FDA APPROVED

FOR PATIENTS WITHOUT PRIOR CHEMOTHERAPY*

In PSMA+ mCRPC,

STRIVE EARLIER FOR

PLUVICTORY

A chance to live longer without progression.[1,2] **That's a Victory.**

The first and only PSMA-targeted radioligand therapy to significantly delay progression after only 1 ARPI.

Median rPFS (primary end point) in the PSMAfore trial with PLUVICTO® vs change in ARPI:

- Primary analysis: 9.3 months vs 5.6 months (HR=0.41 [95% CI, 0.29-0.56]; *P*<0.0001)[1]
- Updated exploratory analysis: 11.6 months vs 5.6 months (HR=0.49 [95% CI, 0.39-0.61])[2,†]

Not an actual patient.

Indication

PLUVICTO® (lutetium Lu 177 vipivotide tetraxetan) is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibition (ARPI) therapy, and

- are considered appropriate to delay taxane-based chemotherapy, or
- have received prior taxane-based chemotherapy

IMPORTANT SAFETY INFORMATION

Risk From Radiation Exposure

PLUVICTO contributes to a patient's long-term cumulative radiation exposure, which is associated with an increased risk for cancer.

Minimize radiation exposure to patients, medical personnel, and others during and after treatment with PLUVICTO consistent with institutional practices, patient treatment procedures, Nuclear Regulatory Commission patient-release guidance, and instructions to the patient for follow-up radiation protection.

ARPI, androgen receptor pathway inhibitor; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; PSMA, prostate-specific membrane antigen; PSMA+, PSMA positive; rPFS, radiographic progression-free survival.

*For patients considered appropriate to delay taxane-based chemotherapy.[1]

†Exploratory rPFS analysis was performed with a median follow-up period of 24 months vs the primary analysis at 7 months. This analysis was not controlled for Type-I error.[2]

Please see additional Important Safety Information throughout and on pages 8-9 and full Prescribing Information.

PLUVICTO®
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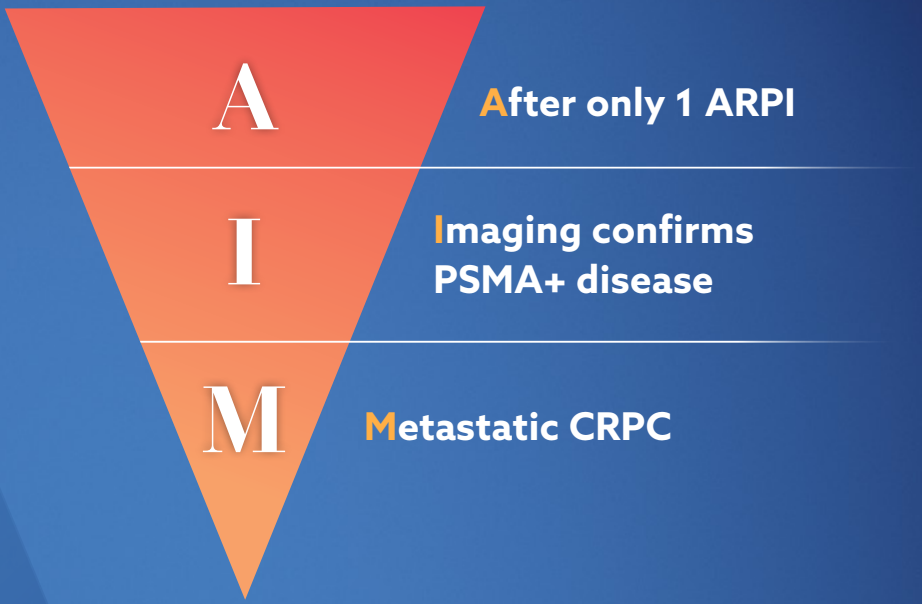
INJECTION FOR INTRAVENOUS USE

FDA APPROVED FOR PATIENTS AFTER ONLY 1 ARPI

AFTER YOUR PATIENTS WITH PSMA+ mCRPC RECEIVE THEIR FIRST ARPI, **BE READY FOR WHAT'S NEXT**

AIM for PLUVICTO even earlier in mCRPC[1,2]



1 ARPI could have been received at **any** point in your patient's prostate cancer journey, including in the castration-sensitive setting[1,2]

FOR YOUR PATIENTS ON ARPI, AT WHAT POINT DO YOU BEGIN CONSIDERING SUBSEQUENT TREATMENT OPTIONS?

CRPC, castration-resistant prostate cancer.

IMPORTANT SAFETY INFORMATION (continued)

Risk From Radiation Exposure (continued)

Ensure patients increase oral fluid intake and advise them to void as often as possible to reduce bladder radiation.

To minimize radiation exposure to others, advise patients to limit close contact (less than 3 feet) with household contacts for 2 days or with children and pregnant women for 7 days, to refrain from sexual activity for 7 days, and to sleep in a separate bedroom from household contacts for 3 days, from children for 7 days, or from pregnant women for 15 days.

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FDA APPROVED FOR PATIENTS AFTER ONLY 1 ARPI

MEET PATIENTS WITH PSMA+ mCRPC WHO **ARE ELIGIBLE FOR PLUVICTO**

Plan for PLUVICTO at first ARPI, which could have been received at **any** point in your patient's journey[1,2]

Retired, volunteers at local food bank

- Robert loves giving back to his community and wants to avoid any further disruptions to his volunteering

Robert, 68—Received 1 ARPI in the mCSPC setting

Disease history

- **Localized prostate cancer:** Radical prostatectomy
- 4 years later, **BCR occurred (nmCSPC):** Monitoring for 12 months
- **mCSPC:** ADT + **ARPI** for 21 months
- **PSA began to rise:** Diagnosed with PSMA+ mCRPC

Current clinical presentation

- PSMA-PET scan confirmed **PSMA+ mCRPC** and identified new bone and lymph node metastases
- ECOG PS: 1
- Asymptomatic disease
- No actionable genomic alterations

Military veteran, plays piano in the VFW orchestra

- James would like to keep playing piano in the VFW orchestra for as long as possible

James, 70—Received 1 ARPI in the mCRPC setting

Disease history

- **Localized prostate cancer:** EBRT
- 2 years later, **BCR occurred (nmCSPC):** ADT for 2 years
- **mCRPC:** ADT + **ARPI** for 11 months
- **PSA began to rise:** PSMA-PET shows positive disease

Current clinical presentation

- PSMA-PET scan confirmed **PSMA+ mCRPC** and identified new bone and lymph node metastases
- ECOG PS: 1
- Mildly symptomatic disease
- No actionable genomic alterations

Hypothetical patient cases.

ADT, androgen deprivation therapy; BCR, biochemical recurrence; EBRT, external beam radiation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; nmCSPC, nonmetastatic castration-sensitive prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; PET, positron emission tomography; PSA, prostate-specific antigen.

IMPORTANT SAFETY INFORMATION (continued)

Myelosuppression

PLUVICTO can cause severe and life-threatening myelosuppression. In the PSMAfore study, grade 3 or 4 decreased hemoglobin (7%), decreased leukocytes (4.4%), decreased neutrophils (3.5%), and decreased platelets (2.7%) occurred in patients treated with PLUVICTO.
One death occurred due to bone marrow failure during long-term follow-up in a patient who received PLUVICTO.
In the VISION study, 4 myelosuppression-related deaths occurred.

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FDA APPROVED FOR PATIENTS AFTER ONLY 1 ARPI

LONGER LIFE WITHOUT PROGRESSION IS POSSIBLE WITH PLUVICTO. THAT'S A VICTORY.

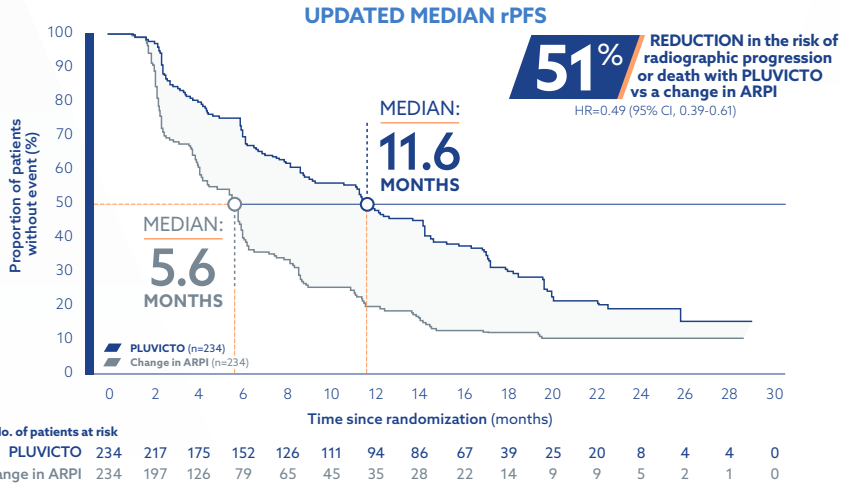
Primary end point

rPFS: In the primary analysis, PLUVICTO achieved statistically significant rPFS[1]

- **Median rPFS was 9.3 months with PLUVICTO vs 5.6 months with a change in ARPI (HR=0.41 [95% CI, 0.29-0.56]; *P*<0.0001)**

In the updated exploratory analysis

PLUVICTO more than doubled median rPFS vs a change in ARPI[2]



No. of patients at risk

PLUVICTO	234	217	175	152	126	111	94	86	67	39	25	20	8	4	4	0
Change in ARPI	234	197	126	79	65	45	35	28	22	14	9	9	5	2	1	0

- Exploratory rPFS analysis was performed with a median follow-up period of 24 months vs the primary analysis at 7 months. This analysis was not controlled for Type-I error[2]

Key secondary end point

OS: Numerically favored PLUVICTO but was not statistically significant; high crossover rate may have confounded OS analysis[1,2]

- **60.3%** of patients randomized to the change in ARPI arm subsequently crossed over to receive PLUVICTO following confirmed radiographic progression[3]
- At the preplanned final analysis,* **HR=0.91** (95% CI, 0.72-1.14); median OS was 24.5 months with PLUVICTO and 23.1 months with a change in ARPI[1]
- With an IPCW method analysis,† **HR=0.59** (95% CI, 0.38-0.91)[3]

IPCW, inverse probability of censoring weighting; OS, overall survival.

*Data cutoff for the final analysis was January 1, 2025, with a total of 299 events occurring.[3]

†IPCW method is a multivariate model that uses time-varying weights estimated for non-crossover control arm patients to reflect how similar they are to crossover patients using propensity methods. Arms are then compared using the weighted Cox model.[3]

IMPORTANT SAFETY INFORMATION (continued)

Myelosuppression (continued)

Perform complete blood counts before and during treatment with PLUVICTO. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity of myelosuppression.

Please see additional Important Safety Information throughout and on pages 8-9 and full Prescribing Information.

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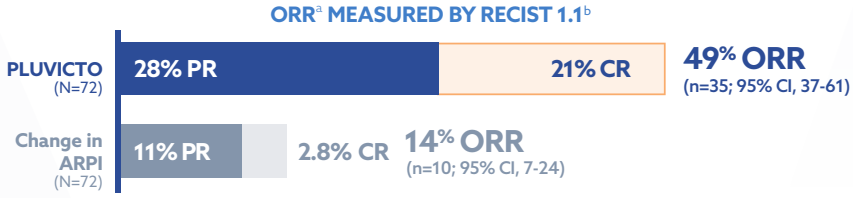
PSMAfore: A study of PLUVICTO after only 1 ARPI

HALF OF PATIENTS TREATED WITH PLUVICTO **ACHIEVED A RESPONSE**

Additional end points

ORR: More patients had a response to PLUVICTO, with >7x more complete responses seen with PLUVICTO vs a change in ARPI[1,*]



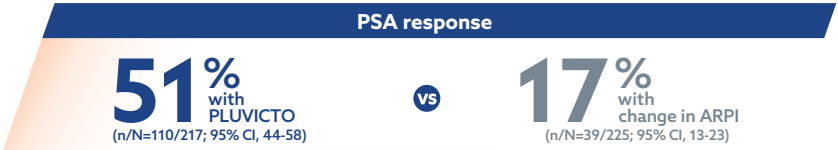
CR, complete response; ORR, overall response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors. ORR=CR+PR.
[a]Responses are based on soft tissue and bone lesion assessment.
[b]Patients with measurable disease at baseline.

DCR (CR+PR+SD): 78% with PLUVICTO vs 56% with a change in ARPI[4,†]

- CR: 21% with PLUVICTO vs 3% with a change in ARPI
- PR: 28% with PLUVICTO vs 11% with a change in ARPI
- SD: 29% with PLUVICTO vs 42% with a change in ARPI

DCR, disease control rate; SD, stable disease.
[†]SD and DCR are exploratory end points from PSMAfore, not validated surrogates for survival or clinical benefit. SD may reflect natural disease course, and its clinical significance, especially short-term, is not established. Efficacy evaluation should focus on rPFS and OS.

PSA: More patients had a PSA decline with PLUVICTO vs a change in ARPI[2,*]



- Data are from patients with available PSA measurements at the time of the third data cutoff
- PSA50 response was defined as a confirmed decrease of 50% or greater

*Not powered for statistical significance.

IMPORTANT SAFETY INFORMATION (continued)

Renal Toxicity

PLUVICTO can cause severe renal toxicity. In the PSMAfore study, grade 3 or 4 acute kidney injury (1.3%) occurred in patients treated with PLUVICTO.

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PSMAfore: A study of PLUVICTO after only 1 ARPI

PLUVICTO HAS A **FAVORABLE SAFETY PROFILE**

Grade ≥3 AE rates were lower in the PLUVICTO group with a longer median duration of exposure[2]

- Incidence of grade ≥3 TEAEs: 36% with PLUVICTO (n=81) vs 48% with a change in ARPI (n=112)
- Median duration of exposure: 8.4 months with PLUVICTO vs 6.5 months with a change in ARPI

PSMAfore: ADVERSE REACTIONS OCCURRING AT ≥10% INCIDENCE IN PATIENTS WHO RECEIVED PLUVICTO[1,a]

	PLUVICTO (n=227)		Change in ARPI (n=232)	
Adverse reactions	All grades (%)	Grades 3 or 4 (%)	All grades (%)	Grades 3 or 4 (%)
Gastrointestinal disorders				
Dry mouth[b]	61	0.9	2.6	0
Nausea	32	0	12	0.4
Constipation	22	0.4	14	0
Diarrhea	17	0	9	0.4
Vomiting	11	0	4.7	0
General disorders				
Fatigue[b]	53	1.3	53	5
Metabolism and nutrition disorders				
Decreased appetite	22	0	19	0.4
Musculoskeletal and connective tissue disorders				
Arthralgia	20	0	23	0.4
Back pain	14	1.3	20	2.6

[a]National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.[5]
[b]Includes multiple similar terms.[1]

- Clinically relevant ARs in <10% of patients who received PLUVICTO included dysgeusia, abdominal pain, peripheral edema, headache, acute kidney injury, weight decreased, urinary tract infection, dry eye, dizziness, dry skin, oral fungal infection, gastroesophageal reflux disease, pyrexia, vertigo, stomatitis, dysphagia, esophagitis, pancytopenia, and bone marrow failure[1]

AE, adverse event; AR, adverse reaction;
TEAE, treatment-emergent adverse event.

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PSMAfore: A study of PLUVICTO after only 1 ARPI

PLUVICTO HAS PROVEN TOLERABILITY

Permanent discontinuation rate due to an AE[1,2]

6% with PLUVICTO (n=13) vs **5%** with change in ARPI (n=12)

- ARs leading to permanent discontinuation of PLUVICTO in ≥1% of patients who received PLUVICTO were thrombocytopenia (1.8%) and dry mouth (1.3%)[1]

Dose modification due to an AE[2]

4% with PLUVICTO (n=8) vs **16%** with change in ARPI (n=36)

- The most frequent (≥0.5%) AR leading to a dose reduction of PLUVICTO in patients who received PLUVICTO was dry mouth (0.9%)[1]

Dose interruption due to an AE[2]

12% with PLUVICTO (n=28) vs **19%** with change in ARPI (n=45)

- The most frequent (≥1%) ARs leading to a dose interruption of PLUVICTO in patients who received PLUVICTO were COVID-19 (3.1%) and anemia (1.8%)[1]

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INDICATION AND IMPORTANT SAFETY INFORMATION

Indication

PLUVICTO® (lutetium Lu 177 vipivotide tetraxetan) is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibition (ARPI) therapy, and

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Ensure patients increase oral fluid intake and advise them to void as often as possible to reduce bladder radiation.

To minimize radiation exposure to others, advise patients to limit close contact (less than 3 feet) with household contacts for 2 days or with children and pregnant women for 7 days, to refrain from sexual activity for 7 days, and to sleep in a separate bedroom from household contacts for 3 days, from children for 7 days, or from pregnant women for 15 days.

Myelosuppression

PLUVICTO can cause severe and life-threatening myelosuppression. In the PSMAfore study, grade 3 or 4 decreased hemoglobin (7%), decreased leukocytes (4.4%), decreased neutrophils (3.5%), and decreased platelets (2.7%) occurred in patients treated with PLUVICTO. One death occurred due to bone marrow failure during long-term follow-up in a patient who received PLUVICTO. In the VISION study, 4 myelosuppression-related deaths occurred.

Perform complete blood counts before and during treatment with PLUVICTO. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity of myelosuppression.

Renal Toxicity

PLUVICTO can cause severe renal toxicity. In the PSMAfore study, grade 3 or 4 acute kidney injury (1.3%) occurred in patients treated with PLUVICTO.

Advise patients to remain well hydrated and to urinate frequently before and after administration of PLUVICTO. Perform kidney function laboratory tests, including serum creatinine and calculated creatinine clearance (CrCl), before and during treatment. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity of renal toxicity.

Embryo-Fetal Toxicity

The safety and efficacy of PLUVICTO have not been established in females. Based on its mechanism of action, PLUVICTO can cause fetal harm. No animal studies using lutetium Lu 177 vipivotide tetraxetan have been conducted to evaluate its effect on female reproduction and embryo-fetal development; however, radioactive emissions, including those from PLUVICTO, can cause fetal harm. Advise males with female partners of reproductive potential to use effective contraception during treatment with PLUVICTO and for 14 weeks after the last dose.

Infertility

The recommended cumulative dose of 44.4 GBq of PLUVICTO results in a radiation-absorbed dose to the testes within the range where PLUVICTO may cause temporary or permanent infertility.

Please see additional Important Safety Information on the following page and full Prescribing Information.

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IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions and Laboratory Abnormalities

In the pooled safety population for the PSMAfore and VISION studies (N=756), the most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased lymphocytes (83%), decreased hemoglobin (65%), fatigue (49%), dry mouth (46%), decreased platelets (40%), decreased estimated glomerular filtration rate (37%), nausea (35%), decreased neutrophils (31%), decreased calcium (29%), decreased sodium (27%), increased aspartate aminotransferase (26%), increased alkaline phosphatase (24%), arthralgia (22%), decreased appetite (21%), increased potassium (21%), constipation (21%), and back pain (21%).

Please see full Prescribing Information.

Trial design: PSMAfore was an open-label, multicenter, randomized phase 3 clinical trial evaluating PLUVICTO in 468 adult taxane-naive patients with PSMA+ mCRPC previously treated with 1 ARPI, who were considered appropriate to delay taxane-based chemotherapy. Participants were randomized in a 1:1 ratio to receive PLUVICTO (7.4 GBq every 6 weeks for 6 cycles) or a change in ARPI. The primary end point was rPFS. Key secondary end point: OS; select additional end points: ORR, PSA response.[1,2]

References: 1. Pluvicto. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Morris MJ, Castellano D, Herrmann K, et al; PSMAfore Investigators. ^{177}Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naive patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): a phase 3, randomised, controlled trial. *Lancet*. 2024;404(10459):1227-1239. doi:10.1016/S0140-6736(24)01653-2 **3.** Fizazi K, Chi KN, Shore ND, et al; PSMAfore Investigators. Final overall survival and safety analyses of the phase 3 PSMAfore trial of [^{177}Lu]Lu-PSMA-617 versus change of androgen receptor pathway inhibitor in taxane-naive patients with metastatic castration-resistant prostate cancer. *Ann Oncol*. Published online July 16, 2025. doi:10.1016/j.annonc.2025.07.003 **4.** Morris MJ, Castellano D, Herrmann K, et al; PSMAfore Investigators. ^{177}Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naive patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): a phase 3, randomised, controlled trial. *Lancet*. 2024:404(10459)(suppl 1):1227-1239. doi:10.1016/S0140-6736(24)01653-2 **5.** Morris MJ, Castellano D, Herrmann K, et al; PSMAfore Investigators. ^{177}Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naive patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): a phase 3, randomised, controlled trial. *Lancet*. 2024;404(10459)(suppl 2):1227-1239. doi:10.1016/S0140-6736(24)01653-2 **6.** Hupe MC, Philippi C, Roth D, et al. Expression of prostate-specific membrane antigen (PSMA) on biopsies is an independent risk stratifier of prostate cancer patients at time of initial diagnosis. *Front Oncol*. 2018;8:623. doi:10.3389/fonc.2018.00623 **7.** Pomykala KL, Czernin J, Grogan TR, Armstrong WR, Williams J, Calais J. Total-body ^{68}Ga-PSMA-11 PET/CT for bone metastasis detection in prostate cancer patients: potential impact on bone scan guidelines. *J Nucl Med*. 2020;61(3):405-411. doi:10.2967/jnumed.119.230318 **8.** Data on file. PLUVICTO NPS Metrics. Novartis Pharmaceuticals Corp; June 2025.

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GBq, gigabecquerel.

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For your patients with PSMA+ mCRPC,

STRIVE EARLIER FOR PLUVICTORY

A chance to live longer without progression.[1] That's a Victory.

PLUVICTO targets PSMA, a biomarker overexpressed in more than 80% of men with prostate cancer[1,6,7]

In the PSMAfore trial after only 1 ARPI,

PLUVICTO more than doubled median rPFS vs a change in ARPI[2]

- Updated exploratory analysis: Median rPFS was 11.6 months with PLUVICTO vs 5.6 months with a change in ARPI (HR=0.49 [95% CI, 0.39-0.61])*

PLUVICTO has a favorable safety profile and proven tolerability[2]

- Grade ≥3 AE rates were lower in the PLUVICTO group with a longer median duration of exposure[2]
- 6% permanent discontinuation rate due to an AE; 4% had a dose modification due to an AE; 12% had a dose interruption due to an AE[1,2]

PLUVICTO can be delivered within 5 days of order placement,† so your patients can begin treatment as soon as possible[8]

CHOOSE PLUVICTO AFTER ONLY 1 ARPI[1]

*Exploratory rPFS analysis was performed with a median follow-up period of 24 months vs the primary analysis at 7 months. This analysis was not controlled for Type-I error.[2]

†Exceptions may apply for syringe form and select geographic locations.[8]

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Novartis Pharmaceuticals Corporation
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