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Sandoz Group
Global Corporate Affairs
Lichtstrasse 35
4056 Basel
Switzerland

sandoz.com

MEDIA RELEASE

Sandoz receives FDA approval for first and only denosumab biosimilars

- Wyost® (denosumab-bddz) and Jubbonti® (denosumab-bddz) interchangeable with and approved by FDA for all indications of reference medicines Xgeva®* (denosumab) and Prolia®* (denosumab)
- FDA approval based on robust clinical studies and totality of evidence, which show no clinically meaningful differences from reference medicines

Basel, March 5, 2024 – Sandoz, the global leader in generic and biosimilar medicines, today announced that the US Food and Drug Administration (FDA) approved Wyost® (denosumab-bbdz) and Jubbonti® (denosumab-bbdz), the first and only FDA-approved denosumab biosimilars, to treat all indications of the reference medicines.

"Sandoz has achieved the first FDA approval for biosimilars to denosumab, a medicine that can address primary and secondary bone loss, such as osteoporosis, as well as cancer-related skeletal events, which are disease states that can profoundly reduce quality of life for patients. I am proud that Sandoz continues to pioneer access to these life-changing medicines for the patients who need them most."

Keren Haruvi
President Sandoz North America

Wyost® is approved to prevent skeletal-related events (SREs) in patients with multiple myeloma and in patients with bone metastases from solid tumors, to treat adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity, and to treat hypercalcemia of malignancy refractory to bisphosphonate therapy.[1]

Bone is the third most frequent site for metastatic tumors.[2] Nearly all types of cancer can spread to the bone and cause pain and fractures, though cancers that often metastasize in bones include breast and prostate.[3]

Jubbonti® is approved to treat postmenopausal women with osteoporosis at high risk for fracture, to increase bone mass in men with osteoporosis at high risk for fracture, to treat glucocorticoid-induced osteoporosis in men and

women at high risk for fracture, to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer, and to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.[4]

Osteoporosis is a bone disease that develops when bone mineral density and bone mass decrease or when bone strength and structure change. People living with osteoporosis typically do not have symptoms and might not know they have the disease until they experience a fracture. More than 10 million US adults aged 50 and over live with osteoporosis, a major cause of fractures in postmenopausal women and in older men.[5,6] Half of all women over the age of 50 will experience an osteoporotic fracture during their lifetime.[7]

The FDA approval is based on robust clinical studies and accompanied by labeling with safety warnings. The Jubbonti® approval is also accompanied by approval of Sandoz's Jubbonti® Risk Evaluation and Mitigation Strategy (REMS) program, which is designed to inform prescribers and patients about the risk of severe hypocalcemia associated with Jubbonti® in patients with advanced chronic kidney disease, including dialysis-dependent patients.

Wyost® and Jubbonti® have the same dosage form, route of administration, dosing regimen and presentation as the respective reference medicines. Wyost® and Jubbonti® are approved as interchangeable with the reference medicines for all indications.

Given ongoing patent litigation around these products, Sandoz will not comment on anticipated launch timing or other launch details at this time.

About Wyost® (denosumab-bbdz)

Wyost® 120 mg/1.7 mL (70 mg/mL) injection has been approved by the FDA as interchangeable with the reference medicine, a human monoclonal antibody designed to bind to the RANKL protein, an activator of osteoclasts (cells involved in breaking down bone tissue).[8,9] Wyost® is indicated in the US to prevent SREs in patients with multiple myeloma and in patients with bone metastases from solid tumors, to treat adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity, and to treat hypercalcemia of malignancy refractory to bisphosphonate therapy.[1]

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Hypocalcemia and known clinically significant hypersensitivity to denosumab products.

WARNINGS AND PRECAUTIONS

Same Active Ingredient: Patients receiving Wyost should not receive other denosumab products concomitantly. *Hypersensitivity* reactions including anaphylaxis may occur. Discontinue permanently if a clinically significant reaction occurs. *Hypocalcemia*: Denosumab products can cause severe symptomatic hypocalcemia. Fatal cases have been reported with denosumab products use. Correct hypocalcemia prior to initiating Wyost. Monitor calcium levels during therapy, especially in the first weeks of initiating therapy, and adequately supplement all patients with calcium and

vitamin D. *Osteonecrosis of the jaw (ONJ)* has been reported in patients receiving denosumab products. Perform an oral examination prior to starting Wyost. Monitor for symptoms. Avoid invasive dental procedures during treatment with Wyost. *Atypical femoral fracture*: Evaluate patients with thigh or groin pain to rule out a femoral fracture. *Hypercalcemia Following Treatment Discontinuation in Patients with Giant Cell Tumor of Bone and in Patients with Growing Skeletons*: Monitor patients for signs and symptoms of hypercalcemia, and manage as clinically appropriate. *Multiple Vertebral Fractures (MVF) Following Treatment Discontinuation*: When Wyost treatment is discontinued, evaluate the individual patient's risk for vertebral fractures. *Embryo-Fetal Toxicity*: Can cause fetal harm. Advise females of reproductive potential of potential risk to the fetus and to use effective contraception.

ADVERSE REACTIONS
Bone Metastasis from Solid Tumors: Most common adverse reactions (≥ 25%) were fatigue/asthenia, hypophosphatemia, and nausea. *Multiple Myeloma*: Most common adverse reactions (≥ 10%) were diarrhea, nausea, anemia, back pain, thrombocytopenia, peripheral edema, hypocalcemia, upper respiratory tract infection, rash, and headache. *Giant Cell Tumor of Bone*: Most common adverse reactions (≥ 10%) were arthralgia, headache, nausea, back pain, fatigue, and pain in extremity. *Hypercalcemia of Malignancy*: Most common adverse reactions (> 20%) were nausea, dyspnea, decreased appetite, headache, peripheral edema, vomiting, anemia, constipation, and diarrhea.

USE IN SPECIFIC POPULATIONS
Pediatric patients: Recommended only for treatment of skeletally mature adolescents with giant cell tumor of bone. *Renal impairment*: Patients with creatinine clearance less than 30 mL/min or receiving dialysis are at risk for hypocalcemia. Adequately supplement with calcium and vitamin D.

This is not the complete list of all the safety information for Wyost. Please click to see full Prescribing Information for Wyost.

About Jubbonti® (denosumab-bbdz)

Jubbonti® 60 mg/1 mL injection has been approved by the FDA as interchangeable with the reference medicine, a human monoclonal antibody designed to bind to the RANKL protein, an activator of osteoclasts (cells involved in breaking down bone tissue).[8,9] Jubbonti® is indicated in the US to treat postmenopausal women with osteoporosis at high risk for fracture, to increase bone mass in men with osteoporosis at high risk for fracture, to treat glucocorticoid-induced osteoporosis in men and women at high risk for fracture, to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer, and to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.[4]

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SEVERE HYPOCALCEMIA IN PATIENTS WITH ADVANCED KIDNEY DISEASE
See full prescribing information for complete boxed warning.

- **Patients with advanced chronic kidney disease are at risk of severe hypocalcemia following denosumab products administration. Severe**

hypocalcemia requiring hospitalization, life-threatening events and fatal cases have been reported.

- **The presence of chronic kidney disease-mineral bone disorder (CKD-MBD) markedly increases the risk of hypocalcemia.**
- **Prior to initiating Jubbonti in patients with advanced chronic kidney disease, evaluate for the presence of CKD-MBD. Treatment with Jubbonti in these patients should be supervised by a healthcare provider with expertise in the diagnosis and management of CKD-MBD.**

CONTRAINDICATIONS

Hypocalcemia; pregnancy; and known hypersensitivity to denosumab products.

WARNINGS AND PRECAUTIONS

Hypocalcemia: Pre-existing hypocalcemia must be corrected before initiating Jubbonti. Adequately supplement all patients with calcium and vitamin D. Concomitant use of calcimimetic drugs may also worsen hypocalcemia risk. Evaluate for presence of chronic kidney disease mineral-bone disorder. Monitor serum calcium. *Same Active Ingredient*: Patients receiving Jubbonti should not receive other denosumab products concomitantly. *Hypersensitivity* including anaphylactic reactions may occur. Discontinue permanently if a clinically significant reaction occurs. *Osteonecrosis of the jaw (ONJ)*: Has been reported with denosumab products. Monitor for symptoms. *Atypical femoral fractures*: Have been reported. Evaluate patients with thigh or groin pain to rule out a femoral fracture. *Multiple vertebral fractures* have been reported following treatment discontinuation. Patients should be transitioned to another antiresorptive agent if Jubbonti is discontinued. *Serious infections including skin infections*: May occur, including those leading to hospitalization. Advise patients to seek prompt medical attention if they develop signs or symptoms of infection, including cellulitis. *Dermatologic reactions*: Dermatitis, rashes, and eczema have been reported. Consider discontinuing Jubbonti if severe symptoms develop. *Severe bone, joint, muscle pain* may occur. Discontinue use if severe symptoms develop. *Suppression of bone turnover*: Significant suppression has been demonstrated. Monitor for consequences of bone over-suppression.

ADVERSE REACTIONS

Postmenopausal osteoporosis: Most common adverse reactions (> 5% and more common than placebo) were: back pain, pain in extremity, hypercholesterolemia, musculoskeletal pain, and cystitis. Pancreatitis has been reported in clinical trials. *Male osteoporosis*: Most common adverse reactions (> 5% and more common than placebo) were: back pain, arthralgia, and nasopharyngitis. *Glucocorticoid-induced osteoporosis*: Most common adverse reactions (> 3% and more common than active-control group) were: back pain, hypertension, bronchitis, and headache. *Bone loss due to hormone ablation for cancer*: Most common adverse reactions (≥ 10% and more common than placebo) were: arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials.

USE IN SPECIFIC POPULATIONS

Pregnant women and females of reproductive potential: Denosumab products may cause fetal harm when administered to pregnant women. Advise females of reproductive potential to use effective contraception during therapy, and for at least 5 months after the last dose of Jubbonti. *Pediatric patients*: Denosumab products are not approved for use in pediatric patients. *Renal impairment*: No dose adjustment is necessary in patients with renal impairment. Patients with advanced chronic kidney disease (eGFR <30 mL/min/1.73 m^2), including dialysis-dependent patients, are at greater risk of severe hypocalcemia. The presence of underlying chronic kidney disease-mineral bone disorder markedly increases the risk of hypocalcemia.

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This is not the complete list of all the safety information for Jubbonti. Please click to see full Prescribing Information for Jubbonti.

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About Sandoz

Sandoz (SIX: SDZ; OTCQX: SDZNY) is the global leader in generic and biosimilar medicines, with a growth strategy driven by its Purpose: pioneering access for patients. 22,000 people of more than 100 nationalities work together to bring Sandoz medicines to some 500 million patients worldwide, generating substantial global healthcare savings and an even larger total social impact. Its leading portfolio of more than 1500 products addresses diseases from the common cold to cancer. Headquartered in Basel, Switzerland, Sandoz traces its heritage back to the year 1886. Its history of breakthroughs includes Calcium Sandoz in 1929, the world's first oral penicillin in 1951, and the first biosimilar in 2006. In 2022, Sandoz achieved sales of USD 9.1 billion and core EBITDA of USD 1.9 billion.

Global Media Relations contacts	Investor Relations contacts
Global.MediaRelations@sandoz.com	**Investor.Relations@sandoz.com**
Joerg E. Allgaeuer +49 171 838 4838	Karen M. King +1 609 722 0982
Chris Lewis +49 174 244 9501	Laurent de Weck +41 79 795 7364