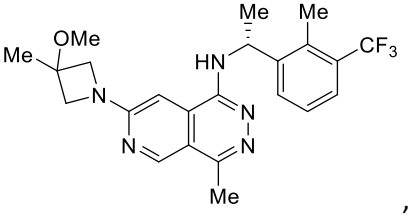
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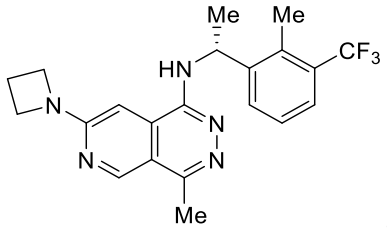
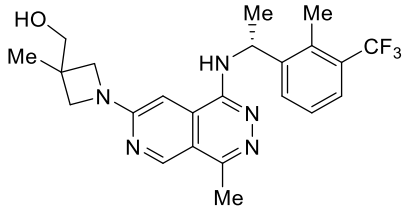
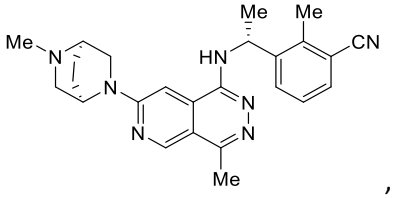
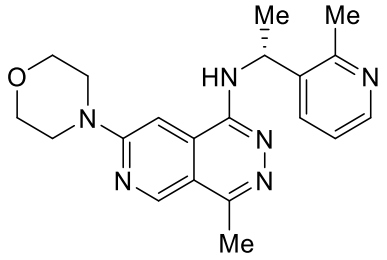
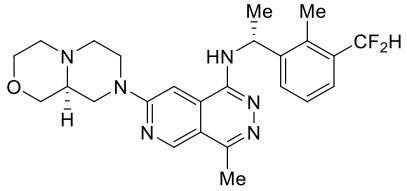
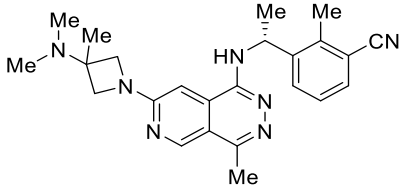
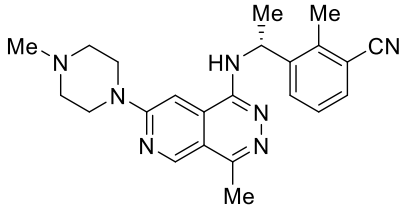
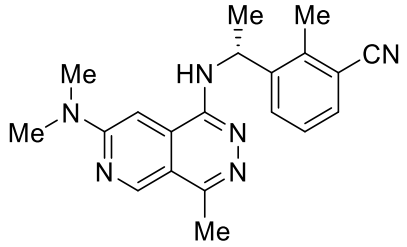
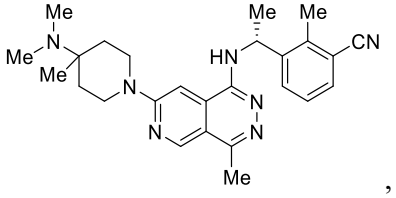
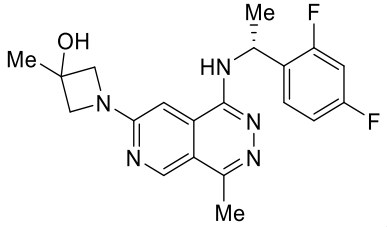
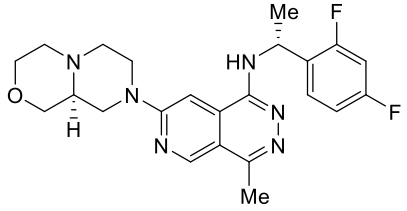
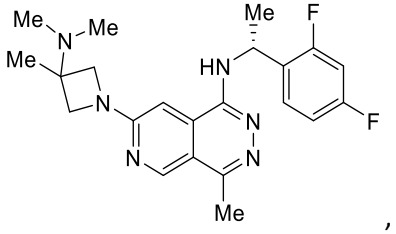
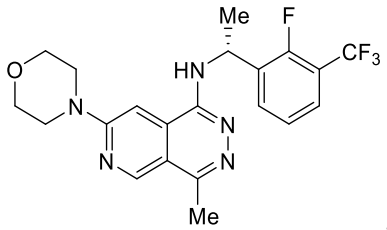
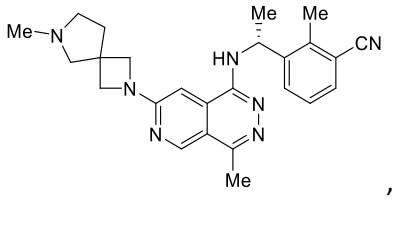
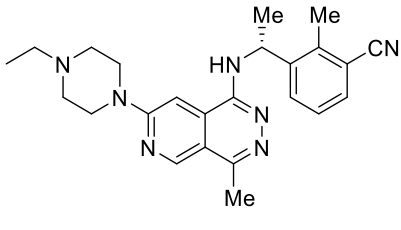
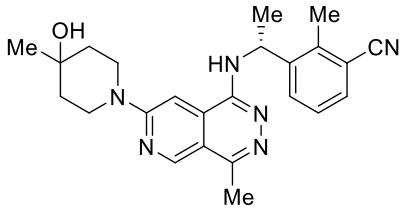
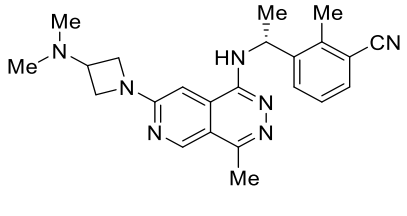
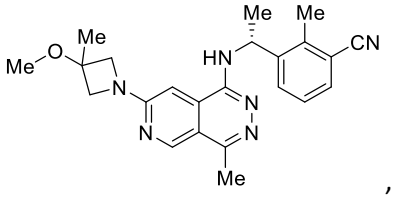
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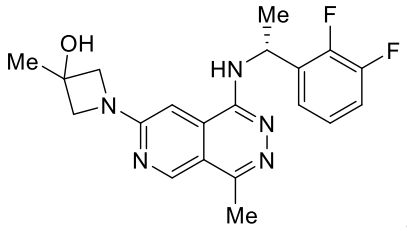
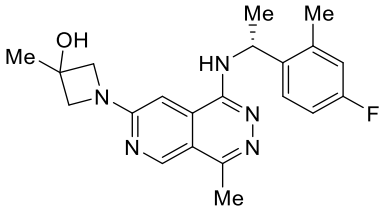
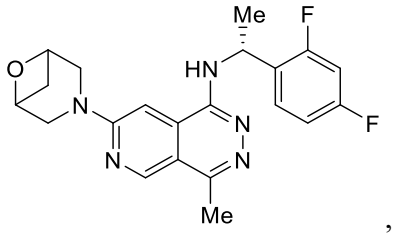
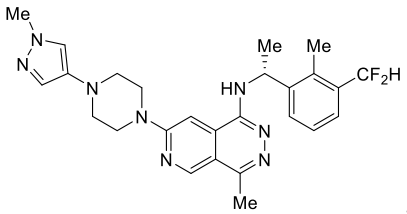
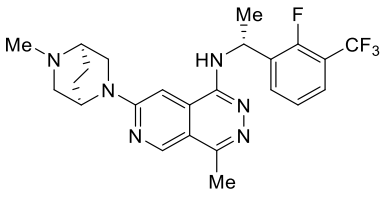
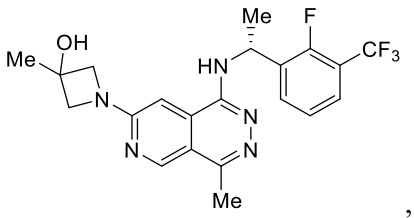
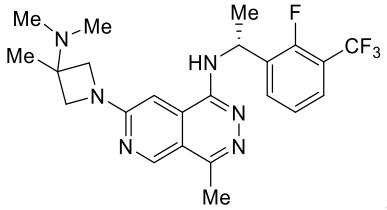
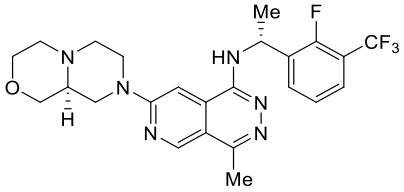
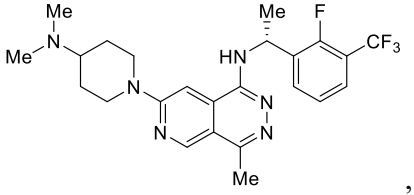
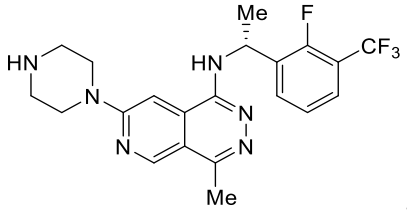
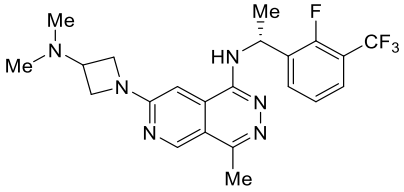
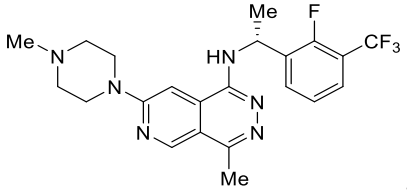
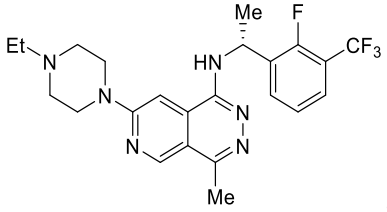
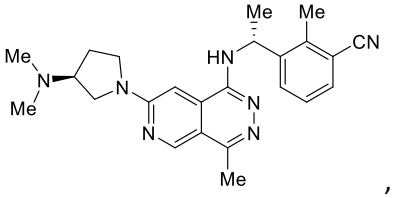
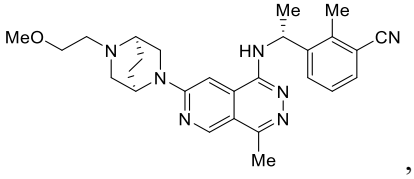
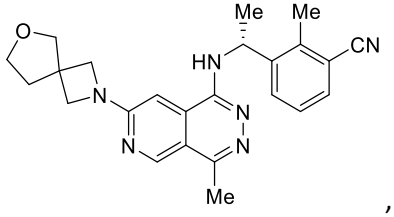
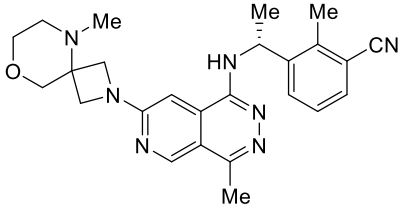
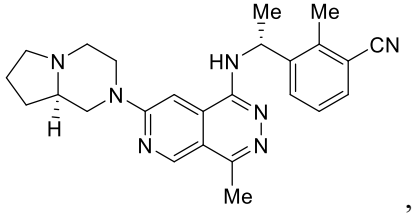
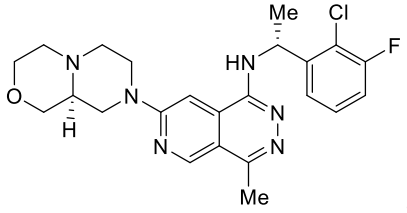
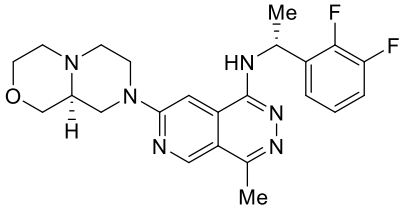
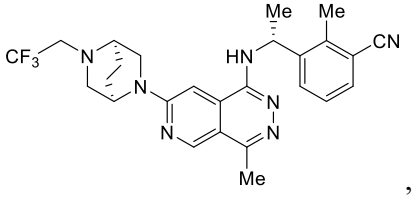
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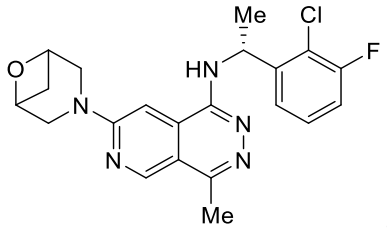
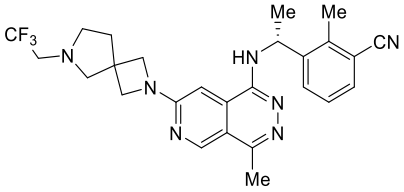
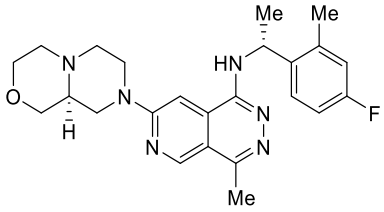
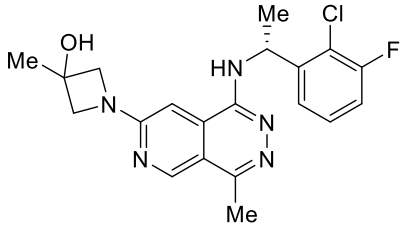
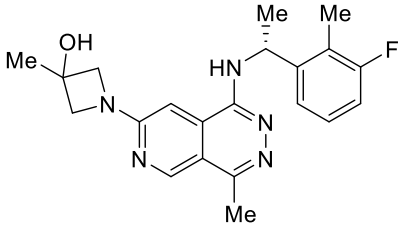
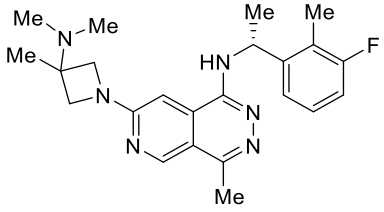
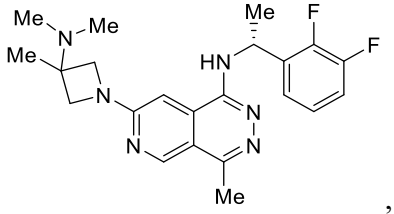
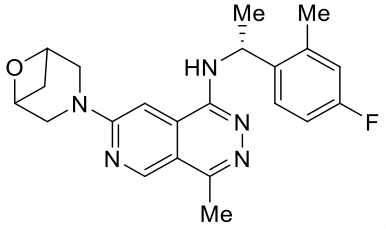
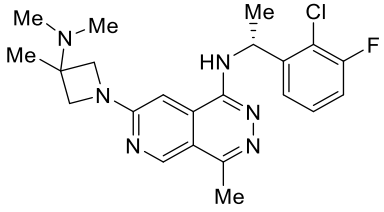
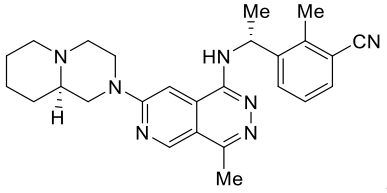
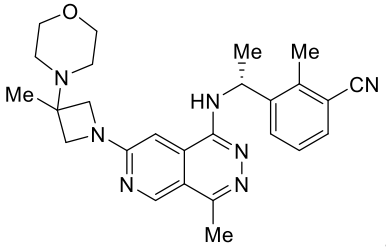
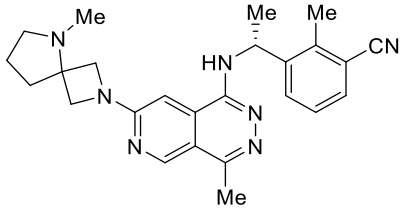
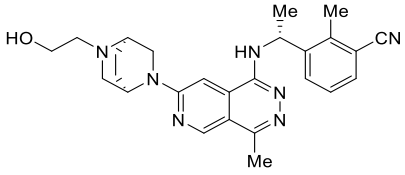
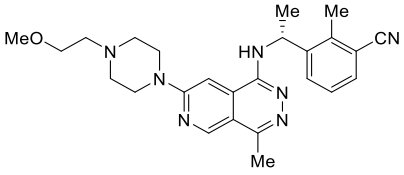
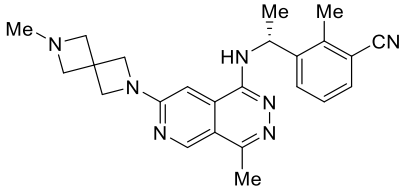
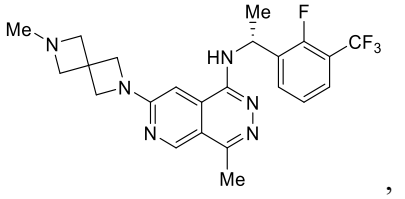
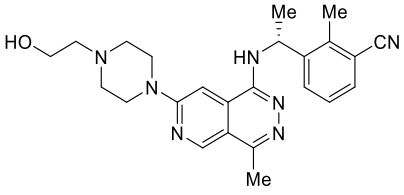
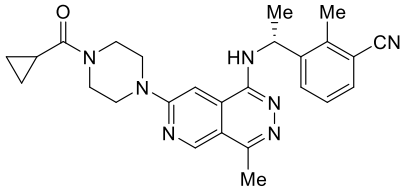
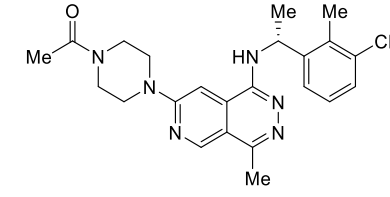
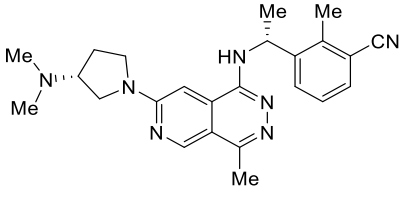
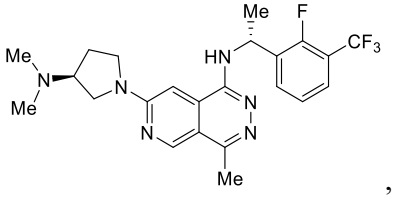
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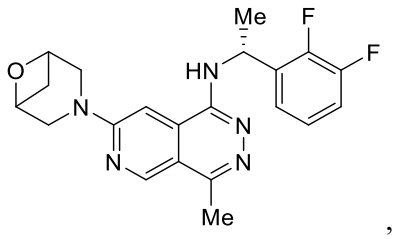
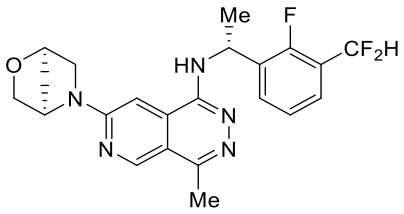
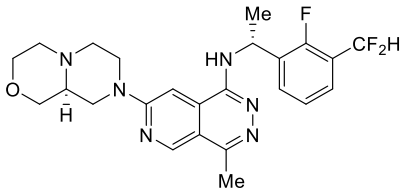
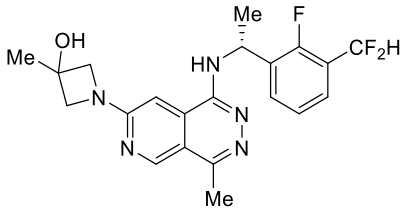
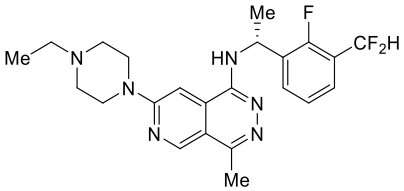
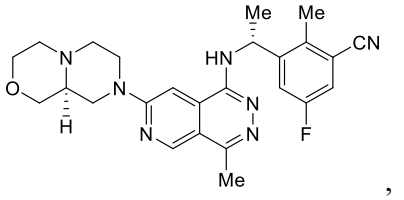
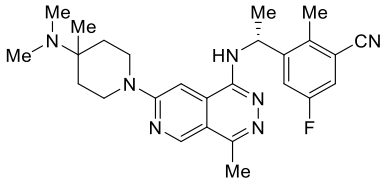
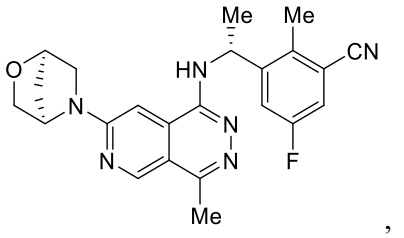
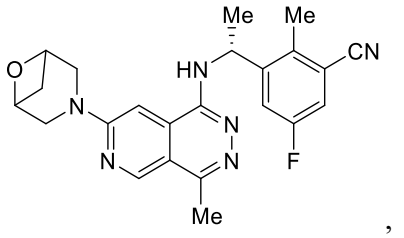
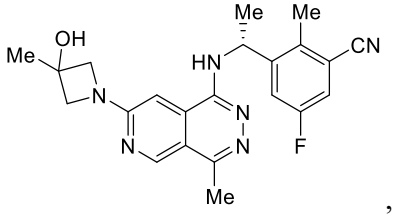
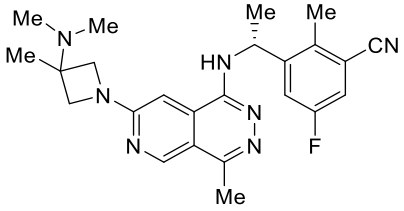
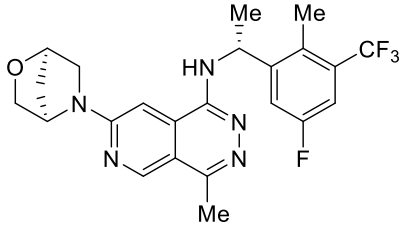
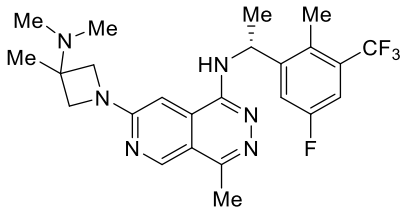
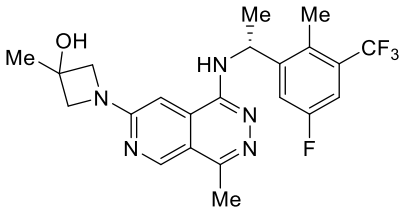
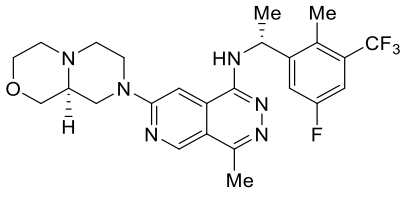
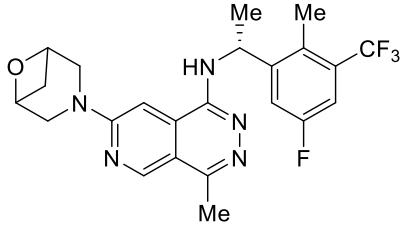
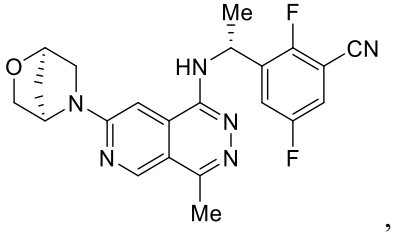
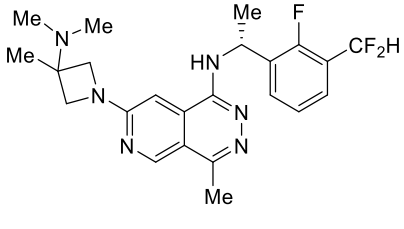
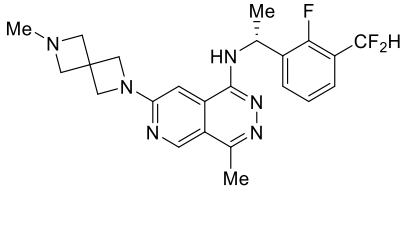
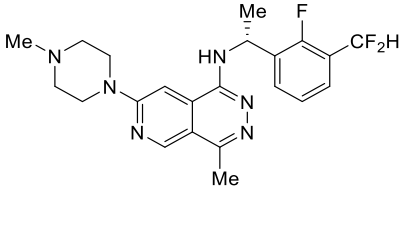
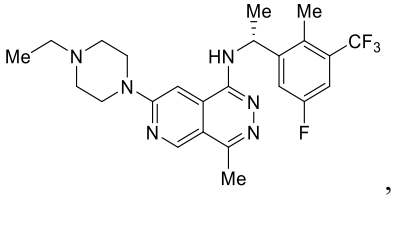
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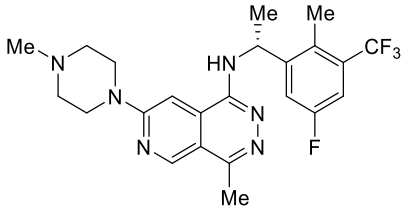
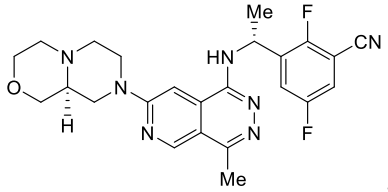
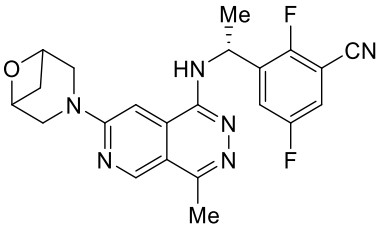
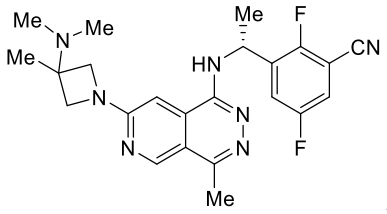
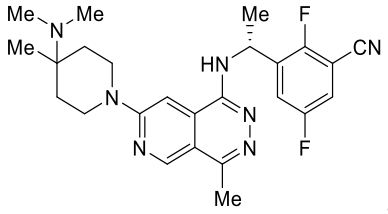
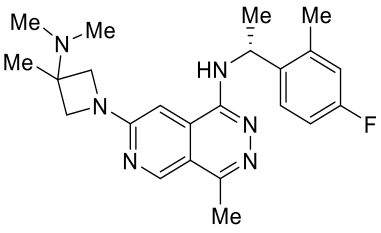
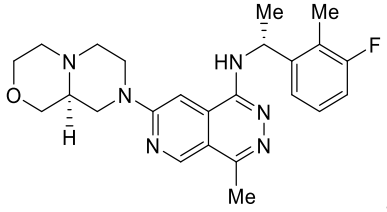
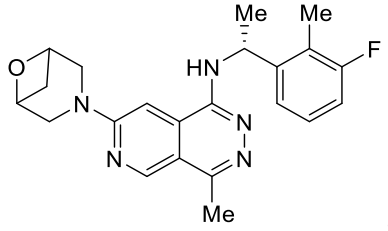
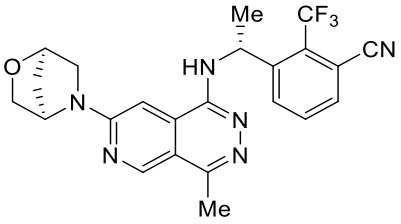
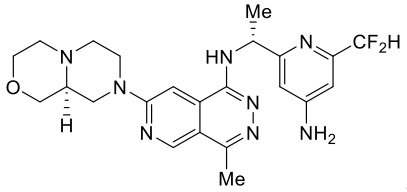
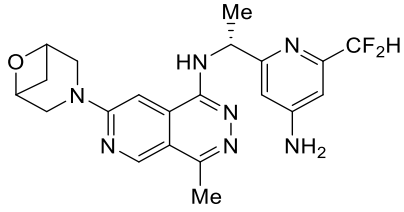
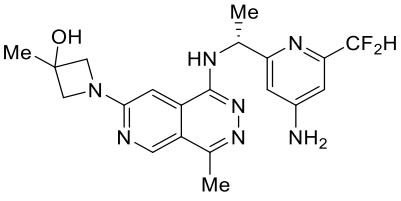
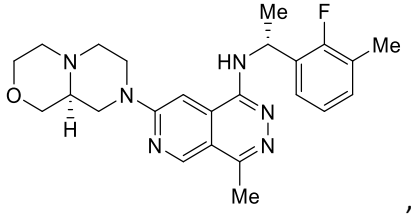
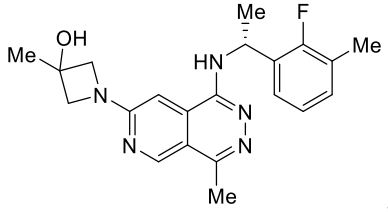
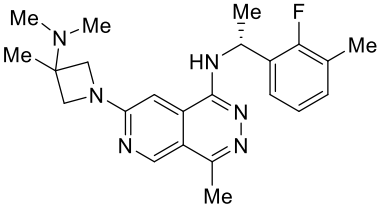
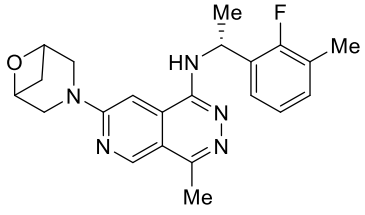
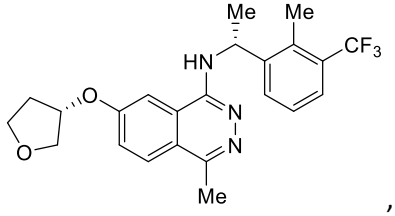
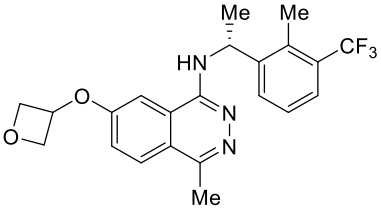
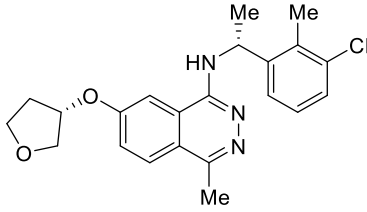
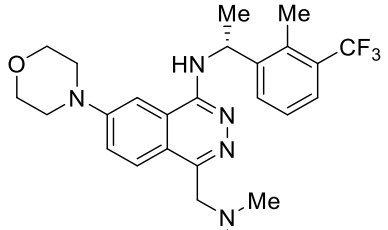
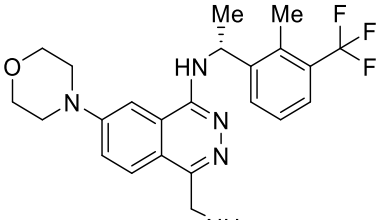
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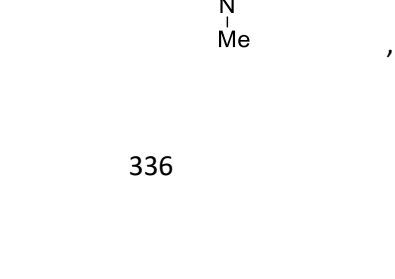
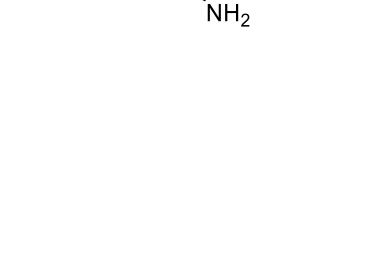

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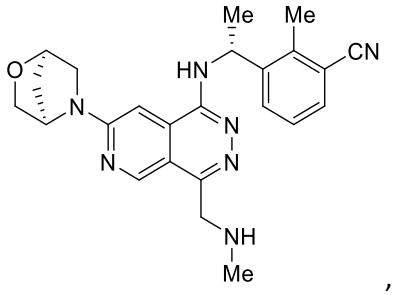
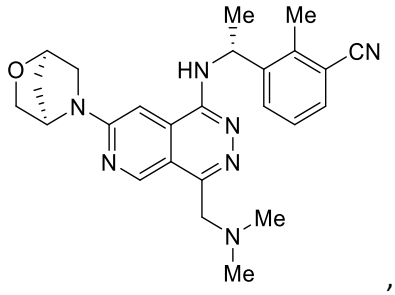
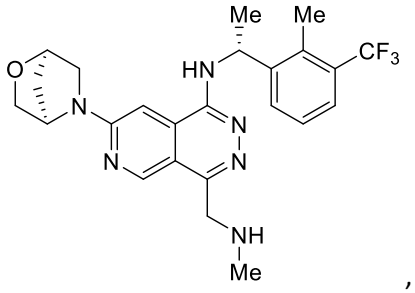
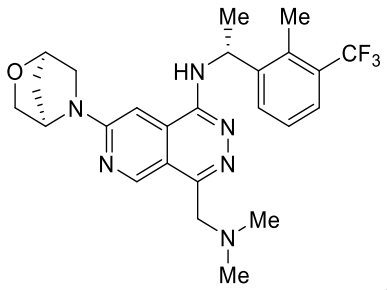
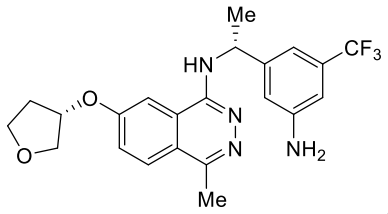
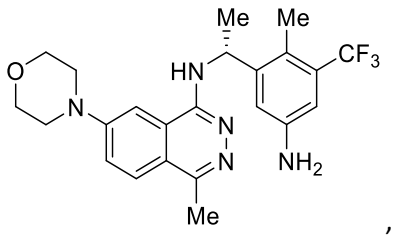
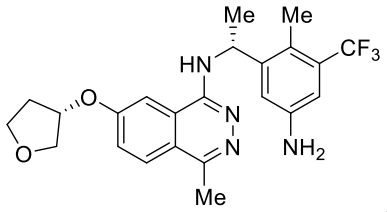
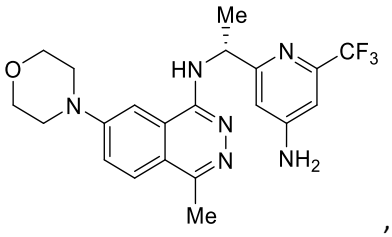
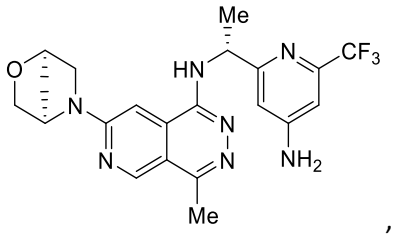
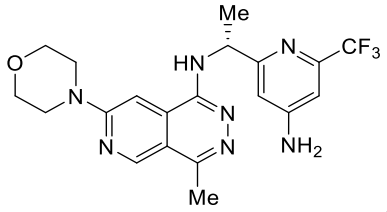
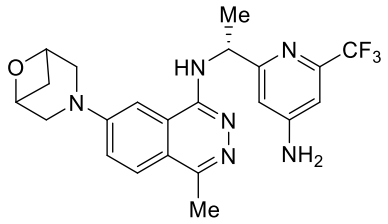
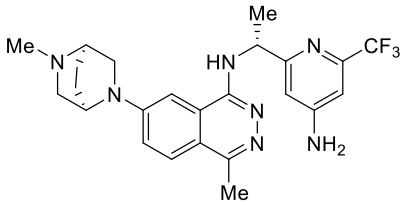
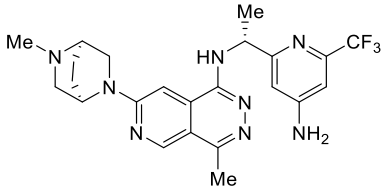
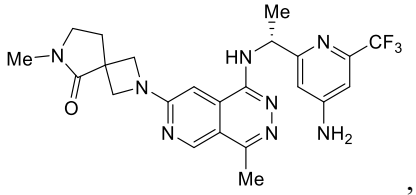
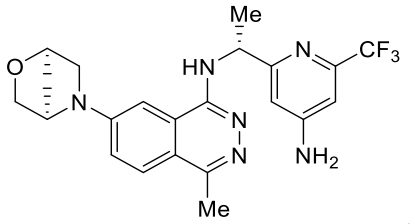
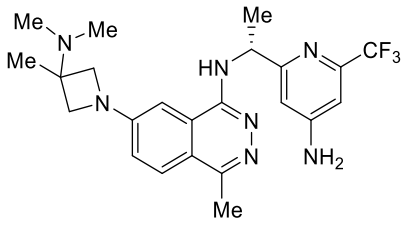
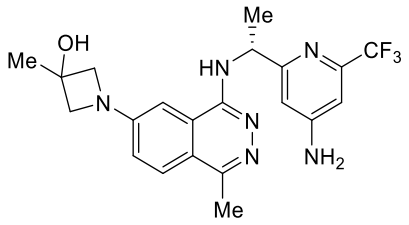
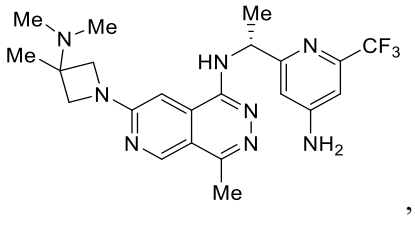
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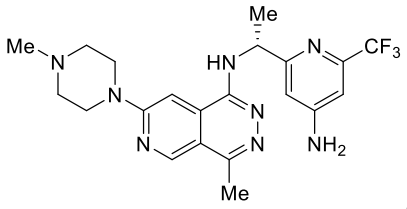
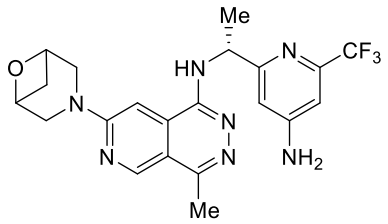
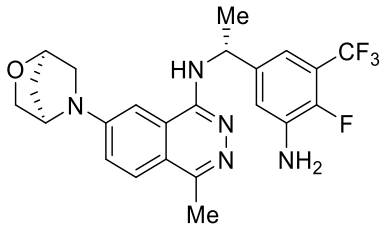
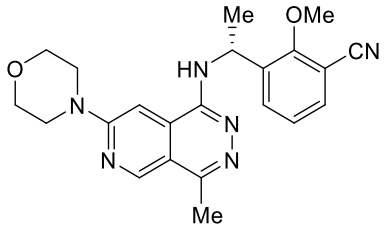
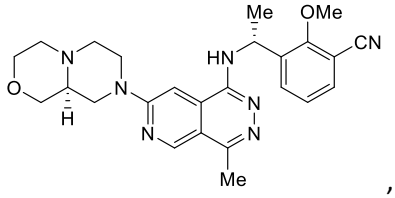
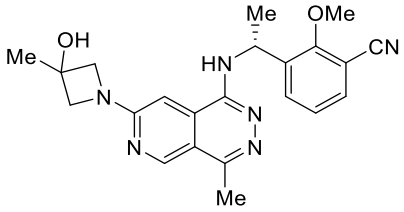
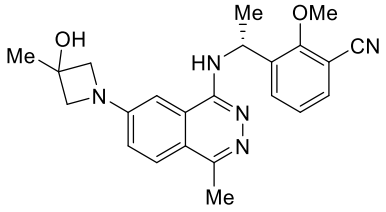
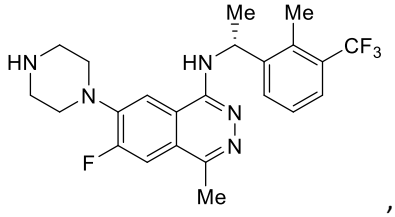
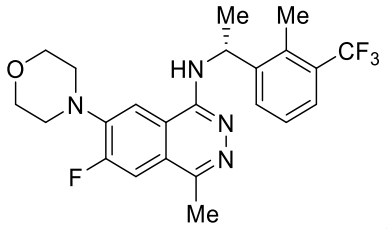
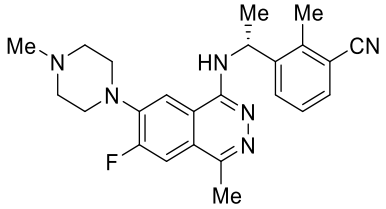
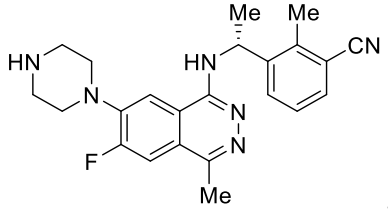
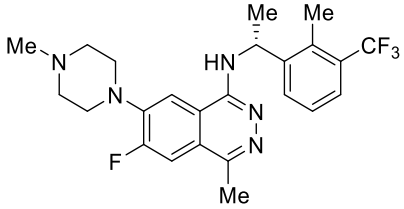
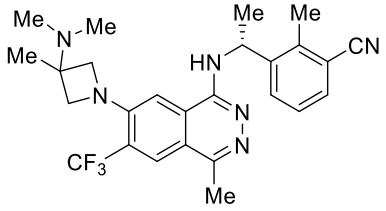
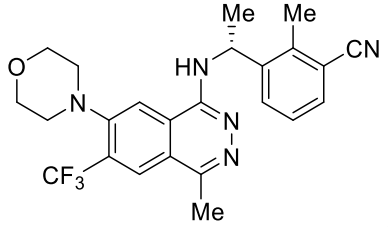
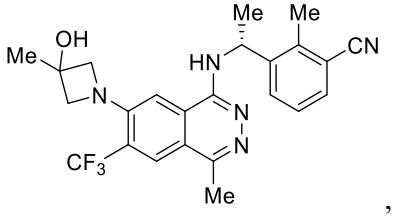
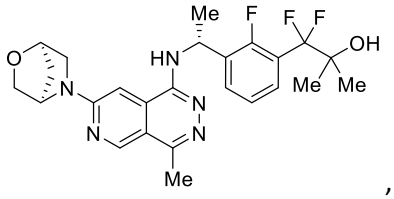
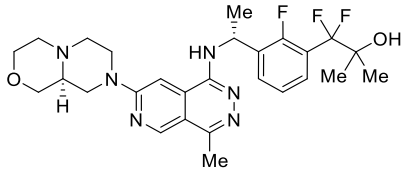
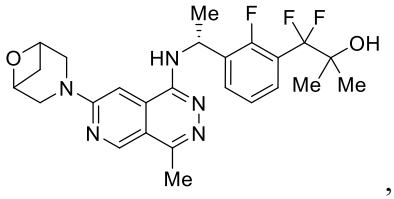
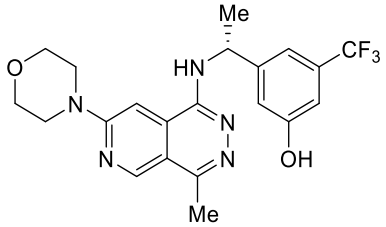
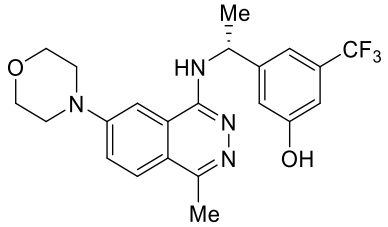
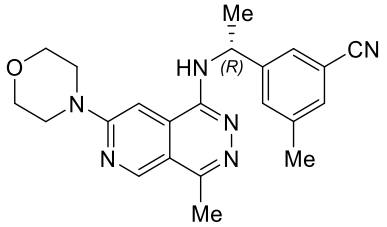
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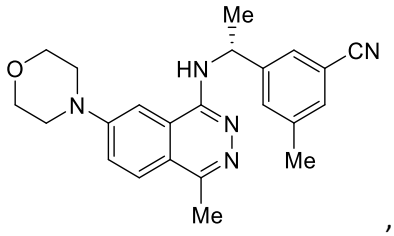
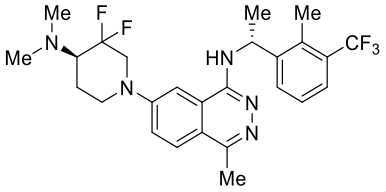
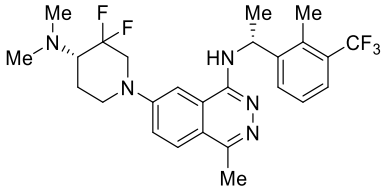
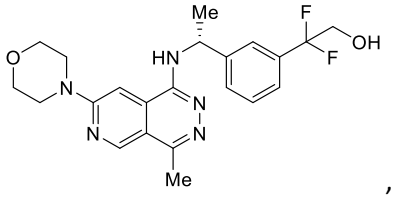
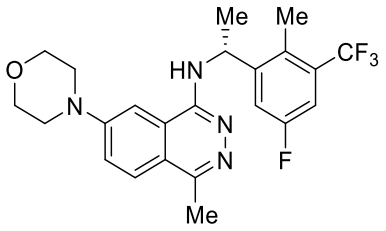
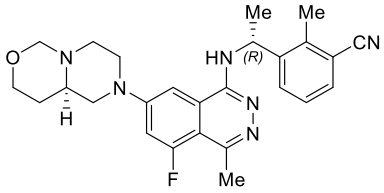
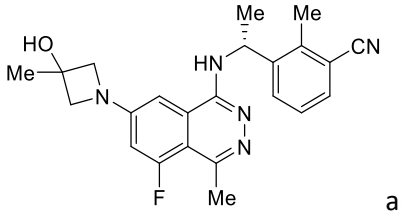
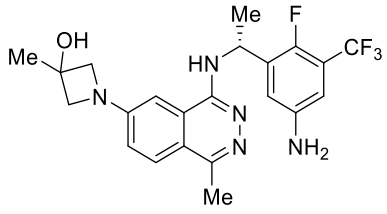

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and pharmaceutically acceptable salts thereof.

2. A pharmaceutical composition, comprising a therapeutically effective amount of a compound of Formula (I) according to claim 1 or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient.

3. A method for inhibiting SOS1 activity in a cell, comprising contacting the cell in which inhibition of SOS1 activity is desired with an effective amount of a compound of Formula (I) according to claim 1 or a pharmaceutically acceptable salt or solvate thereof, or a pharmaceutical composition according to claim 2.

4. The method according to claim 3, wherein the cell harbors an activating mutation in a RAS family-member gene.

5. The method according to claim 3, wherein the cell harbors an activating mutation in SOS1 gene.

6. The method according to claim 3, wherein the cell harbors an activating mutation in NF-1 or NF-2 gene.

7. Use of a therapeutically effective amount of a compound according to claim 1or a pharmaceutically acceptable salt or solvate thereof, , alone or combined with a

pharmaceutically acceptable carrier, excipient or diluents, in the manufacture of a medicament for treating cancer in a patient.

8. The use according to claim 7, wherein the therapeutically effective amount of the compound is between about 0.01 to 300 mg/kg per day.

9. The use according to claim 8, wherein the therapeutically effective amount of the compound is between about 0.1 to 100 mg/kg per day.

10. The use according to any one of claims 7-9, wherein the cancer is selected from the group consisting of Cardiac: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract: kidney (adenocarcinoma, Wilm's tumor (nephroblastoma), lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Biliary tract: gall bladder carcinoma, ampullary carcinoma, cholangiocarcinoma; Bone: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochronfroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma (pinealoma), glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological: uterus (endometrial wcarcinoma (serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma), granulosa-thecal cell tumors, Sertoli-Leydig cell tumors, dysgerminoma,

malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma); Hematologic: blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma); Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; and Adrenal glands: neuroblastoma.

11. The use according to any one of claims 7-10, wherein the cancer is a Ras family-associated cancer.

12. The use according to claim 11, wherein the Ras family-associated cancer is a KRas, HRas or NRas G12C-associated cancer, a KRas, HRas or NRas G12D-associated cancer, a KRas, HRas or NRas G12S-associated cancer, a KRas, HRas or NRas G12A-associated cancer, a KRas, HRas or NRas G13D-associated cancer, a KRas, HRas or NRas G13C-associated cancer, a KRas, HRas or NRas Q61X-associated cancer, a KRas, HRas or NRas A146T-associated cancer, a KRas, HRas or NRas A146V-associated cancer or a KRas, HRas or NRas A146P-associated cancer.

13. The use according to claim 12, wherein the Ras family-associated cancer is a KRas G12C-associated cancer.

14. The use according to claim 13, wherein the Ras family-associated cancer is non-small cell lung cancer or pancreatic cancer.

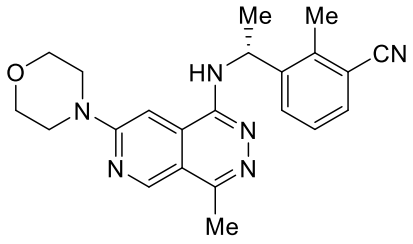
15. The use according to any one of claims 7-13, wherein the cancer is a SOS1-associated cancer.

16. The use according to claim 15, wherein the SOS1-associated cancer is a SOS1 N233S-associated cancer or a SOS1 N233Y-associated cancer.

17. The use according to any one of claims 15 or 16, wherein the SOS1-associated cancer is lung adenocarcinoma, embryonal rhabdomyosarcoma, Sertoli cell testis tumor or granular cell tumors of the skin.

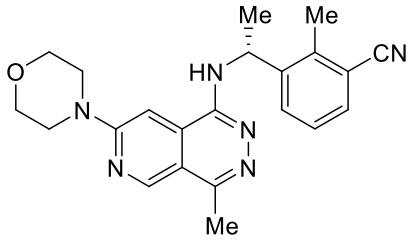
18. The use according to any one of claims 7-10, wherein the cancer is a NF-1/NF-2-associated cancer.

19. A compound of the following formula



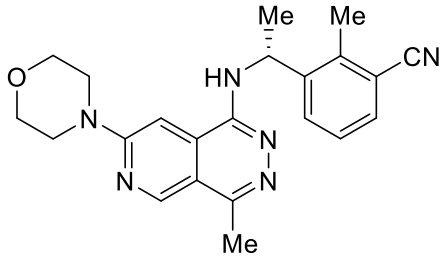
, or a pharmaceutically acceptable salt thereof.

20. A compound of the following formula:



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21. A pharmaceutically acceptable salt of a compound of the following formula:



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22. Use of a therapeutically effective amount of a compound of claim 19, or a pharmaceutically acceptable salt or solvate thereof, , alone or combined with a pharmaceutically acceptable carrier, excipient or diluents, in the manufacture of a medicament for treating cancer in a patient.

23. The use according to claim 22, wherein the therapeutically effective amount of the compound is between about 0.01 to 300 mg/kg per day.

24. The use according to claim 22, wherein the therapeutically effective amount of the compound is between about 0.1 to 100 mg/kg per day.

25. The use according to any one of claims 22-24, wherein the cancer is selected from the group consisting of Cardiac: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract: kidney (adenocarcinoma, Wilm's tumor (nephroblastoma), lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Biliary tract: gall bladder carcinoma, ampullary carcinoma, cholangiocarcinoma; Bone: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochronfroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma (pinealoma), glioblastoma

multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological: uterus (endometrial wcarcinoma (serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma), granulosa-thecal cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma); Hematologic: blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma); Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; and Adrenal glands: neuroblastoma.

26. The use according to any one of claims 22-25, wherein the cancer is a Ras family-associated cancer.

27. The use according to calim 26, wherein the Ras family-associated cancer is a KRas, HRas or NRas G12C-associated cancer, a KRas, HRas or NRas G12D-associated cancer, a KRas, HRas or NRas G12S-associated cancer, a KRas, HRas or NRas G12A-associated cancer, a KRas, HRas or NRas G13D-associated cancer, a KRas, HRas or NRas G13C-associated cancer, a KRas, HRas or NRas Q61X-associated cancer, a KRas, HRas or NRas A146T-associated cancer, a KRas, HRas or NRas A146V-associated cancer or a KRas, HRas or NRas A146P-associated cancer.

28. The use according to claim 26, wherein the Ras family-associated cancer is a KRas G12C-associated cancer.

29. The use according to claim 27, wherein the Ras family-associated cancer is non-small cell lung cancer or pancreatic cancer.

30. The use according to any one of claims 22-29, wherein the cancer is a SOS1-associated cancer.

31. The use according to claim 30, wherein the SOS1-associated cancer is a SOS1 N233S-associated cancer or a SOS1 N233Y-associated cancer.

32. The use according to any one of claims 30-31, wherein the SOS1-associated cancer is lung adenocarcinoma, embryonal rhabdomyosarcoma, Sertoli cell testis tumor or granular cell tumors of the skin.

33. The use according to any one of claims 31-32, wherein the cancer is a NF-1/NF-2-associated cancer.