

P†PǫPŸPŸP PJPљP|P†Pİ

PrP»Cİ PjPµPrPëC‡PSPsPiPs P·P°CÍC,PsCÍCíPIP°PSPSCİ P»C-PeP°CĤCÍCĤPePsPiPs
P·P°CÍPsP±Cí

PћPњPǫP†Pљ PћPљPћPŸ

(OMNIC OCAS)

PŸPeP»P°Pr:

PrC-CĤC‡P° CĤPµC‡PsPIPëPSP°: C,P°PjCÍCíP»PsP·PëPSCí PiC-PrCĤPsC...P»PsCĤPëPr;

1 C,P°P±P»PµC,PeP° PjC-CÍC,PëC,CĤ 0,4 PjPi C,P°PjCÍCíP»PsP·PëPSCí
PiC-PrCĤPsC...P»PsCĤPëPrCí;

PrPsPiPsPjC-P¶PSC- CĤPµC‡PsPIPëPSPë: PjP°PeCĤPsPiPsP» 8000, PjP°PeCĤPsPiPsP»
7000000, PjP°PiPSC-CĤ CÍC,PµP°CĤP°C,, PIPsPrP° PsC‡PëC‰PµPSP°, PsPiP°PrCĤC-
P¶PsPIC,PëPN 03F22733.

P»C-PeP°CĤCÍCĤPeP° C,,PsCĤPjP°. PŸP°P±P»PµC,PePë, PIPeCĤPëC,C-
PİP»C-PIPePsPIPsCĤ PsP±PsP»PsPSPePsCĤ, PİCĤPsP»PsPSPiPsPIP°PSPsC— PrC-C— P·
PİPµCĤPsCĤP°P»CĤPSPsCĤ CÍPëCÍC,PµPjPsCĤ PePsPSC,CĤPsP»CĤPsPIP°PSPsC—
P°P±CÍPsCĤP±C†C-C—.

PћCÍPSPsPIPSC- C,,C-P·PëPePs-C...C-PjC-C‡PSC- PIP»P°CÍC,PëPIPsCÍC,C-:
C,P°P±P»PµC,PePë PeCĤCíPiP»C-, PrPIPsPsPİCíPeP»C-, PIPeCĤPëC,C- P¶PsPIC,PsCĤ
PİP»C-PIPePsPIPsCĤ PsP±PsP»PsPSPePsCĤ, PjP°CĤPePsPIP°PSC- C,PëCÍPSPµPSPSCİPj B«04B».

P»P°CĤPjP°PePsC,PµCĤP°PİPµPIC,PëC‡PSP° PiCĤCíPİP°. P—P°CÍPsP±Pë, C‰Ps
P·P°CÍC,PsCÍPsPICíCĤC,CĤCÍCİ PİCĤPë PrPsP±CĤPsCİPeC-CÍPSC-PN
PiC-PİPµCĤPİP»P°P·C-C— PİPµCĤPµPrPjC-C...CíCĤPsPIPsC— P·P°P»PsP·Pë.
PћPSC,P°PiPsPSC-CÍC,Pë α₁-P°PrCĤPµPSPµCĤPiC-C‡PSPëC... CĤPµC†PµPİC,PsCĤC-PI. B PљPsPr
PћPŸPİ G04C A02.

P»P°CĤPjP°PePsP»PsPiC-C‡PSC- PIP»P°CÍC,PëPIPsCÍC,C-.

P»P°CĤPjP°PePsPrPëPSP°PjC-PeP°.

PћPjPSC-Pe PћPeP°CÍ PIPëP±C-CĤPePsPIPs C- PePsPSPeCíCĤPµPSC,PSPs
P±P»PsPeCíC” PİPsCÍC,CÍPëPSP°PİC,PëC‡PSC-B α₁-

P°PrC₇H₉PμPSPsC₇H₉PμC†PμPīC,PsC₇H₉Pē, P·PsPeC₇H₉PμPjP° α_{1A} C,P° α_{1D}, C%₀Ps
P·PSP°C...PsPrC₇H₉C,CHC₇H₉C₇ C₇ PiP»P°PrPeC-PN₂ PjC₇H₉C₇PeC₇H₉P»P°C,C₇H₉C-
PīPμC₇H₉PμPrPjC-C...C₇H₉PsPIPSC— P·P°P»PsP·Pē, C€PēPN₂PePē C₇H₉PμC†PsPIPSPiPs
PjC-C...C₇H₉P° C- PīC₇H₉PsC₇H₉,P°C,PēC†PSPSC— C†P°C₇H₉,PēPSPē C₇H₉PμC,C₇H₉Pē. P₁Pμ
PīC₇H₉PēP·PIPSPPrPēC,CH PrPs P·PSPēP¶PμPSPSC₇ C,PsPSC₇H₉C₇ PiP»P°PrPePsC—
PjC₇H₉C₇PeC₇H₉P»P°C,C₇H₉Pē PīPμC₇H₉PμPrPjC-C...C₇H₉PsPIPSC— P·P°P»PsP·Pē,
C€PēPN₂PePē C₇H₉PμC†PsPIPSPiPs PjC-C...C₇H₉P° C- PīC₇H₉PsC₇H₉,P°C,PēC†PSPSC—
C†P°C₇H₉,PēPSPē C₇H₉PμC,C₇H₉Pē C,P° PīPsP»C-PīC€PμPSPSC₇ PIPēPrC-P»PμPSPSC₇
C₇H₉PμC†C-.

PhPrPSPSC†P°C₇H₉Ps P·PjPμPSC€C₇H₉C,CHC₇H₉C₇ C₇PēPjPīC,PsPjPē
PsP±C₇H₉,C₇H₉C₇PeC†C-C— C,P° PīPsPrC₇H₉P°P·PSPμPSPSC₇, PīPsPIB₇™ C₇H₉P·P°PSC- P·
PrPsP±C₇H₉PsC₇H₉PeC-C₇H₉PsC₇H₉ PiC-PīPμC₇H₉PīP»P°P·C-C”C₇H₉
PīPμC₇H₉PμPrPjC-C...C₇H₉PsPIPSC— P·P°P»PsP·Pē (C₇H₉C₇PrPSPμPSPSC₇
PīPsC†P°C,PeC₇ C₇H₉PμC†PsPIPēPīC₇H₉C₇PeP°PSPSC₇, PīPsC₇H₉P»P°P±P»PμPSPSC₇
C₇H₉C₇PrPjPμPSC₇ C₇H₉PμC†C-, PeC₇H₉P°PīP°PSPSC₇ PīC-C₇H₉P»C₇H₉
P·P°PeC-PSC†PμPSPSC₇ C₇H₉PμC†PsPIPēPīC₇H₉C₇PeP°PSPSC₇, PIC-PrC†C₇H₉,C,C₇H₉
PSPμPīPsPIPSPSPiPs C₇H₉PīPsC₇H₉PsP¶PSPμPSPSC₇ C₇H₉PμC†PsPIPSPiPs PjC-C...C₇H₉P°,
C†P°C₇H₉,C- PīPsP·PēPIPē PrPs C₇H₉PμC†PsPIPēPīC₇H₉C₇PeP°PSPSC₇, PīPsP·PēPIPē PrPs
C₇H₉PμC†PsPIPēPīC₇H₉C₇PeP°PSPSC₇ PI PSC-C†PSPēPN₂ C†P°C₇H₉,
PSPμPIC-PrPeP»P°PrPSC-C₇H₉ C₇H₉PμC†PsPIPēPīC₇H₉C₇PeP°PSPSC₇).

P—PrP°C,PSC-C₇H₉,CH α_{1A}-P°PrC₇H₉PμPSPSP±P»PsPeP°C,PsC₇H₉-PI P·PjPμPSC€C₇H₉PiP°C,Pē
P°C₇H₉,PμC₇H₉-P°P»CHPSPēPN₂ C,PēC₇H₉Pe PīPsPIB₇™ C₇H₉P·P°PSP° P·C- P·PjPμPSC€PμPSPSC₇Pj
PīPμC₇H₉PēC,,PμC₇H₉PēC†PSPSPiPs PsPīPsC₇H₉C₇. PhPjPSC-Pe PhPeP°C₇ C₇ PrPsP±PsPIC-PN₂ PrPsP·C-
0,4 PjPi PSPμ C₇H₉PīC₇H₉PēC†PēPSC₇C” PeP»C-PSC-C†PSPs P·PSP°C†C₇H₉C%₀PsPiPs
P·PSPēP¶PμPSPSC₇ C₇H₉PēC₇H₉,PμPjPSPSPiPs P°C₇H₉,PμC₇H₉-P°P»CHPSPSPiPs C,PēC₇H₉PeC₇ (PhPj)
C₇H₉Pe C₇ C...PIPSPēC... PSP° P°C₇H₉,PμC₇H₉-P°P»CHPSC₇ PiC-PīPμC₇H₉,PμPSP·C-C₇H₉, C,P°Pe C-
C₇ PīP°C†C-C”PSC,C-PI P· PSPSC₇H₉PjP°P»CHPSPēPj PīPsC†P°C,PePsPIPēPj PhPj.

PαP°C₇H₉PjP°PePsPeC-PSPμC,PēPeP°.

PhP±C₇H₉PsC₇H₉P±C†C-C₇H₉. PhPjPSC-Pe PhPeP°C₇ C₇H₉PIP»C₇H₉C” C₇H₉PsP±PsC₇H₉ C,P°P±P»PμC,PeC₇
PīC₇H₉PsP»PsPSPiPsPIP°PSPSC— PrC-C— P· PePsPSC,C₇H₉PsP»CHPSPiP°PSPēPj
PIPēPIC-P»CHPSPμPSPSC₇Pj PSP° PsC₇H₉PsPIC- PjP°C,C₇H₉PēPeC₇H₉C₇ P·
PIPēPePsC₇H₉PēC₇H₉,P°PSPSC₇Pj PiPμP»C₇H₉ PSPμC-PsPSPSPSPiPs C,PēPīC₇H₉. PαPsC₇H₉PjP°
PhPeP°C₇H₉C₇ P·P°P±PμP·PīPμC†C₇H₉” C,C₇H₉PēPIP°P»Pμ C,P° PīPsPIC-P»CHPSPμ
PIPēPIC-P»CHPSPμPSPSC₇ C,P°PjC₇H₉C₇PsP·PēPSC₇, C%₀Ps PrP°C” PμPeC₇H₉PīPsP·PēC†C-C₇H₉
P·C- C₇H₉P»P°P±PePēPjPē PePsP»PēPIP°PSPSC₇PjPē PīC₇H₉PsC,C₇H₉PiPsPj 24 PiPsPrPēPS.
PμC-C₇H₉C₇ PīPμC₇H₉PsC₇H₉P°P»CHPSPSPiPs PīC₇H₉PēPN₂PsPjC₇ PSP°C,C%₀Pμ 57 %
C,P°PjC₇H₉C₇PsP·PēPSC₇ P°P±C₇H₉PsC₇H₉P±C†C-C₇H₉,CHC₇H₉C₇ PI PePēC€PμC†PSPēPeC₇.
PēPIPēPrPeC-C₇H₉,CH C- PsP±B₇™ C”Pj P°P±C₇H₉PsC₇H₉P±C†C-C— PīC₇H₉PμPīP°C₇H₉P°C,C₇ PI
P»C-PeP°C₇H₉C₇CHPeC-PN₂ C,,PsC₇H₉PjC- C,P°P±P»PμC,PsPe PīC₇H₉PsP»PsPSPiPsPIP°PSPSC—
PrC-C— PSPμ P·PjC-PSC₇H₉C,CHC₇H₉C₇ PīC₇H₉Pē PīC₇H₉PēPN₂PsPjC- C—P¶C- C-P· PSPēP·CHPePēPj
PIPjC-C₇H₉,PsPj P¶PēC₇H₉C₇. PμPsPeP°P·PSPēPePē PIC₇H₉PjPsPeC,C₇PIP°PSPSC₇
PīC-PrPIPēC%₀C₇H₉C,CHC₇H₉C₇ PSP° 64 % C,P°B 149 % (AUC C,P° P₇max
PIC-PrPīPsPIC-PrPSPs) PīC₇H₉Pē PīC₇H₉PēPN₂PsPjC- C—P¶C- P· PIPēC₇H₉PsPePēPj PIPjC-C₇H₉,PsPj
P¶PēC₇H₉C₇ PīPsC₇H₉-PIPSC₇SPSPs P· PīC₇H₉PēPN₂PsPjPsPj PSP°C,C%₀Pμ.

PjP°PjC₇H₉C₇PsP·PēPS PrPμPjPsPSC₇H₉C₇C₇ P»C-PSC-PN₂PSC₇

C,,P°CḡPjP°PePsPeC-PSPμC,PëPeCř.

B PμC-CřP»Cł PsPrPSPsCḡP°P·PsPIPsPiPs PİCḡPëPNëPsPjCř PİCḡPμPİP°CḡP°C,Cř PhPjPSC-Pe PhPeP°Cř PSP°C,C%oPμ PjP°PeCřPëPjP°P»CHbPSP° PePsPSC†PμPSC,CḡP°C†C-Cł P°PeC,PëPIPSPsC— CḡPμC†PsPIPëPSPë Cř PİP»P°P·PjC- PeCḡPsPIC- CřPiPsCřC,PμCḡC-PiP°C”C,CHbCřCł C†PμCḡPμP· 6 PiPsPrPëPS. Pj CḡC-PIPSPsPIP°P¶PSPsPjCř CřC,P°PSC-, CłPePëPNë PrPsCřCłPiP°C”C,CHbCřCł PSP° C†PμC,PIPμCḡC,PëPNë PrPμPSCḡ PİCḡPëPNëPsPjCř PİCḡPμPİP°CḡP°C,Cř, PİC-Pe PePsPSC†PμPSC,CḡP°C†C-C— PSP°CřC,P°C” C†PμCḡPμP· 4bḡ”6 PiPsPrPëPS PSPμP·P°P»PμP¶PSPs B PIC-Pr B PİCḡPëPNëPsPjCř B C—P¶C-. B PμC-Pe B PePsPSC†PμPSC,CḡP°C†C-C— B Cř B PİP»P°P·PjC- B PeCḡPsPIC- PİC-PrPIPëC%oCřC”C,CHbCřCł PİCḡPëP±P»PëP·PSPs P·

6 PSPi/PjP» PİC-CřP»Cł PİPμCḡC€PsPiPs PİCḡPëPNëPsPjCř PrPs 11 PSPi/PjP» Cř CḡC-PIPSPsPIP°P¶PSPsPjCř CřC,P°PSC-.

PİPe CḡPμP·CřP»CHbC,P°C, C,CḡPëPIP°P»PsPiPs PIPëPIC-P»CHbPSPμPSPSCł PSP°PNëPSPëP¶C†PëPNë CḡC-PIPμPSCḡ PePsPSC†PμPSC,CḡP°C†C-C— C,P°PjCřCřP»PsP·PëPSCř Cř PİP»P°P·PjC- CřC,P°PSPsPIPëC,CHb 40 % PjP°PeCřPëPjP°P»CHbPSPsC— PePsPSC†PμPSC,CḡP°C†C-C— PSPμP·P°P»PμP¶PSPs PIC-Pr PİCḡPëPNëPsPjCř C—P¶C-.B B B B

P PsP·PiPsPrC-P». B P—PIbḡ™ CłP·CřPIP°PSPSCł B P· B P±C-P»PeP°PjPë PİP»P°P·PjPë bḡ” 99 %B PhP±bḡ™C”Pj CḡPsP·PiPsPrC-P»Cř PSPμP·PSP°C†PSPëPNëB (PİCḡPëP±P»PëP·PSPs

0,2 P»/PePi).

PḡPμC,P°P±PsP»C-P·Pj. PŷP°PjCřCřP»PsP·PëPSCř PiC-PrCḡPsC...P»PsCḡPëPr PjP°C” PSPëP·CHbPePëPNë PμC,,PμPeC, PİPμCḡC€PsPiPs PİCḡPsC...PsPrP¶PμPSPSCł, PİPsPIC-P»CHbPSPs PjPμC,P°P±PsP»C-P·CřCḡC†PëCřCḡ. P’C-P»CHbC€P° C†P°CřC,PëPSP° P°PeC,PëPIPSPsC— CḡPμC†PsPIPëPSPë PİCḡPëCřCřC,PSCł PI PeCḡPsPIC- Cř PSPμP·PjC-PSPμPSPsPjCř PIPëPiP»CłPrC-. PhPμC,P°P±PsP»C-P·CřC”C,CHbCřCł Cř PİPμC†C-PSC†C-. P PμP·CřP»CHbC,P°C,Pë in vitro PİPsPeP°P·CřCḡC,CHb, C%oPs CYP3A4 C- C,P°PePsP¶ CYP2D6 PIPëP»CḡC†P°CḡC,CHbCřCł Cř PjPμC,P°P±PsP»C-P·Pj, C-PSC€C- C-P·PsC,,PμCḡPjPμPSC,Pë CYP PSPμP·PSP°C†PSPs PIPİP»PëPIP°CḡC,CHb PSP° C,P°PjCřCřP»PsP·PëPS. PμCḡPëPiPSC-C†PμPSPSCł PjPμC,P°P±PsP»C-P·CřCḡC†PëC... C,,PμCḡPjPμPSC,C-PI B CYP3A4 C- CYP2D6 PjPsP¶Pμ PİCḡPëP·PIPμCřC,Pë PrPs PİC-PrPIPëC%oPμPSPSCł PμPeCřPiPsP·PëC†C-C— C,P°PjCřCřP»PsP·PëPSCř PiC-PrCḡPsC...P»PsCḡPëPrCř (PrPëPI. CḡPsP·PrC-P»Pë B«PhCřPsP±P»PëPIPsCřC,C- P·P°CřC,PsCřCřPIP°PSPSCłB», B«P’P·P°C”PjPsPrC-Cł P· C-PSC€PëPjPë P»C-PeP°CḡCřCHbPePëPjPë P·P°CřPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C”PjPsPrC-PNëB»). P-PsPrPμPS P· PjPμC,P°P±PsP»C-C,C-PI PSPμ C” P°PeC,PëPIPSC-C€PëPj P·P° PrC-CḡC†Cř CḡPμC†PsPIPëPSCř.

P’PëPIPμPrPμPSPSCł. PŷP°PjCřCřP»PsP·PëPS C,P° PNëPsPiPs PjPμC,P°P±PsP»C-C,Pë PIPëPIPsPrCłC,CHbCřCł PI PsCřPSPsPIPSsPjCř PSPëCḡPeP°PjPë, 4bḡ”6 % PrPsP·Pë PIPëPrC-P»CłC”C,CHbCřCł Cř PSPμP·PjC-PSPμPSPsPjCř PIPëPiP»CłPrC-. PμPμCḡC-PsPr PSP°PİC-PIIPëPIPμPrPμPSPSCł C,P°PjCřCřP»PsP·PëPSCř PİCḡPë PsPrPSPsCḡP°P·PsPIPsPjCř PİCḡPëPNëPsPjC- C,P° Cř CḡC-PIPSsPIP°P¶PSPsPjCř CřC,P°PSC- CřC,P°PSPsPIPëC,CHb 19 C- 15 PiPsPrPëPS PIC-PrPİPsPIC-PrPSPs.

PḡP»C-PSC-C†PSC- C...P°CḡP°PeC,PμCḡPëCřC,PëPePë.

PuPsPeP°P·P°PSPSCI.

P>C-PeCrPIP°PSPSCI CÍPëPjPiC,PsPjC-PI P· P±PsPeCr PSPëP¶PSC-C... PIC-PrPrC-P»C-PI
CÍPµC±PsPIPëPIC-PrPSPëC... C€P»CÍC...C-PI PiC¶Pë PrPsP±C¶PsC¶PeC-CÍPSC-PNë
PiC-PiPµC¶PiP»P°P·C-C— PiC¶PsCÍC,P°C,Pë.

PuC¶PsC,PëPiPsPeP°P·P°PSPSCI.

P“C-PiPµC¶C±CrC,P»PëPIC-CÍC,CH PrPs C,P°PjCÍCrP»PsP·PëPSCr
PiC-PrC¶PsC...P»PsC¶PëPrCr, PIPeP»C¶C±P°C¶C±Pë PjPµPrPëPeP°PjPµPSC,PsP·PSPs
C-PSPrCrPePsPIP°PSPëPNë P°PSPiC-PsPSPµPIC¶PsC,PëC±PSPëPNë PSP°P±C¶C¶Pe,
P°P±Ps PrPs P±CrPrCH-C¶PePsC— P· PrPsPiPsPjC-P¶PSPëC... C¶PµC±PsPIPëPS;
PSP°C¶PIPSC-CÍC,CH PI P°PSP°PjPSPµP·C- PsC¶C,PsCÍC,P°C,PëC±PSPsC—
PiC-PiPsC,PµPSP·C-C—; C,C¶P¶PeP° PiPµC±C-PSPePsPIP°
PSPµPrPsCÍC,P°C,PSC-CÍC,CH.

P'P·P°C" PjPsPrC-C¶ P· C-PSC€PëPjPë P»C-PeP°C¶CÍCHPePëPjPë P·P°CÍPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PNë.

P"PsCÍP»C-PrP¶PµPSPSCI PIP·P°C" PjPsPrC-C— PiC¶PsPIPsPrPëP»PëCÍC¶
C,C-P»CHPePë P·P° CÍC±P°CÍC,CH PrPsC¶PsCÍP»PëC....

PµC¶Pë PsPrPSPsC±P°CÍPSPsPjCr P·P°CÍC,PsCÍCrPIP°PSPSC- C,P°PjCÍCrP»PsP·PëPSCr
PiC-PrC¶PsC...P»PsC¶PëPrCr P· P°C,PµPSPsP»PsP»PsPj, PµPSP°P»P°PiC¶PëP»PsPj,
PSC-C,,PµPrPëPiC-PSPsPj P°P±Ps C,PµPsC,,C-P»C-PSPsPj P»C-PeP°C¶CÍCHPePsC—
PIP·P°C" PjPsPrC-C— PSPµ PIC-PrP·PSP°C±P°P»PsCÍC¶. PhPrPSPsC±P°CÍPSPµ
P·P°CÍC,PsCÍCrPIP°PSPSCI P· C±PëPjPµC,PëPrPëPSPsPj PiC-PrPIPëC%CrC", P° P·
C,,CrC¶PsCÍPµPjC-PrPsPj б¶ P·PSPëP¶CÍC" PePsPSC±PµPSC,C¶P°C±C-CH
C,P°PjCÍCrP»PsP·PëPSCr Cr PiP»P°P·PjC- PeC¶PsPIC-, P°P»Pµ PsCÍPeC-P»CHPePë C±C-
C¶C-PIPSC- P·P°P»PëC€P°C¶C,CHCÍC¶ Cr PjPµP¶P°C... PSPsC¶PjPë, Cr
CÍPiPµC±C-P°P»CHPSC-PNë PePsC¶PµPeC±C-C— PrPsP·CrPIP°PSPSCI C,P°PjCÍCrP»PsP·PëPSCr
PSPµPjP°C" PSPµPsP±C...C-PrPSPsCÍC,C-.

Pj PrPsCÍP»C-PrP¶PµPSPSCI... *in vitro* PrC-P°P·PµPiP°Pj, PiC¶PsPiC¶P°PSPsP»PsP»,
C,C¶PëC...P»PsC¶PjPµC,C-P°P·PëPr, C...P»PsC¶PjP°PrPëPSPsPS,
P°PjC-C,C¶PëPiC,PëP»C-PS, PrPëPeP»PsC,,PµPSP°Pe, PiP»C-P±PµPSPeP»P°PjC-Pr,
CÍPëPjPIP°CÍC,P°C,PëPS C,P° PIP°C¶C,,P°C¶PëPS PSPµ PIPiP»PëPIP°C¶C,CH PSP°
PIC-P»CHPSCr C,,C¶P°PeC±C-CH C,P°PjCÍCrP»PsP·PëPSCr Cr PiP»P°P·PjC- PeC¶PsPIC-
P»CHPrPëPSPë. PµPsPrC-P±PSPëPj C±PëPSPsPj C,P°PjCÍCrP»PsP·PëPS PSPµ
P·PjC-PSC¶C" C¶C-PIPµPSC¶ PIC-P»CHPSPëC... C,,C¶P°PeC±C-PNë PrC-P°P·PµPiP°PjCr,
PiC¶PsPiC¶P°PSPsP»PsP»Cr, C,C¶PëC...P»PsC¶PjPµC,C-P°P·PëPrCr C,P°
C...P»PsC¶PjP°PrPëPSPsPSCr Cr PiP»P°P·PjC- PeC¶PsPIC- P»CHPrPëPSPë.

PµC¶PsC,Pµ PrPëPeP»PsC,,PµPSP°Pe C,P° PIP°C¶C,,P°C¶PëPS PjPsP¶CrC,CH
PiC-PrPIPëC%CrPIP°C,Pë C€PIPëPrPeC-CÍC,CH PµP»C-PjC-PSP°C±C-C—
C,P°PjCÍCrP»PsP·PëPSCr.

PhPrPSPSc†P°CÍPSPµ P·P°CÍC,PsCÍCÍPIP°PSPSCÍ C,P°PjCÍCÍP»PsP·PëPSCÍ
 PiC-PrCḡPsC...P»PsCḡPëPrCÍ P· CÍPëP»CHBPSPëPjPë C-PSPiC-P±C-C,PsCḡP°PjPë
 CYP3A4 PjPsP¶Pµ PiCḡPëP·PIPµCÍC,Pë PrPs P·P±C-P»CHC€PµPSPSCÍ PIPiP»PëPICÍ
 C,P°PjCÍCÍP»PsP·PëPSCÍ PiC-PrCḡPsC...P»PsCḡPëPrCÍ. PhPrPSPSc†P°CÍPSPµ
 P·P°CÍC,PsCÍCÍPIP°PSPSCÍ P· PePµC,PsPePsPSP°P·PsP»PsPj (PIC-PrPsPjPëPñ
 CÍPëP»CHBPSPëPñ C-PSPiC-P±C-C,PsCḡ CYP3A4) PíCḡPëP·PIPsPrPëP»Ps PrPs
 P·P±C-P»CHC€PµPSPSCÍ AUC C- PŸ_{max} PrPs 2,8 C- 2,2 CḡP°P·P° PIC-PrPíPsPIC-PrPSPs.

PŸP°PjCÍCÍP»PsP·PëPSCÍ PiC-PrCḡPsC...P»PsCḡPëPr PSPµ CÍP»C-Pr
 PíCḡPëP·PSP°C†P°C,Pë CÍ PePsPjP±C-PSP°C†C-C— P· CÍPëP»CHBPSPëPjPë
 C-PSPiC-P±C-C,PsCḡP°PjPë CYP3A4 PíP°C†C-C”PSC,P°Pj P· PSPëP·CHPePëPj
 PjPµC,P°P±PsP»C-P·PjPsPj CYP2D6.

PŸP°PjCÍCÍP»PsP·PëPSCÍ PiC-PrCḡPsC...P»PsCḡPëPr CÍP»C-Pr
 P·P°CÍC,PsCÍPsPICÍPIP°C,Pë P· PsP±PµCḡPµP¶PSC-CÍC,Cḡ CÍ PePsPjP±C-PSP°C†C-C—
 P· CÍPëP»CHBPSPëPjPë C- PíPsPjC-CḡPSPëPjPë C-PSPiC-P±C-C,PsCḡP°PjPë CYP3A4.

PhPrPSPSc†P°CÍPSPµ P·P°CÍC,PsCÍCÍPIP°PSPSCÍ C,P°PjCÍCÍP»PsP·PëPSCÍ
 PiC-PrCḡPsC...P»PsCḡPëPrCÍ C- PíP°CḡPsPeCÍPµC,PëPSCÍ (CÍPëP»CHBPSPëPñ
 C-PSPiC-P±C-C,PsCḡ PŸYP2D6) PíCḡPëP·PIPsPrPëP»Ps PrPs P·P±C-P»CHC€PµPSPSCÍ
 PŸ_{max} C- AUC PrPs 1,3 C- 1,6 CḡP°P·P° PIC-PrPíPsPIC-PrPSPs, P°P»Pµ C†Pµ PSPµ C”
 PeP»C-PSC-C†PSPs P·PSP°C†CÍC‰PëPj.

PhPrPSPSc†P°CÍPSPµ P·P°CÍC,PsCÍCÍPIP°PSPSCÍ P· C-PSC€PëPjPë α₁-
 P°PrCḡPµPSPsP±P»PsPeP°C,PsCḡP°PjPë PjPsP¶Pµ PíPsCÍPëP»CHPIP°C,Pë
 PiC-PíPsC,PµPSP·PëPIPSPëPñ PµC,,PµPeC,.

PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCÍPIP°PSPSCÍ.

PíPe C- PíCḡPë P·P°CÍC,PsCÍCÍPIP°PSPSC- C-PSC€PëC... α₁-
 P°PrCḡPµPSPsP±P»PsPeP°C,PsCḡC-PI, PI PsPeCḡPµPjPëC... PIPëPíP°PrPeP°C... PíCḡPë
 P·P°CÍC,PsCÍCÍPIP°PSPSC- P»C-PeP°CḡCÍCHPePsPiPs P·P°CÍPsP±CÍ PhPjPSC-Pe
 PhPeP°CÍ PjPsP¶P»PëPIPµ P·PSPëP¶PµPSPSCÍ P°CḡC,PµCḡC-P°P»CHBPSPsPiPs C,PëCÍPeCÍ,
 C‰Ps CḡC-PrPePs PjPsP¶Pµ PíCḡPëP·PIPsPrPëC,Pë PrPs PIC,CḡP°C,Pë CÍPIC-PrPsPjPsCÍC,C-.
 PµCḡPë PíPµCḡC€PëC... PsP·PSP°PeP°C... PsCḡC,PsCÍC,P°C,PëC†PSPsC— PiC-PíPsC,PµPSP·C-C—
 (P·P°PíP°PjPsCḡPsC†PµPSPSCÍ, CÍP»P°P±PeC-CÍC,CH) PíP°C†C-C”PSC, PíPsPIPëPSPµPS
 CÍC-CÍC,Pë P°P±Ps P»CÍPiC,Pë C- P·P°P»PëC€P°C,PëCÍCÍ PI C,P°PePsPjCÍ
 PíPsP»PsP¶PµPSPSC- PrPs P·PSPëPePSPµPSPSCÍ PIPëC‰PµP·PíP°PrP°PSPëC...
 CÍPëPjPiC,PsPjC-PI.

PµPµCḡPµPr C,PëPj CÍPe CḡPsP·PíPsC†P°C,Pë P»C-PeCÍPIP°PSPSCÍ
 PíCḡPµPíP°CḡP°C,PsPj PhPjPSC-Pe PhPeP°CÍ, CÍP»C-Pr PíCḡPsPñC,Pë PjPµPrPëC†PSPµ
 PsP±CÍC,PµP¶PµPSPSCÍ P· PjPµC,PsCḡ PIPëCÍPIP»PµPSPSCÍ C-PSC€PëC...
 CÍCÍPiCÍC,PSC-C... P·P°C...PIPsCḡCHPIP°PSCH, C‰Ps PjPsP¶CÍC,CH CÍPíCḡPëC†PëPSPëC,Pë
 C,P°PeC- CÍP°PjC- CÍPëPjPíC,PsPjPë, CÍPe PrPsP±CḡPsCÍPeC-CÍPSP°
 PiC-PíPµCḡPíP»P°P·C-CÍ PíPµCḡPµPrPjC-C...CÍCḡPsPIPsC— P·P°P»PsP·Pë. PµPµCḡPµPr
 PíPsC†P°C,PePsPj P»C-PeCÍPIP°PSPSCÍ PSPµPsP±C...C-PrPSPs PíCḡPsPIPµCÍC,Pë
 CḡPµPeC,P°P»CHBPSPµ PsP±CÍC,PµP¶PµPSPSCÍ PíPµCḡPµPrPjC-C...CÍCḡPsPIPsC—

P·P°P»PsP·Pë C,P° PïCḡPë PSPμPsP±C...C-PrPSPsCíC,C- вḡ“ C,PμCíC, PSP°
PIPëP·PSP°C±PμPSPSCí CḡC-PIPSCí CíPïPμC†PëC,,C-C±PSPsPiPs P°PSC,PëPiPμPSCí
PïPμCḡPμPrPjC-C...CíCḡPsPIPSC— P·P°P»PsP·Pë (PSA) PrPs PïPsC±P°C,PëCí C,P°
C±PμCḡPμP· PsPrPSP°PePsPIC- PïCḡPsPjC-PḡPëPë C±P°CíCí PïC-Pr C±P°Cí
P»C-PëCíPIP°PSPSCí.

PμCḡPëP·PSP°C±P°C,Pë PïCḡPμPïP°CḡP°C, PïP°C†C-C”PSC,P°Pj C-P· C,CḡPḡPePsCḡ
CíC,P°PrC-C”Cḡ PSPëCḡPePsPIPsC— PSPμPrPsCíC,P°C,PSPsCíC,C- (PeP»C-CḡPμPSCí
PeCḡPμP°C,PëPSC-PSCí <10 PjP»/C...PI) PSPμPsP±C...C-PrPSPs P·
PsCíPsP±P»PëPIPsCḡ PsP±PμCḡPμPḡPSC-CíC,Cḡ, PsCíPeC-P»CḡPePë
PeP»C-PSC-C±PSPëC... PrPsCíP»C-PrPḡPμPSCḡ PrP»Cí C,P°PePëC...
PïP°C†C-C”PSC,C-PI PSPμ PïCḡPsPIPsPrPëP»Pë.

Pj PrPμCḡPePëC... PïP°C†C-C”PSC,C-PI, CḡPeC- PïCḡPëPNḡPjP°P»Pë P°P±Ps
PïCḡPëPNḡPjP°CḡC,Cḡ C,P°PjCíCíP»PsP·PëPS, PïC-Pr C±P°Cí
C...C-CḡCíCḡPiC-C±PSPsPiPs PIC,CḡCíC±P°PSPSCí P· PïCḡPëPIPsPrCí
PIPëPrP°P»PμPSPSCí PeP°C,P°CḡP°PeC,Pë C- PiP»P°CíPePsPjPë
PIC-PrP·PSP°C±P°PICíCí CíPëPSPrCḡPsPj P°C,PsPSC-C±PSPsC— P·C-PSPëC†C- (IFIS,
PIP°CḡC-P°PSC, CíPëPSPrCḡPsPjCí P·PICíPḡPμPSPsC— P·C-PSPëC†C-), C%Ps PjPsPḡPμ
CíC,P°C,Pë PïCḡPëC±PëPSPsCḡ P·P±C-P»CḡCḡPμPSPSCí PeC-P»CḡPePsCíC,C-
CíCíPeP»P°PrPSPμPSCḡ PïC-Pr C±P°Cí C±Pë PïC-CíP»Cí PïCḡPsPIPμPrPμPSPSCí
C,P°PePsC— PsPïPμCḡP°C†C-C—.

PïPe PïCḡP°PIPëP»Ps, P·P° 1вḡ“2 C,PëPḡPSC- PrPs PïCḡPsPIPμPrPμPSPSCí
PsPïPμCḡP°C†C-C— P· PïCḡPëPIPsPrCíB PIPëPrP°P»PμPSPSCí PeP°C,P°CḡP°PeC,Pë C-
PiP»P°CíPePsPjPë CḡPμPePsPjPμPSPrCíC”C,CḡCíCí PïCḡPëPïPëPSPëC,Pë
P»C-PëCíPIP°PSPSCí C,P°PjCíCíP»PsP·PëPSPsPj, PïCḡPsC,Pμ PePsCḡPëCíC,Cḡ PIC-Pr
PïCḡPëPïPëPSPμPSPSCí P»C-PëCíPIP°PSPSCí C,P°PjCíCíP»PsP·PëPSPsPj PSP°
CíCḡPsPiPsPrPSC- C,PsC±PSPs PSPμ PICíC,P°PSPsPIP»PμPSP°. PμCḡPs
CíPëPSPrCḡPsPj P°C,PsPSC-C±PSPsC— P·C-PSPëC†C- PïPsPIC-PrPsPjP»CḡP»PsCíCí
C,P°PePsPḡ Cí PïP°C†C-C”PSC,C-PI, CḡPePëPj PïCḡPëPïPëPSPëP»Pë
P·P°CíC,PsCíCíPIP°PSPSCí C,P°PjCíCíP»PsP·PëPSCí PïCḡPsC,CḡPiPsPj
C,CḡPëPIP°P»PsPiPs C±P°CíCí PrPs PïCḡPsPIPμPrPμPSPSCí PsPïPμCḡP°C,PëPIPsPiPs
PIC,CḡCíC±P°PSPSCí P· PïCḡPëPIPsPrCí PeP°C,P°CḡP°PeC,Pë.

PμP°C†C-C”PSC,P°Pj PïPμCḡPμPr PïP»P°PSPsPIPsCḡ PsPïPμCḡP°C†C-C”Cḡ P·
PïCḡPëPIPsPrCí PeP°C,P°CḡP°PeC,Pë C±Pë PiP»P°CíPePsPjPë PSPμ
CḡPμPePsPjPμPSPrCíC”C,CḡCíCí CḡPsP·PïPsC±PëPSP°C,Pë PïCḡPëPNḡPsPj
C,P°PjCíCíP»PsP·PëPSCí PiC-PrCḡPsC...P»PsCḡPëPrCí. P— PjPμC,PsCḡ
PïPsPïPμCḡPμPrPḡPμPSPSCí PjPsPḡP»PëPIPëC... CíCíPeP»P°PrPSPμPSCḡ,
PïPsPIвḡ™CḡP·P°PSPëC... C-P· IFIS, PïCḡPë PïC-PrPiPsC,PsPIC†C- PrPs
PsPïPμCḡP°C†C-C— C...C-CḡCíCḡPiPë C,P° PsC,,C,P°P»CḡPjPsP»PsPiPë PjP°CḡC,Cḡ
PrC-P·PSP°C,PëCíCí, C±Pë PïCḡPëPNḡPjP°PI (P°P±Ps PïCḡPëPNḡPjP°C”) PïP°C†C-C”PSC,
C,P°PjCíCíP»PsP·PëPS.

PḡP°PjCíCíP»PsP·PëPSCí PiC-PrCḡPsC...P»PsCḡPëPr PSPμ CíP»C-Pr
PïCḡPëP·PSP°C±P°C,Pë Cí PePsPjP±C-PSP°C†C-C— P· CíPëP»CḡPSPëPjPë
C-PSPiC-P±C-C,PsCḡP°PjPë CYP3A4 PïP°C†C-C”PSC,P°Pj P· PSPëP·CḡPePëPj

PjPμC,P°P±PsP»C-P·PjPsPj CYP2D6.

PŸP°PjCÍCfP»PsP·PëPSCr PiC-PrCḡPsC...P»PsCḡPëPr CÍP»C-Pr
P·P°CÍC,PSCÍPsPICrPIP°C,Pë P· PsP±PμCḡPμP¶PSC-CÍC,Cḡ Cr PePsPjP±C-PSP°C†C-C—
P· CÍPëP»CHbPSPëPjPë C- PiPsPjC-CḡPSPëPjPë C-PSPiC-P±C-C,PSCḡP°PjPë CYP3A4
(PrPëPI. B«P'P·P°C"PjPsPrC-CÍ P· C-PSCëPëPjPë P»C-PeP°CḡCÍCHbPePëPjPë
P·P°CÍPsP±P°PjPë C,P° C-PSCëC- PIPëPrPë PIP·P°C"PjPsPrC-PNëB»).

P†PSPsPrC- PjPsP¶PSP° PIPëCÍPIPIëC,Pë P·P°P»PëCëPePë C,P°P±P»PμC,PePë Cr
C,,PμPeP°P»C-CÍC....

PμPsPIC-PrPsPjP»CÍP»Pë PiCḡPs PIPëPiP°PrPePë P°P»PμCḡPiC-C†PSPëC...
CḡPμP°PeC†C-PNë PSP° C,P°PjCÍCfP»PsP·PëPS Cr PiP°C†C-C"PSC,C-PI P·
PSP°CÍPIIPSC-CÍC,Cḡ PI P°PSP°PjPSPμP·C- P°P»PμCḡPiC-C— PSP°
CÍCfP»CHbC,,P°PSC-P»P°PjC-PrPë. PŸP»C-Pr PrPsC,CḡPëPjCfPIP°C,PëCÍCÍ
PsP±PμCḡPμP¶PSPsCÍC,C- PiCḡPë P·P°CÍC,PSCÍCfPIP°PSPSC-
C,P°PjCÍCfP»PsP·PëPSCr PiC-PrCḡPsC...P»PsCḡPëPrCr PiP°C†C-C"PSC,P°Pj, Cr
CÍPePëC... CḡP°PSC-CëPμ PIC-PrP·PSP°C†P°P»P°CÍCÍ P°P»PμCḡPiC-CÍ PSP°
CÍCfP»CHbC,,P°PSC-P»P°PjC-PrPë.

*P—P°CÍC,PSCÍC¿PIP°PSPSCÍ C¿ PiPμCḡC-PsPr PIP°PiC-C,PSPsCÍC,C- P°P±Ps
PiPsPrC¿PIP°PSPSCÍ PiCḡC¿PrPrCḡ.*

PhPjPSC-Pe PhPeP°CÍ PSPμ PiPsPeP°P·P°PSPëPNë PrP»CÍ P·P°CÍC,PSCÍCfPIP°PSPSCÍ
P¶C-PSPeP°Pj.

PαPμCḡC,PëP»CHbPSC-CÍC,Cḡ

PμC-Pr C†P°CÍ PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PμPSCḡ
C,P°PjCÍCfP»PsP·PëPSCr PiCḡPsC,CÍPiPsPj PePsCḡPsC,PePsPiPs C,P°
C,CḡPëPIP°P»PsPiPs C†P°CÍCf PIC-PrP·PSP°C†P°P»PëCÍCÍ PiPsCḡCfCëPμPSPSCÍ
PμCÍPeCfP»CÍC†C-C—. P'PëPiP°PrPePë PiPsCḡCfCëPμPSPSCÍ PμCÍPeCfP»CÍC†C-C—,
CḡPμC,CḡPsPiCḡP°PrPSPsC— PμCÍPeCfP»CÍC†C-C— C- PSPμPrPsCÍC,P°C,PSCḡPsC—
PμCÍPeCfP»CÍC†C-C— PIC-PrP·PSP°C†P°P»PëCÍCÍ Cr
PiC-CÍP»CÍCḡPμC"CÍC,CḡP°C†C-PNëPSPëPNë PiPμCḡC-PsPr.

*P—PrP°C,PSC-CÍC,Cḡ PIPiP»PëPIP°C,Pë PSP° CëPIPëPrPeC-CÍC,Cḡ CḡPμP°PeC†C-C— PiCḡPë
PePμCḡC¿PIP°PSPSC- P°PIC,PSC,CḡP°PSCÍPiPsCḡC,PSPj P°P±Ps C-PSCëPëPjPë
PjPμC...P°PSC-P·PjP°PjPë.*

P"PsCÍP»C-PrP¶PμPSPSCÍ PIPiP»PëPICr PiCḡPμPiP°CḡP°C,Cr PSP°
P·PrP°C,PSC-CÍC,Cḡ PePμCḡCfPIP°C,Pë P°PIC,PSC,CḡP°PSCÍPiPsCḡC,PSPj P°P±Ps
C-PSCëPëPjPë B PjPμC...P°PSC-P·PjP°PjPë PSPμ PiCḡPsPIPsPrPëP»Pë. PhPrPSP°Pe
PiP°C†C-C"PSC,C-PI PiPsC,CḡC-P±PSPs PiPsPiPμCḡPμPrPëC,Pë PiCḡPs
PjPsP¶P»PëPIC-CÍC,Cḡ PIPëPSPëPePSPμPSPSCÍ P·P°PiP°PjPsCḡPsC†PμPSPSCÍ.

PŸPİPsCÍC-P± P·P°CÍC,PsCÍC¿PIP°PSPSCİ C,P° PrPsP·Pë.

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° бҒ“ 1 C,P°P±P»PµC,PeP° C%PsPrPµPSPSPs,
PSPµP·P°P»PµP¶PSPs PIC-Pr PİCҒPëPµPsPjCÍ C—P¶C-. PŸP°P±P»PµC,PeCÍ CÍP»C-Pr
PePsPIC,P°C,Pë C†C-P»PsCҒ, PSPµ CҒPsP·P»P°PjCÍCҒC†Pë C,P° PSPµ CҒPsP·P¶PsPICÍCҒC†Pë
C—C—, PsCÍPeC-P»CHPePë C†Pµ P±CÍPrPµ PİPµCҒPµC€PePsPrP¶P°C,Pë
PrPsPIPiPsC,CҒPëPIP°P»PsPjCÍ C,P° PePsPSC,CҒPsP»CHPsPIP°PSPsPjCÍ
PIPëPIC-P»CHPSPµPSPSCҒ P°PeC,PëPIPSsPiPs C-PSPİCҒPµPrC-C”PSC,P°.
PŸCҒPëPIP°P»C-CÍC,CH P»C-PeCÍPIP°PSPSCİ PICÍC,P°PSPsPIP»CҒC”C,CHCÍCİ
C-PSPPrPëPIC-PrCÍP°P»CHPSPs.

PµP°C†C-C”PSC,P°Pj C-P· PSPëCҒPePsPIPsCҒ PSPµPrPsCÍC,P°C,PSC-CÍC,CҒ PSPµ
PİPsC,CҒC-P±PSP° PePsCҒPµPeC†C-Cİ PrPsP·Pë. PµP°C†C-C”PSC,P°Pj C-P· PİPsPjC-CҒPSPsCҒ
C,P° CÍPµCҒPµPrPSCҒPsPiPs CÍC,CÍPİPµPSCİ C,CİP¶PePsCÍC,C- PİPµC†C-PSPePsPIPsCҒ
PSPµPrPsCÍC,P°C,PSC-CÍC,CҒ PSPµ PİPsC,CҒC-P±PSP° PePsCҒPµPeC†C-Cİ PrPsP·Pë (PrPëPI.
C,P°PePsP¶ CҒPsP·PrC-P» B«PµCҒPsC,PëPİPsPeP°P·P°PSPSCİB»).

P”C-C,Pë.

PµCҒPµPİP°CҒP°C, PSPµ P·P°CÍC,PsCÍPsPICÍCҒC,CH PrC-C,CİPj.

P’PµP·PİPµPeCÍ C,P° PµC,,PµPeC,PëPIPSC-CÍC,CH P·P°CÍC,PsCÍCÍPIP°PSPSCİ
C,P°PjCÍCÍP»PsP·PëPSCÍ PrC-C,CİPj PSPµ PsC†C-PSCҒPIP°P»Pë.

PµPµCҒPµPrPsP·C¿PIP°PSPSCİ.

PŸPëPjPiC,PsPjPë.

PµPµCҒPµPrPsP·CÍPIP°PSPSCİ C,P°PjCÍCÍP»PsP·PëPSCÍ
PiC-PrCҒPsC...P»PsCҒPëPrPsPj PjPsP¶Pµ PİPsC,PµPSC†C-PN₂PSPs
CÍPİCҒPëC†PëPSPëC,Pë C,CİP¶PeCÍ PiC-PİPsC,PµPSP·PëPIPSCÍ PrC-CҒ. PŸCİP¶PeP°
PiC-PİPsC,PµPSP·PëPIPSP° PrC-Cİ PIC-PrP·PSP°C†P°P»P°CÍCİ PİCҒPë CҒC-P·PSPëC...
CÍC,CÍPİPµPSCİC... PİPµCҒPµPrPsP·CÍPIP°PSPSCİ.

P>C-PeC¿PIP°PSPSCİ.

PJ CҒP°P·C- CҒC-P·PePsPiPs P·PSPëP¶PµPSPSCİ C,PëCÍPeCÍ PIPSP°CÍP»C-PrPsPe
PİPµCҒPµPrPsP·CÍPIP°PSPSCİ CÍP»C-Pr PİCҒPsPIPsPrPëC,Pë PİC-PrC,CҒPëPjCÍCҒC†CÍ
C,PµCҒP°PİC-CҒ, CÍPİCҒCİPjPsPIP°PSCÍ PSP° PIC-PrPSPsPIP»PµPSPSCİ
PSPsCҒPjP°P»CHPSPsC— C,,CÍPSPeC†C-C— CÍPµCҒC†PµPIPs-CÍCÍPrPëPSPSPsC—
CÍPëCÍC,PµPjPëB (PSP°PİCҒPëPeP»P°Pr, PİP°C†C-C”PSC,P° CÍP»C-Pr
PİPsPeP»P°CÍC,Pë PI PİPsCҒPëP·PsPSC,P°P»CHPSPµ PİPsP»PsP¶PµPSPSCİ). PİPeC%Ps
C†PµPN₂ P·P°C...C-Pr PSPµ PrC-C”, PİCҒPsPIPµCÍC,Pë C-PSC,,CÍP·C-PN₂PSCÍ
C,PµCҒP°PİC-CҒ C,P° PİCҒPëP·PSP°C†PëC,Pë PIP°P·PsPİCҒPµCÍPsCҒPSC-
P·P°CÍPsP±Pë. PќPµPsP±C...C-PrPSPs CÍP»C-PrPeCÍPIP°C,Pë P·P° C,,CÍPSPeC†C-C”CҒ
PSPëCҒPsPe C,P° PİCҒPsPIPsPrPëC,Pë P·P°PİP°P»CHPSCÍ PİC-PrC,CҒPëPjCÍCҒC†CÍ

$P''P \gg C \sqcup \text{P}i\text{C}\text{H}P\ddot{e}P\ddot{i}P\ddot{e}PSP_{\mu}PSPSC \sqcup \text{P}\ddot{i}PsPrP^{\circ}P \gg \text{CH}C\epsilon PsPiPs \text{PIC}\acute{r}PjPsPeC, CrPIP^{\circ}PSPSC \sqcup$
 $\text{P}i\text{C}\text{H}P_{\mu}P\ddot{i}P^{\circ}C\text{H}P^{\circ}C, Cr PjPsP\text{H}PSP^{\circ} C\epsilon C, CrC\ddagger PSPs \text{PIP}\ddot{e}PeP \gg P\ddot{e}PeP^{\circ}C, P\ddot{e}$
 $P\pm P \gg C\text{H}PIP^{\circ}PSPSC \sqcup. P_{\mu}C\text{H}P\ddot{e} \text{P}\ddot{i}P_{\mu}C\text{H}P_{\mu}PrPsP \cdot CrPIP^{\circ}PSPSC - P \cdot PSP^{\circ}C\ddagger PSPsC -$
 $PeC - P \gg \text{CH}PePsC\acute{r}C, C - \text{P}i\text{C}\text{H}P_{\mu}P\ddot{i}P^{\circ}C\text{H}P^{\circ}C, Cr \text{P}\ddot{i}P^{\circ}C\ddagger C - P^{\circ}PSC, Cr PSP_{\mu}PsP\pm C \dots C - PrPSPs$
 $\text{P}i\text{C}\text{H}PsPjP\ddot{e}C, P\ddot{e} C\epsilon P \gg CrPSPsPe C - P \cdot P \cdot P^{\circ}C\acute{r}C, PsC\acute{r}CrPIP^{\circ}PSPSC \sqcup Pj$
 $P^{\circ}PeC, P\ddot{e}PIPsPIP^{\circ}PSPsPiPs \text{PIC}\acute{r}PiC - P \gg P \gg C \sqcup C, P^{\circ} PSP\ddot{e}P \cdot \text{CH}PePsPsC\acute{r}PjPsC, P\ddot{e}C\ddagger PSP\ddot{e}C \dots$
 $\text{P}i\text{C}\text{H}PsPSPsC\acute{r}PSP\ddot{e}C \dots P \cdot P^{\circ}C\acute{r}PsP\pm C - PI, C, P^{\circ}PeP\ddot{e}C \dots C \sqcup Pe C\acute{r}CrP \gg \text{CH}C, P^{\circ}C,$
 $PSP^{\circ}C, C\text{H}C - C\text{H}.$

[illegible]

$\text{P}_{\mu}\text{C}-\text{Pr}\text{C}\text{P}^{\circ}\text{C}\dot{\text{I}}\text{P}\ddot{\text{I}}\text{C}-\text{C}\dot{\text{I}}\text{P}\ddot{\text{I}}\text{C}\text{P}_{\mu}\text{C}''\text{C}\dot{\text{I}}\text{C},\text{C}\dot{\text{I}}\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C}-\text{P}\text{N}_{\circ}\text{PSPsPiPs}\text{PSP}^{\circ}\text{PiP}\ddot{\text{I}}\text{C}\text{P}\ddot{\text{I}}\text{C}\text{PrC}\dot{\text{I}}\text{C}$
 $\text{PsPiP}\ddot{\text{I}}\text{C}\dot{\text{I}}\text{P}^{\circ}\text{PSPs}\text{PiP}\ddot{\text{I}}\text{P}^{\circ}\text{PrPeP}\ddot{\text{I}}\text{C}-\text{PSC},\text{C}\dot{\text{I}}\text{P}^{\circ}\text{PsPiP}_{\mu}\text{C}\dot{\text{I}}\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C}-\text{P}\text{N}_{\circ}\text{PSPsC}-$
 $\text{PSP}_{\mu}\text{C}\dot{\text{I}}\text{C},\text{P}^{\circ}\text{P}\pm\text{C}-\text{P}\ddot{\text{I}}\text{C}\text{PSPsC}\dot{\text{I}}\text{C},\text{C}-\text{C}\dot{\text{I}}\text{P}^{\circ}\text{P}\text{N}_{\circ}\text{PrC}\dot{\text{I}}\text{P}\ddot{\text{I}}\text{C}\text{PSPsC}-\text{PsP}\pm\text{PsP}\ddot{\text{I}}\text{C}\text{PSPeP}\ddot{\text{I}}\text{C}\text{PsPeP}^{\circ}$
 $(\text{C}\dot{\text{I}}\text{P}\ddot{\text{I}}\text{C}\text{PSPPrC}\dot{\text{I}}\text{P}\text{PsPj}\text{P}\cdot\text{PiC}\dot{\text{I}}\text{P}\ddot{\text{I}}\text{C}\text{P}_{\mu}\text{PSPsC}-\text{P}\cdot\text{C}-\text{PSP}\ddot{\text{I}}\text{C}\dot{\text{I}}\text{C}-)\text{PiC}\dot{\text{I}}\text{P}\ddot{\text{I}}\text{C}\text{PsPiP}_{\mu}\text{C}\dot{\text{I}}\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C}-\text{C}-\text{P}\cdot$
 $\text{PiC}\dot{\text{I}}\text{P}\ddot{\text{I}}\text{C}\text{PiPsPrC}\dot{\text{I}}\text{C}\text{PeP}^{\circ}\text{C},\text{P}^{\circ}\text{C}\dot{\text{I}}\text{P}^{\circ}\text{PeC},\text{P}\ddot{\text{I}}\text{C},\text{P}^{\circ}\text{PiP}\ddot{\text{I}}\text{C}\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C}\text{PePsPjP}\ddot{\text{I}}\text{C}\text{C}\dot{\text{I}}\text{C}\text{PiP}^{\circ}\text{C}\dot{\text{I}}\text{C}-\text{C}''\text{PSC},\text{C}-\text{Pi},$
 $\text{C}\dot{\text{I}}\text{PeC}-\text{PiC}\dot{\text{I}}\text{P}\ddot{\text{I}}\text{C}\text{P}\text{N}_{\circ}\text{PjP}^{\circ}\text{P}\ddot{\text{I}}\text{C},\text{P}^{\circ}\text{PjC}\dot{\text{I}}\text{C}\dot{\text{I}}\text{C}\text{P}\ddot{\text{I}}\text{C}\text{PsP}\cdot\text{P}\ddot{\text{I}}\text{CPS}(\text{PrP}\ddot{\text{I}}\text{C}\text{Pi},\text{C}\dot{\text{I}}\text{PsP}\cdot\text{PrC}-\text{P}\ddot{\text{I}}\text{C})$
 $\text{B}\ddot{\text{I}}\text{C}\dot{\text{I}}\text{C}\text{PsP}\pm\text{P}\ddot{\text{I}}\text{C}\text{PiPsC}\dot{\text{I}}\text{C},\text{C}-\text{P}\cdot\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C},\text{PsC}\dot{\text{I}}\text{C}\dot{\text{I}}\text{C}\text{PiP}^{\circ}\text{PSPSC}\dot{\text{I}}\text{B}\ddot{\text{I}}\text{C}).$

$P_{\mu}C-ClP \gg ClC\bar{C}P_{\mu}C''C\bar{C}C, C\bar{C}P^{\circ}C\bar{C}C-PN_2PSP\bar{C}PN_2PrPsClP\bar{C}IC-Pr.$ $P_{\mu}C\bar{C}C-P_j$
 $PIP\bar{C}C\%P_{\mu}PIPeP^{\circ}P\cdot P^{\circ}PSP\bar{C}C... PiPsP\pm C-C\bar{C}PSP\bar{C}C... C\bar{C}P_{\mu}P^{\circ}PeC\bar{C}C-PN_2,$
 $PiPsPIC-PrPsP_jP \gg ClP \gg PsCl\bar{C}Cl PiC\bar{C}Ps PIP\bar{C}PiP^{\circ}PrPeP\bar{C} C,,C-P\pm C\bar{C}P\bar{C}P \gg ClC\bar{C}C-C-$
 $PiP_{\mu}C\bar{C}P_{\mu}PrClP_{\mu}C\bar{C}PrCH, P^{\circ}C\bar{C}P\bar{C}C,P_jC-C-, C,P^{\circ}C...C-PeP^{\circ}C\bar{C}PrC-C- C,P^{\circ} PrP\bar{C}ClPiPSPsP_{\mu}.$
 $P_{\mu}C\bar{C}Ps P\cdot P^{\circ}P\cdot PSP^{\circ}C\bar{C}P_{\mu}PSC- PIP\bar{C}PiP^{\circ}PrPeP\bar{C} PiPsPIC-PrPsP_jP \gg ClP \gg PsCl\bar{C}Cl$
 $ClPiPsPSC,P^{\circ}PSPSPs, C\bar{C}P^{\circ}Cl\bar{C},PsC,Cr PiPsPIC-PrPsP_jP \gg P_{\mu}PSC\bar{C} C,P^{\circ} C\bar{C}PsP \gg CH$
 $C,P^{\circ}P_jClCrP \gg PsP\cdot P\bar{C}PSCr Cr C-C... PIP\bar{C}PSP\bar{C}PePSP_{\mu}PSPSC- PSP_{\mu} P_jPsP\bar{C}PSP^{\circ}$

PrPsCfC,PsPIC-CfPSPs PICfC,P°PSPsPIPeC,Pë.B

PuPsPIC-PrPsPjP»PuPSPSCu PicfPs PiC-PrPsP·CfCfPIP°PSC- PiPsP±C-CfPSC-
CfPuP°PeCfC-C—

PuPsPIC-PrPsPjP»PuPSPSCu PicfPs PiPsP±C-CfPSC- CfPuP°PeCfC-C— PiC-CfP»Cu
CfPuC”CfC,CfP°CfC-C— P»C-PeP°CfCfCHPePsPiPs P·P°CfPsP±Cf PjP°C” PIP°P¶P»PëPIPu
P·PSP°CfPuPSPSCu. P|Pu PrP°C” P·PjPsPiCf PicfPsPIPsPrPëC,Pë PjPsPSC-C,PsCfPëPSPi
CfPiC-PIPIC-PrPSPsCfPuPSPSCu PePsCfPëCfC,CH/CfPëP·PëPe PicfPë
P·P°CfC,PsCfCfPIP°PSPSC- CfCHPePsPiPs P»C-PeP°CfCfCHPePsPiPs P·P°CfPsP±Cf.
P¶PuPrPëCfPSPëPj C,P° C„P°CfPjP°CfPuPIC,PëCfPSPëPj PicfP°CfC-PIPSPëPeP°Pj, P°
C,P°PePsP¶ PiP°CfC-C”PSC,P°Pj P°P±Ps C—C... P·P°PePsPSPSPëPj PicfPuPrCfC,P°PIPSPëPeP°Pj
CfP»C-Pr PiPsPIC-PrPsPjP»CuC,Pë PicfPs CfCfC- PIPëPiP°PrPePë PiC-PrPsP·CfCfPIP°PSPëC...
PiPsP±C-CfPSPëC... CfPuP°PeCfC-PNë C,P° PIC-PrCfCfC,PSPsCfC,C-
PuC„PuPeC,PëPIPSPsCfC,C- P»C-PeP°CfCfCHPePsPiPs P·P°CfPsP±Cf CfPuCfPuP·
P¶PIC,PsPjP°C,PëP·PsPIP°PSCf C-PSC„PsCfPjP°CfC-PNëPSCf CfPëCfC,PuPjCf P·
C„P°CfPjP°PePsPSP°PiP»CuPrCf P·P° PiPsCfPëP»P°PSPSCuPj: <https://aisf.dec.gov.ua>.

PŸPuCfPjC-PS PicfPëPrP°C,PSPsCfC,C-. 3 CfPsPePë.

PJPjPsPIPe P·P±PuCfC-PiP°PSPSCu. P—P±PuCfC-PiP°C,Pë Cf PSPuPrPsCfC,CfPiPSPsPjCf
PrP»Cu PrC-C,PuPNë PjC-CfCfC-.

P—P±PuCfC-PiP°C,Pë PicfPë C,PuPjPiPuCfP°C,CfCfC- PSPu PIPëC‰Pu 25 °PŸ.

PJPiP°PePsPIPeP°. PuPs 10 C,P°P±P»PuC,PsPe Cf P±P»C-CfC,PuCfC-, PiPs 3
P±P»C-CfC,PuCfPë PI PeP°CfC,PsPSPSC-PNë PePsCfPsP±CfC-.

P¶P°C,PuPiPsCfC-Cu PIC-PrPiCfCfPeCf. P—P° CfPuCfPuPiC,PsPj.

P’PëCfPsP±PSPëPe. P”PuP»C„P°CfPj P¶PuPiPiPuP» P’.P’./Delpharm Meppel B.V.

**P¶C-CfCfPuP·PSP°C...PsPrP¶PuPSPSCu PIPëCfPsP±PSPëPeP° C,P° PNëPsPiPs
P°PrCfPuCfP° PjC-CfCfCu PicfPsPIP°PrP¶PuPSPSCu PrC-CuP»CHPSPsCfC,C-.**

PIPsPiPuPjP°C, 2, 7942 P”P- P¶PuPiPiPuP», PkC-PrPuCfP»P°PSPrPë/Hogemaat 2, 7942 JG
Meppel, the Netherlands.

P—P°CuPIPSPëPe. P¶CfC,PuP»P»P°Cf P¶P°CfPjP° P®CfPsPi P’.P’./Astellas Pharma Europe
B.V.

РѢС-СІС†РμР•PSP°С...PsPrP¶PμPSPSCЦ P•P°CЦPIPSPëPeP° C,P° PN₂PsPiPs
P°PrCЃPμCІP° PjC-СІС†CЦ PïCЃPsPIP°PrP¶PμPSPSCЦ PrC-СЦP»CḤPSPsCІC,C-.
PŸPëP»CḤPIC-СrCІPIPμPi, 62, 2333 P'P• P>PμPN₂PrPμPS, PќC-PrPμCЃP»P°PSPrPë/Sylviusweg,
62, 2333 P'P• Leiden, the Netherlands.