

Р†РќРЎРЎР РЈРЉР†Р†РЇ

**Р†Р»СІ РјРјР†РёС†РЎРЎРіРЎ Р•Р°СІС,РЎСІСІРІР°РЎРЎСІ Р»С-РёР°СІСІСІРёРёРЎРіРЎ
Р•Р°СІСРЎСІ**

Р”РЈРЎРђРђРђ РЎ

В (DUTAFORCE)

РЎРёР»Р°Р†:

*Р†С-СІСІС- СІРјС†РЎРІРёРЎРЎРё: Р†СІС,Р°СІС,РјСІРёР†Р†, С,Р°РјСІСІР»РЎР•РЎСІ
РіС-Р†СІРЎС...Р»РЎСІРёР†;*

1 РёР°РёСІСІР»Р° РјС-СІС,РёС,СІ Р†СІС,Р°СІС,РјСІРёР†Р† 0,5 РјРі С,Р°
С,Р°РјСІСІР»РЎР•РЎСІ РіС-Р†СІРЎС...Р»РЎСІРёР† 0,4 РјРі;

Р†РЎРіРјСРјС-РІРЎС- СІРјС†РЎРІРёРЎРЎРё:

*РЎР±РЎР»РЎРЎРёР° С,РІРјСІР†Р†— РёР°РёСІСІР»Рё: РіС-РіСІРјРјР»РЎР•Р°,
РёР°СІР°РіС-РЎР°С (Р• 407), РёР°Р»С-СІС...Р»РЎСІРёР†, С,РёС,Р°РЎСІ Р†С-РЎРёСІРёР†
(Р• 171), РІРјРіС,РёР№ Б«СІРЎРЎСІСІСІРёР» Р•Р°С...С-Р†В» (Е 110), Р•Р»С-Р• РЎРёСІР†Р†
С†РјСІРІРЎРЎРё (Р• 172);*

*Р†СІС,Р°СІС,РјСІРёР†Р†, РёР°РёСІСІР»Рё РјРёСІ™ СІРёС- 0,5 РјРі: РіР»С-С†РјСІРЎР»
РјРЎРЎРёРёР°РіСІРёР»Р»РЎРёР°РіСІР°С, С,РёРі Р†, Р±СІС,РёР»РіС-РіС-Р†СІРЎРЎРёСІР†Р†,РЎР»СІР»Р»
(Р• 321), РІРјР»Р»Р°С,РёРЎ, РіР»С-С†РјСІРёРЎ, С,РёС,Р°РЎСІ Р†С-РЎРёСІР†Р† (Р• 171),
Р•РлС-Р• РЎРёСІР†Р† РІРјРіС,РёР№ (Р• 172), С,СІРёРіС-С†РјСІРёР†Р†
СІРјСІР†РЎСІРіРіРЎ Р»Р°РЎСІСІР° Р»Р°РЎСІСІР†РіРіР°, Р»РјС†РёС,РёРЎ (Р• 322);*

*С,Р°РјСІСІР»РЎР•РЎСІ РіС-Р†СІРЎС...Р»РЎСІРёР†, РіРјР»Р»Рµ 0,4 РјРі:
С†РјР»Р»СІР»Р»РЎР•Р° РјС-РёСІРЎРёСІРёР†Р†СІС,Р°Р»С-С†РЎР°, РјР°РіРЎС-СІС
СІС,РјР°СІР°С, РјРјС,Р°РёСІР»Р»РЎРІ РёРёСІР»Р»Р»Р»Р»Р»Р»Р» Р»Р»Р» Р»С,Р° РІ” РјС,РёР»
Р°РёСІР»Р»Р»Р»Р», СІРіРіРіС-РјСІР» (1:1) Р†РёСІРіРіРјСІСІС-СІ 30 %,
РјРјС,Р°РёСІР»Р»Р»Р»Р»Р» РёРёСІР»Р»Р»Р»Р»Р» Р»С,Р° РІ” РјС,РёР» Р°РёСІР»Р»Р»Р»Р»Р»,
СІРіРіРіРіС-РјСІР» (1:1), РЎР°С,СІС-СІ РіС-Р†СІРЎРЎРёСІР†Р†, С,СІРёР°С†РјС,РёРЎ,
С,Р°Р»РёС, С,РёС,Р°РЎСІ Р†С-РЎРёСІР†Р† (Р• 171).*

Р»С-РёР°СІСІСІРёРёР° С„РЎСІРјР°. РљР°РіСІСІР»Р»Р» С,РІРјСІР†Р†.

*РђСІРЎРЎРІС- С„С-Р•РёРёС-С...С-РјС-С†РЎС- РІР»Р°СІС,РёРІРіСІС,С-: РёР°РіСІСІР»Р»Р»Р»
С,РІРјСІР†Р† Р• РЎСІР°РЎРІРІРіРіРі РёСІРёСІР»Р»Р»Р» С,Р° РёР�СІРёСІСІР»Р»Р»Р»Р»Р»Р»
РёР�СІРіСІСІРј, С%РЎ РјС-СІС,СІС,СІ Р±С-Р»С- Р°Р±РЎ Р±С-Р»СІРІР°С,С- РіРмР»Р»Р»Р»Р»Р»*

C,P° PsPrPSCr P¶PsPIC,Cr PjḄḤ™ CḄPeCr P¶PμP»P°C,PëPSPsPICr PeP°PīCfCrP»Cr P·
PjP°CfP»CḄPSPëCfC,PsCḤ P¶PsPIC,CrPIP°C,PsCḤ CḤC-PrPëPSPsCḤ.

PḄP°CḤPjP°PePsC,PμCḤP°PīPμPIC,PëC‡PSP° PiCḤCrPīP°. P—P°CfPsP±Pë, C%Ps
P·P°CfC,PsCfPsPICrCḤC,CH PīCḤPë PrPsP±CḤPsCḄPeC-CfPSC-PNë PiC-PīPμCḤPīP»P°P·C-C—
PīPμCḤPμPrPjC-C...CrCḤPsPIPsC— P·P°P»PsP·Pë. PhPSC,P°PiPsPSC-CfC, α1-
P°PrCḤPμPSPsCḤPμC‡PμPīC,PsCḤC-PI. PḤPsPr PhPḡPḤ G04C Ph52.

PḄP°CḤPjP°PePsP»PsPiC-C‡PSC- PIP»P°CfC,PëPIPsCfC,C-.

PḄP°CḤPjP°PePsPrPëPSP°PjC-PeP°.

P"CrC,P°C,,PsCḤCf C" PePsPjP±C-PSP°C‡C-C"Ḥ PrPIPsC... P»C-PeP°CḤCfCHPePëC...
P·P°CfPsP±C-PI: PrCrC,P°CfC,PμCḤPëPrCr, PīPsPrPIC-PNëPSPsPiPs
C-PSPiC-P±C-C,PsCḤP° 5α-CḤPμPrCrPeC,P°P·Pë (5 PhP P†), C- C,P°PjCfCrP»PsP·PëPSCr
PiC-PrCḤPsC...P»PsCḤPëPrCr, P°PSC,P°PiPsPSC-CfC,P°
P°PrCḤPμPSPsCḤPμC‡PμPīC,PsCḤC-PI α_{1P°} C- α_{1d}. P|C- P»C-PeP°CḤCfCHPeC-
P·P°CfPsP±Pë PjP°CḤC,CH PIP·P°C"PjPsPrPsPīPsPIPSCḤPIP°P»CHPSPëPNë
PjPμC...P°PSC-P·Pj PrC-C—, P·P°PIPrCḄPePë CḄPePsPjCr PIC-PrP±CrPIP°C"C,CHCfCḄ
C€PIPëPrPePμ PīPsCfP»P°P±P»PμPSPSCḄ CfPμC‡PsPIPëPrC-P»PμPSPSCḄ,
P·PSPëP¶CfC"C,CHCfCḄ CḤPëP·PëPe PiPsCfC,CḤPsC— P·P°C,CḤPëPjPePë CfPμC‡C-
(P"P—Pḡ) C,P° P·PjPμPSC€CfC"C,CHCfCḄ C-PjPsPIC-CḤPSC-CfC,CH
PSPμPsP±C...C-PrPSPsCfC,C- PīCḤPsPIPμPrPμPSPSCḄ C...C-CḤCrCḤPiC-C‡PSPsC—
PsPīPμCḤP°C‡C-C— P· PīCḤPëPIPsPrCr PrPsP±CḤPsCḄPeC-CfPSPsC—
PiC-PīPμCḤPīP»P°P·C-C— PīPμCḤPμPrPjC-C...CrCḤPsPIPsC— P·P°P»PsP·Pë.

PkPμ PsC‡C-PeCrC"C,CHCfCḄ, C%Ps C,,P°CḤPjP°PePsPrPëPSP°PjC-C‡PSC-
PμC,,PμPeC,Pë C,,C-PeCfPsPIP°PSPsC— PrPsP·PsPIP°PSPsC— PePsPjP±C-PSP°C‡C-C—
PrCrC,P°CfC,PμCḤPëPrCr C,P° C,P°PjCfCrP»PsP·PëPSCr
PIC-PrCḤC-P·PSCḄC,PëPjCrC,CHCfCḄ PIC-Pr C,PëC..., C%Ps PsC,CḤPëPjP°PSC-
PīCḤPë PsPrPSPsC‡P°CfPSPsPjCr P·P°CfC,PsCfCrPIP°PSPSC- PrCrC,P°CfC,PμCḤPëPrCr
C,P° C,P°PjCfCrP»PsP·PëPSCr CḄPe PsPeCḤPμPjPëC... PePsPjPīPsPSPμPSC,C-PI.

P"CzC,P°CfC,PμCḤPëPr

P"CrC,P°CfC,PμCḤPëPr PīCḤPëPiPSC-C‡CrC" P°PeC,PëPIPSC-CfC,CH CḄPe 1-PiPs,
C,P°Pe C- 2-PiPs C,PëPīCr C-P·PsC,,PμCḤPjPμPSC,C-PI 5-α-CḤPμPrCrPeC,P°P·Pë, CḄPeC-
PIC-PrPīPsPIC-PrP°CḤC,CH P·P° PīPμCḤPμC,PIPsCḤPμPSPSCḄ
C,PμCfC,PsCfC,PμCḤPsPSCr PSP° PrPëPiC-PrCḤPsC,PμCfC,PsCfC,PμCḤPsPS (P"P"Pḡ).
P"P"Pḡ C" P°PSPrCḤPsPiPμPSPsPj, CḄPePëPNë PSP°CfP°PjPīPμCḤPμPr
PIC-PrPīPsPIC-PrP°C" P·P° CḤC-CfC, PīPμCḤPμPrPjC-C...CrCḤPsPIPsC— P·P°P»PsP·Pë
C- CḤPsP·PIPëC,PsPe PrPsP±CḤPsCḄPeC-CfPSPsC— PiC-PīPμCḤPīP»P°P·C-C—
PīPμCḤPμPrPjC-C...CrCḤPsPIPsC— P·P°P»PsP·Pë. PḡP°PjCfCrP»PsP·PëPS
PīCḤPëPiPSC-C‡CrC" P°PeC,PëPIPSC-CfC,CH P°PrCḤPμPSPsCḤPμC‡PμPīC,PsCḤC-PI α_{1P°}
C- α_{1d} Cr CfC,CḤPsPjP°P»CHPSC-PNë PiP»P°PrPeC-PNë PjCrCfPeCrP»P°C,CrCḤC-

PeC₇PsPIC- (C_{ss}), C₄PeP° C₇C, P°PSPsPIPëC, CH₃ P_iC₇PëP±P»PëP·PSPs 40 PSPi/PjP», PrPsC₇C₄PiP°C''C, CH₃C₇C₄ C₄P_μC₇P_μP· 6 PjC-C₇C₄C₇C-PI PIPiP_μPrP_μPSPSC₄ PrPsP·Pë 0,5 PjPi PSP° PrPsP±C₇. P_YP_μC₇P_μPrPSC'' P·PSP°C₄P_μPSPSC₄ PSP°PrC...PsPrP_μPSPSC₄ PrC₇C, P°C₇C, P_μC₇PëPrC₇ P·C- C₇PëC₇PsPIP°C, PePë PeC₇PsPIC- C₇ C₇C-PjB₇TM C₄PSC₇ C₇C-PrPëPSC₇ C₇C, P°PSPsPIPëC, CH₃ 11,5 %.

P_YP°PjC₇C₇P»PsP·PëPS

Pj C₄PsP»PsPIC-PeC-PI C, P°PjC₇C₇P»PsP·PëPS P·PiB₇TM C₄P·C₇C''C, CH₃C₇C₄ P· P±C-P»PeP°PjPë P_iP»P°P·PjPë PeC₇PsPIC- P_iC₇PëP±P»PëP·PSPs PSP° 99 %. PhP±B₇TM C''Pj C₇PsP·P_iPsPrC-P»C₇ C'' PSP_μPIP_μP»PëPePëPj (P_iC₇PëP±P»PëP·PSPs 0,21/PePi).

PhP_μC, P°P±PsP»C-P·Pj

P''C₇C, P°C₇C, P_μC₇PëPr

P''C₇C, P°C₇C, P_μC₇PëPr P°PeC, PëPIPSPs PjP_μC, P°P±PsP»C-P·C₇C''C, CH₃C₇C₄ *in vivo*. P' C₇PjPsPIP°C... *in vitro* PrC₇C, P°C₇C, P_μC₇PëPr PjP_μC, P°P±PsP»C-P·C₇C''C, CH₃C₇C₄ C₇PëC, PsC...C₇PsPjPsPj P450 3A4 C- 3A5, C₇C, PIPsC₇C₇C₇C₄Pë C, C₇Pë PjPsPSPsPiC-PrC₇PsPeC₇PëP»CH₃PsPIP°PSPëC... PjP_μC, P°P±PsP»C-C, Pë C- PsPrPëPS PrPëPiC-PrC₇PsPecPëP»CH₃PsPIP°PSPëPN₆ PjP_μC, P°P±PsP»C-C,.

P_μC-C₇P»C₄ P_iP_μC₇PsC₇P°P»CH₃PSPsPiPs P·P°C₇C, PsC₇C₇PIP°PSPSC₄ PrC₇C, P°C₇C, P_μC₇PëPrC₇ PI PrPsP·C- 0,5 PjPi PSP° PrPsP±C₇ PrPs PrPsC₇C₄PiPSP_μPSPSC₄ C₇C-PIPSPsPIP°P_μPSPsC— PePsPSC₇P_μPSC, C₇P°C₇C-C— 1,0B₇''15,4 % (C₇P_μC₇P_μPrPSC'' P·PSP°C₄P_μPSPSC₄ B₇'' 5,4 %) PIPiP_μPrP_μPSPsC— PrPsP·Pë PrC₇C, P°C₇C, P_μC₇PëPrC₇ PIPëPrC-P»C₄C''C, CH₃C₇C₄ C₇ PeP°P» C₇ PSP_μP·PjC-PSP_μPSPsPjC₇ PIPëPiP»C₄PrC-. P P_μC₇C, P° PIPëPrC-P»C₄C''C, CH₃C₇C₄ C₇ PeP°P» C₇ PIPëPiP»C₄PrC- 4 PsC₇PSPsPIPSPëC... PjP_μC, P°P±PsP»C-C, C-PI, C%₀₀Ps PjC-C₇C, C₄C, CH₃ 39 %, 21 %, 7 % C- 7 % PePsP_μPSPsC— P· C₇P_μC₄PsPIPëPS, P_iPsPiB₇TM C₄P·P°PSPëC... C-P· P»C-PeP°C₇C₇CH₃PePëPj P·P°C₇PsP±PsPj, C- 6 PrC₇C₇PiPsC₇C₄PrPSPëC... PjP_μC, P°P±PsP»C-C, C-PI (PjP_μPSC€P_μ 5 % PePsP_μP_μPS). Pj C₇P_μC₄C- P»C₇PrPëPSPë PIPëC₄PIP»P_μPSPs P»PëC€P_μ PSP_μP·PSP°C₄PSC- PeC-P»CH₃PePsC₇C, C- PSP_μP·PjC-PSP_μPSPsPiPs PrC₇C, P°C₇C, P_μC₇PëPrC₇ (PjP_μPSC€P_μ PSC-P_μ 0,1 % PrPsP·Pë).

P_YP°PjC₇C₇P»PsP·PëPS

P·PSP°PSC, C-PsPjP_μC₇PSP° P±C-PsPePsPSPIP_μC₇C₇C-C₄ P· C, P°PjC₇C₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPrC₇ [R(-) C-P·PsPjP_μC₇] C₇ S() C-P·PsPjP_μC₇ C₇ P»C₇PrPëPSPë PSP_μ PIC-PrP±C₇PIP°C''C, CH₃C₇C₄. P_YP°PjC₇C₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPr P°PeC, PëPIPSPs PjP_μC, P°P±PsP»C-P·C₇C''C, CH₃C₇C₄ C,, P_μC₇PjP_μPSC, P°PjPë C₇PëC, PsC...C₇PsPjC₇ P450 C₇ P_iP_μC₄C-PSC₇C-, C- PjP_μPSC€P_μ 10 % PrPsP·Pë PIPëPrC-P»C₄C''C, CH₃C₇C₄ C₇ C₇P_μC₄C₇ PI PSP_μP·PjC-PSP_μPSPsPjC₇ PIPëPiP»C₄PrC-. PhP»P_μ C,, P°C₇PjP°PePsPeC-PSP_μC, PëC₄PSPëPN₆ P_iC₇PsC,, C-P»CH₃ PjP_μC, P°P±PsP»C-C, C-PI C₇ P»C₇PrPëPSPë PSP_μ PIC₇C, P°PSPsPIP»P_μPSPëPN₆. P P_μP·C₇P»CH₃C, P°C, Pë PrPsC₇P»C-PrP_μP_μPSCH₃ *in vitro* PIPeP°P·C₇CH₃, CH₃ PSP° C, P_μ, C%₀₀Ps PrPs PjP_μC, P°P±PsP»C-P·PjC₇ C, P°PjC₇C₇P»PsP·PëPSC₇

P·P°P»CfC±P°CHC,CHCfCfC C„PµCHPjPµPSC,Pë CYP3A4 C- CYP2D6, P° C,P°PePsP¶
PSPµP·PSP°C±PSPsCH C” CfC±P°CfC,CH C-PSC€PëC... C-P·PsC„PµCHPjPµPSC,C-PI CYP.

PµCHPëPiPSC-C±PµPSPSCfC P°PeC,PëPIPSPsCfC,C- C„PµCHPjPµPSC,C-PI, C¶PeC-
P±PµCHCfC,CH CfC±P°CfC,CH Cf PïPµC±C-PSPePsPIPsPjCf PjPµC,P°P±PsP»C-P·PjC-,
PjPsP¶Pµ PïCHPëP·PIPµCfC,Pë PrPs PïPsCfPëP»PµPSPsC— PrC-C—
C,P°PjCfCfP»PsP·PëPSCf. PµPµCHPµPr PIPëPIPµPrPµPSPSCfPj P·C- CfPµC±PµCH
PjPµC,P°P±PsP»C-C,Pë C,P°PjCfCfP»PsP·PëPSCf PïC-PrCHPµC...P»PsCHPëPrCf
PïC-PrPrP°CHC,CHCfCfC C€PëCHPsPePsPjCf P·PIB¶™ C¶P·CfPIP°PSPSCH P·
PiP»CHPeCfCHPsPSC-PrPsPj P°P±Ps CfCfP»CHC„P°C,PsPj.

P’PëPIPµPrPµPSPSCfC

P”CfC,P°CfC,PµCHPëPr

P’PëPIPµPrPµPSPSCfC PrCfC,P°CfC,PµCHPëPrCf P·P°P»PµP¶PëC,CH PIC-Pr PrPsP·Pë, C-
C†PµPNë PïCHPsC†PµCf CfP»C-Pr PsPïPëCfCfPIP°C,Pë C¶Pe C,P°PePëPNë, C%Ps
PIC-PrP±CfPIP°C”C,CHCfCfC PrPIPsPjP° PïP°CHP°P»PµP»CHPSPëPjPë
C€P»C¶C...P°PjPë: PsPrPëPS C” PSP°CfPëC±CfPIP°PSPëPj PïCHPë PeP»C-PSC-C±PSPs
P·PSP°C±CfC%PëC... PePsPSC†PµPSC,CHP°C†C-C¶C..., P° PrCHCfPïPëPNë B¶”
PSPµPSP°CfPëC±CfPIP°PSPëPj. PµCHPë PSPëP·CHPePëC...
PePsPSC†PµPSC,CHP°C†C-C¶C... Cf CfPëCHPsPIP°C,C†C- PeCHPsPIC- (PjPµPSC€Pµ 3
PSPi/PjP») PrCfC,P°CfC,PµCHPëPr C€PIPëPrPePs PIPëPIPsPrPëC,CHCfCfC C¶Pe
P·P°P»PµP¶PSPëPj PIC-Pr PePsPSC†PµPSC,CHP°C†C-C—, C,P°Pe C-
PSPµP·P°P»PµP¶PSPëPj PIC-Pr PePsPSC†PµPSC,CHP°C†C-C— C€P»C¶C...PsPj. PµCHPë
P·P°CfC,PsCfCfPIP°PSPSC- PsPrPSPsCHP°P·PsPIPëC... PrPsP· 5 PjPi P°P±Ps
PjPµPSC€PëC... PrPsP· P±CfP»Ps PIPëC¶PIP»PµPSPs PsP·PSP°PePë C€PIPëPrPePsPiPs
PeP»C-CHPµPSCfCf C- PICfC,P°PSPsPIP»PµPSPs PïPµCHC-PsPr
PSP°PïC-PIIPëPIPµPrPµPSPSCfC, C¶PePëPNë C,CHPëPIP°C” PIC-Pr 3 PrPs 9 PrPSC-PI.

PµCHPë C,PµCHP°PïPµPIC,PëC±PSPëC... PePsPSC†PµPSC,CHP°C†C-C¶C... PïC-CfP»C¶
PïPsPIC,PsCHPSPsPiPs PIIPµPrPµPSPSCfC PrPsP·Pë 0,5 PjPi PSP° PrPsP±Cf
PrPsPjC-PSCfC” PïPsPIC-P»CHPSC-C€PëPNë, P»C-PSC-PNëPSPëPNë C€P»C¶C...
PIPëPIPµPrPµPSPSCfC, P° PïPµCHC-PsPr PSP°PïC-PIIPëPIPµPrPµPSPSCfC
CfC,P°PSPsPIPëC,CH PïCHPëP±P»PëP·PSPs 3B¶”5 C,PëP¶PSC-PI.

PÿP°PjCfCfP»PsP·PëPS

PÿP°PjCfCfP»PsP·PëPS C- PNëPsPiPs PjPµC,P°P±PsP»C-C,Pë PIPëPIPsPrC¶C,CHCfCfC
PïPµCHPµPIP°P¶PSPs P·C- CfPµC±PµCH, PI C¶PeC-PNë PïCHPëP±P»PëP·PSPs 9 %
PrPsP·Pë B¶” Cf PIPëPiP»C¶PrC- PSPµP·PjC-PSPµPSPsC— P°PeC,PëPIPSPsC—
CHPµC±PsPIPëPSPë.

PµC-CfP»C¶ PIPSCfC,CHC-C€PSCHPsPIPµPSPSPsPiPs P°P±Ps
PïPµCHPsCHP°P»CHPSPsPiPs P·P°CfC,PsCfCfPIP°PSPSCfC Cf P»C-PeP°CHCfCHPeC-PNë
C„PsCHPjC- P· PSPµPiP°PNëPSPëPj PIPëPIC-P»CHPSPµPSPSCfCfC PïPµCHC-PsPr
PSP°PïC-PIIPëPIPµPrPµPSPSCfC C,P°PjCfCfP»PsP·PëPSCf, C%Ps
PjC-CfC,PëC,CHCfCfC Cf PïP»P°P·PjC- PeCHPsPIC-, PePsP»PëPIP°C”C,CHCfCfC PI
PrC-P°PïP°P·PsPSC- PIC-Pr 5 PrPs 7 PiPsPrPëPS. P¶PµCHPµP·

C,,P°CḡPjP°PePsPeC-PSPµC,PëPeCř, CḡPµPiCřP»CHbPsPIP°PSCř C€PIPëPrPeC-CřC,Cḡ
 PİPsPiP»PëPSP°PSPSCḡ Cř PIPëPiP°PrPeCř P· C,P°PjCřCřP»PsP·PëPSPsPj Cř
 PeP°PiCřCřP»P°C... P· PjPsPrPëC,,C-PePsPIP°PSPëPj PIPëPIC-P»CHbPSPµPSPSCḡPj,
 CřPİCḡP°PIP¶PSC-PNë PİPµCḡC-PsPr PSP°PiC-PIPIPëPIPµPrPµPSPSCḡ
 C,P°PjCřCřP»PsP·PëPSCř, PiCḡPëPNëPSCḡC,PsiPiPs PiC-CřP»Cḡ C—PrPë,
 CřC,P°PSPsPIPëC,CHb PiCḡPëP±P»PëP·PSPs 10 PiPsPrPëPS, P° PI
 CḡC-PIPSPsPIP°P¶PSC-PNë PePsPSC†PµPSC,CḡP°C†C-C— Cř PİP°C†C-C”PSC,C-PI Bḡ”
 PiCḡPëP±P»PëP·PSPs 13 PiPsPrPëPS.

PµP°C†C-C”PSC,Pë P»C-C,PSCHbPsPiPs PIC-PeCž

P”CřC,P°CřC,PµCḡPëPr

PαP°CḡPjP°PePsPeC-PSPµC,PëPeP° PrCřC,P°CřC,PµCḡPëPrCř
 PsC†C-PSCḡPIP°P»P°CřCḡ Cř 36 P·PrPsCḡPsPIPëC... C†PsP»PsPIC-PeC-PI-
 PrPsP±CḡPsPIPsP»CHbC†C-PI PIC-PePsPj PIC-Pr 24 PrPs 87 CḡPsPeC-PI PİC-CřP»Cḡ
 PIPIPµPrPµPSPSCḡ PsPrPSPsCḡP°P·PsPIPsC— PrPsP·Pë 5 PjPi. P—PSP°C†PSPsC—
 P·P°P»PµP¶PSPsCřC,C- PIPİP»PëPICř PrCřC,P°CřC,PµCḡPëPrCř PIC-Pr PIC-PeCř
 PİP°C†C-C”PSC,P° PSPµ CřPİPsCřC,PµCḡC-PiP°P»PsCřCḡ, P°P»Pµ PİPµCḡC-PsPr
 PSP°PiC-PIPIPëPIPµPrPµPSPSCḡ P±CřPI PePsCḡPsC,C€PëPj Cř C†PsP»PsPIC-PeC-PI
 PIC-PePsPj PrPs 50 CḡPsPeC-PI. PŸC,P°C,PëCřC,PëC†PSPëC...
 PIC-PrPjC-PSPSPsCřC,PµPNë Cř PİPµCḡC-PsPrC- PSP°PiC-PIPIPëPIPµPrPµPSPSCḡ PSPµ
 P±CřP»Ps PiCḡPë PİPsCḡC-PIPSCḡPSPSC- PiCḡCřPİPë 50Bḡ”69-CḡC-C†PSPëC...
 PrPsCřP»C-PrP¶CřPIP°PSPëC... C-P· PiCḡCřPİPsCḡ PrPsCřP»C-PrP¶CřPIP°PSPëC...
 PIC-PePsPj PIC-Pr 70 CḡPsPeC-PI.

PŸP°PjCřCřP»PsP·PëPS

PµPµCḡPµC...CḡPµCřPSPµ PİPsCḡC-PIPSCḡP»CHbPSPµ PrPsCřP»C-PrP¶PµPSPSCḡ
 P·P°PiP°P»CHbPSPsPiPs PIPİP»PëPICř C,P°PjCřCřP»PsP·PëPSCř
 PiC-PrCḡPsC...P»PsCḡPëPrCř (AUC) C- PİPµCḡC-PsPrCř
 PSP°PiC-PIPIPëPIPµPrPµPSPSCḡ PIPeP°P·CřC” PSP° C,Pµ, C‰Ps
 C,,P°CḡPjP°PePsPeC-PSPµC,PëC†PSP° PrC-Cḡ C,P°PjCřCřP»PsP·PëPSCř
 PiC-PrCḡPsC...P»PsCḡPëPrCř PjPsP¶Pµ P±CřC,Pë C,CḡPsC...Pë C,CḡPëPIP°P»C-C€PsCḡ
 Cř PİP°C†C-C”PSC,C-PI P»C-C,PSCHbPsPiPs PIC-PeCř PİPsCḡC-PIPSCḡPSPs P·
 PjPsP»PsPrPëPjPë P·PrPsCḡPsPIPëPjPë PrPsP±CḡPsPIPsP»CHbC†CḡPjPë
 C†PsP»PsPIC-C†PsC— CřC,P°C,C-. P’P»P°CřPSPëPNë PeP»C-CḡPµPSCř PSPµ
 P·P°P»PµP¶PëC,CHb PIC-Pr P·PIBḡ™ CḡP·CřPIP°PSPSCḡ C,P°PjCřCřP»PsP·PëPSCř
 PiC-PrCḡPsC...P»PsCḡPëPrCř P· α-1-PePëCřP»PëPj PiP»C-PePsPİCḡPsC,PµC—PSPsPj,
 P°P»Pµ P·PSPëP¶CřC”C,CHbCřCḡ P· PIC-PePsPj PİP°C†C-C”PSC,P°, Cř
 CḡPµP·CřP»CHbC,P°C,C- C†PsPiPs P·P°PiP°P»CHbPSP° PrC-Cḡ C” PSP° 40 %
 CřPëP»CHbPSC-C€PsCḡ (AUC) Cř PİP°C†C-C”PSC,C-PI PIC-PePsPj 55Bḡ”75 CḡPsPeC-PI
 PİPsCḡC-PIPSCḡPSPs P· PrC-C”Cḡ Cř PİP°C†C-C”PSC,C-PI PIC-PePsPj 20Bḡ”32
 CḡPsPePë.

PkPëCḡPePsPIP° PSPµPrPsCřC,P°C,PSC-CřC,CHb

P”CřC,P°CřC,PµCḡPëPr

P'PīP»PēPI PSPēCḡPePsPIPsC— PSPμPrPsCfC,P°C,PSPsCfC,C- PSP°
C,,P°CḡPjP°PePsPeC-PSPμC,PēPeCf PrCfC,P°CfC,PμCḡPēPrCf PSPμ PIPēPIC‡P°P»Pē.
PḡP»Pμ Cf CfPμC‡C- P»CḡPrPēPSPē PIPēCḡPIP»CḡC" C,CHCfCḡ PjPμPSC€Pμ 0,1 %
PrPsP·Pē PrCfC,P°CfC,PμCḡPēPrCf 0,5 PjPi Cf CḡC-PIPSPIPsP°PḡPSC-PNē
PePsPSC‡PμPSC,CḡP°C‡C-C—, C,PsPjCf PeP»C-PSC-C‡PSPs P·PSP°C‡CfC%PsPiPs
PīC-PrPIPēC%PμPSPSCḡ PePsPSC‡PμPSC,CḡP°C‡C-C— PrCfC,P°CfC,PμCḡPēPrCf Cf
PīP»P°P·PjC- PeCḡPsPIC- Cf PīP°C‡C-C" PSC,C-PI P· PSPēCḡPePsPIPsCḡ
PSPμPrPsCfC,P°C,PSC-CfC,Cḡ PsC‡C-PeCfPIP°C,Pē PSPμ CfP»C-Pr (PrPēPI.
CḡPsP·PrC-P» B«PŸPīPsCfC-P± P·P°CfC,PsCfCfPIP°PSPSCḡ C,P° PrPsP·PēB»).

PŸP°PjCfCfP»PsP·PēPS

PαP°CḡPjP°PePsPeC-PSPμC,PēPeP° C,P°PjCfCfP»PsP·PēPSCf
PiC-PrCḡPsC...P»PsCḡPēPrCf PīPsCḡC-PIPSCHPIP°P»P°CfCḡ Cf 6 PīP°C‡C-C" PSC,C-PI
P· PSPēCḡPePsPIPsCḡ PSPμPrPsCfC,P°C,PSC-CfC,Cḡ PIC-Pr CfP»P°P±PePsPiPs PrPs
PīPsPjC-CḡPSPsPiPs ($30 \leq CL_{cr} < 70 PjP»/C...PI/1,73 Pj^2$) P°P±Ps PIC-Pr
PīPsPjC-CḡPSPsPiPs PrPs C,CḡPḡPePsPiPs ($10 \leq CL_{cr} < 30 PjP»/C...PI/1,73 Pj^2$)
CfC,CfPīPμPSCḡ C- Cf 6 PrPsCfP»C-PrPḡCfPIP°PSPēC... P· PSPsCḡPjP°P»CHBPSPēPj
PeP»C-CḡPμPSCfPsPj ($CL_{cr} < 90 PjP»/C...PI/1,73 Pj^2$). Pj C,PsPNē C‡P°Cf CḡPe Cf
P·P°PiP°P»CHBPSC-PNē PePsPSC‡PμPSC,CḡP°C‡C-C— C,P°PjCfCfP»PsP·PēPSCf
PiC-PrCḡPsC...P»PsCḡPēPrCf Cf PīP»P°P·PjC- PeCḡPsPIC-
CfPīPsCfC,PμCḡC-PiP°P»P°CfCḡ P·PjC-PSP° PI CḡPμP·CfP»CHC,P°C,C-
P·PjC-PSPSPsPiPs P·PIbḡ™ CḡP·CfPIP°PSPSCḡ P· α-1-PePēCfP»PēPj
PīP»C-PePsPīCḡPsC,PμC—PSPsPj, PePsPSC‡PμPSC,CḡP°C‡C-Cḡ
PSPμP·PIbḡ™ CḡP·P°PSPsPiPs (P°PeC,PēPIPSPsPiPs) C,P°PjCfCfP»PsP·PēPSCf
PiC-PrCḡPsC...P»PsCḡPēPrCf, P° C,P°PePsPḡ PIP»P°CfPSPēPNē PeP»C-CḡPμPSCf
P·P°P»PēC€P°P»PēCfCḡ PIC-PrPSPsCfPSPs CfC,P°P±C-P»CHBPSPēPjPē. PŸPsPjCf
PīP°C‡C-C" PSC,P°Pj P· PSPēCḡPePsPIPsCḡ PSPμPrPsCfC,P°C,PSC-CfC,Cḡ PSPμ
PīPsC,CḡC-P±PSP° PePsCḡPμPeC‡C-Cḡ PrPsP·Pē C,P°PjCfCfP»PsP·PēPSCf
PiC-PrCḡPsC...P»PsCḡPēPrCf PI PeP°PīCfCfP»P°C.... PḡP»Pμ PīP°C‡C-C" PSC,Pē P·
C,PμCḡPjC-PSP°P»CHBPSPsCḡ CfC,P°PrC-C" Cḡ PSPēCḡPePsPIPsC—
PSPμPrPsCfC,P°C,PSPsCfC,C- ($CL_{cr} < 10 PjP»/C...PI/1,73 Pj^2$) PSPμ
PrPsCfP»C-PrPḡCfPIP°P»PēCfCḡ.

PμPμC‡C-PSPePsPIP° PSPμPrPsCfC,P°C,PSC-CfC,CH

P" CfC,P°CfC,PμCḡPēPr

P'PīP»PēPI PīPμC‡C-PSPePsPIPsC— PSPμPrPsCfC,P°C,PSPsCfC,C- PSP°
C,,P°CḡPjP°PePsPeC-PSPμC,PēPeCf PrCfC,P°CfC,PμCḡPēPrCf PSPμ PIPēPIC‡P°PICfCḡ
(PrPēPI. CḡPsP·PrC-P» B«PμCḡPsC,PēPīPsPeP°P·P°PSPSCḡB»). PḡCfPeC-P»CHPePē
PrCfC,P°CfC,PμCḡPēPr PIPēPIPsPrPēC,CHCfCḡ PīPμCḡPμPIP°PḡPSPs C€P»CḡC...PsPj
PjPμC,P°P±PsP»C-P·PjCf, PsC‡C-PeCfC" C,CHCfCḡ, C%Ps CḡC-PIPμPSCḡ
PrCfC,P°CfC,PμCḡPēPrCf PI PīP»P°P·PjC- PeCḡPsPIC- C‡PēC... PīP°C‡C-C" PSC,C-PI
P±CfPrPμ PiC-PrPIPēC%PμPSPēPj, P° PīPμCḡC-PsPr PSP°PīC-PIPIPēPIPμPrPμPSPSCḡ
bḡ" C,CḡPēPIP°P»C-C€PēPj (PrPēPI. CḡPsP·PrC-P»Pē B«PḡCfPsP±P»PēPIPsCfC,C-
P·P°CfC,PsCfCfPIP°PSPSCḡB» C,P° B«PŸPīPsCfC-P± P·P°CfC,PsCfCfPIP°PSPSCḡ C,P°
PrPsP·PēB»).

Py°PjCfCfP»PsP·PëPS

PαP°CfPjP°PePsPeC-PSPμC,PëPeCf C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCfPsC...P»PsCfPëPrCf PiPsCfC-PIPSCfPIP°P»Pë Cf 8 PiP°CfC-C"°PSC,C-PI P·
PiPsPjC-CfPSPëPjPë PiPsCfCfC€PμPSPSCfPjPë C,,CfPSPeCfC-C— PiPμCfC-PSPePë
(PeP»P°CfPëC,,C-PeP°CfC-Cf P·P° P\$P°PNëP»PrPsPj бг " Pμбг™ Cф: CfC,CfPiPμPSC- A C-
B) C- Cf 8 PrPsCfP»C-PrP¶CfPIP°PSPëC... P· PSPSCfPjP°P»CHbPSPsCf
C,,CfPSPeCfC-C"°Cf PiPμCfC-PSPePë. P' C,PsPNë CfP°Cf CfPe P·PjC-PSP° Cf
P·P°PiP°P»CHbPSC-PNë PePsPSCfPμPSC,CfP°CfC-C— C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCfPsC...P»PsCfPëPrCf PI PiP»P°P·PjC- PeCfPsPIC-
CfPiPsCfC,PμCfC-PiP°P»P°CfCf PI CfPμP·CfP»CHbC,P°C,C- P·PjC-PSPSPsPiPs
P·Piбг™ CfP·CfPIP°PSPSCf P· α-1-PePëCfP»PëPj PiP»C-PePsPiCfPsC,PμC—PSPsPj,
PePsPSCfPμPSC,CfP°CfC-Cf PSPμP·Piбг™ CfP·P°PSPsPiPs (P°PeC,PëPIPSPsPiPs)
C,P°PjCfCfP»PsP·PëPSCf PiC-PrCfPsC...P»PsCfPëPrCf PSPμ P·P°P·PSP°PIP°P»P°
P·PSP°CfPSPëC... P·PjC-PS, PIC-PrP·PSP°CfP°P»P°CfCf C,C-P»CHbPePë PiPsPjC-CfPSP°
(32 %) P·PjC-PSP° PIP»P°CfPSPsPiPs PeP»C-CfPμPSCfCf PSPμP·Piбг™ CfP·P°PSPsPiPs
C,P°PjCfCfP»PsP·PëPSCf PiC-PrCfPsC...P»PsCfPëPrCf. PyPsPjCf PiP°CfC-C"°PSC,Pë P·
PiPsPjC-CfPSPëPjPë PiPsCfCfC€PμPSPSCfPjPë C,,CfPSPeCfC-C— PiPμCfC-PSPePë
PSPμ PiPsC,CfPμP±CfCfC,CHb PePsCfPμPeCfC-C— PrPsP·Pë C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCfPsC...P»PsCfPëPrCf. P"C-Cf C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCfPsC...P»PsCfPëPrCf PSPμ PIPëPICfP°P»P°CfCf Cf PiP°CfC-C"°PSC,C-PI P·
C,CfP¶PePëPjPë PiPsCfCfC€PμPSPSCfPjPë C,,CfPSPeCfC-C— PiPμCfC-PSPePë.

P'PμP·PiPμPeP° C,P° PeP»C-PSC-CfPSC- PrPsCfP»C-PrP¶PμPSPSCf

PYpμCfCfPμPIP° PSPμPrPsCfC,P°C,PSC-CfC,CHb

PJ 4-CfC-CfPSPsPjCf PeP»C-PSC-CfPSPsPjCf PrPsCfP»C-PrP¶PμPSPSC-
P·P°CfC,PsCfCfPIP°PSPSCf PrCfC,P°CfC,PμCfPëPrCf Cf PiPsC"PrPSP°PSPSC- P·
C,P°PjCfCfP»PsP·PëPSPsPj PrP»Cf P»C-PeCfPIP°PSPSCf PrPsP±CfPsCfPeC-CfPSPsC—
PiC-PiPμCfPiP»P°P·C-C— PiPμCfPμPrPjC-C...CfCfPsPIPsC— P·P°P»PsP·Pë Cf 4844
CfPsP»PsPIC-PeC-PI (PrPsCfP»C-PrP¶PμPSPSCf CombAT) CfP°CfC,PsC,P°
PIPëPSPëPePSPμPSPSCf CfPμCfCfPμPIPsC— PSPμPrPsCfC,P°C,PSPsCfC,C- (P·P±C-CfPSPμ
PiPsPSCfC,C,Cf) Cf PiCfCfPiC- PePsPjP±C-PSPIPIP°PSPsC— C,PμCfP°PiC-C— P±CfP»P°
PIPëC%PsCf (14/1610, 0,9 %), PSC-P¶ Cf P±CfPrCHb-CfPeC-PNë PiCfCfPiC-
PjPsPSPsC,PμCfP°PiC-C— PrCfC,P°CfC,PμCfPëPrPsPj (4/1623, 0,2 %) P°P±Ps
C,P°PjCfCfP»PsP·PëPSPsPj (10/1611, 0,6 %).

P' PsPeCfPμPjPsPjCf 4-CfC-CfPSPsPjCf PeP»C-PSC-CfPSPsPjCf PiPsCfC-PIPSCfP»CHbPSPsPjCf
PrPsCfP»C-PrP¶PμPSPSC- PiP»P°CfPμP±Ps P· C...C-PjC-CfPSPsCf
PiCfPsC,,C-P»P°PeC,PëPePsCf PrCfC,P°CfC,PμCfPëPrPsPj P·P° CfCfP°CfC,Cf 8231
CfPsP»PsPIC-PeP° PIC-PePsPj PIC-Pr 50 PrPs 75 CfPsPeC-PI P· PiPsPiPμCfPμPrPSC-PjPë
PSPμPiP°C,PëPIPSPëPjPë PrP°PSPëPjPë P±C-PsPiCfC-C— PSP° CfP°Pe
PiPμCfPμPrPjC-C...CfCfPsPIPsC— P·P°P»PsP·Pë C- PIPëC...C-PrPSPëPj CfC-PIPSPμPj PSA
PjC-P¶ 2,5 PSPI/PjP» C- 10,0 PSPI/PjP» Cf CfPsP»PsPIC-PeC-PI PIC-PePsPj PIC-Pr 50 PrPs 60
CfPsPeC-PI P°P±Ps 3 PSPI/PjP» C- 10,0 PSPI/PjP» Cf CfPsP»PsPIC-PeC-PI PIC-PePsPj PIC-Pr 60
CfPsPeC-PI (PrPsCfP»C-PrP¶PμPSPSCf REDUCE) P±CfP»Ps PICfC,P°PSPsPIP»PμPSPs, C%Ps
CfP°CfC,PsC,P° PIPëPSPëPePSPμPSPSCf CfPμCfCfPμPIPsC—
PSPμPrPsCfC,P°C,PSPsCfC,C- Cf PiP°CfC-C"°PSC,C-PI, CfPeC- PiCfPëPNëPjP°P»Pë
PrCfC,P°CfC,PμCfPëPr 0,5 PjPi 1 CfP°P· PSP° PrPsP±Cf (30/4105, 0,7 %), P±CfP»P°

PIPëC%PsCĤ PĭPsCĤC-PIPSCĬPSPs P· PĭP°C†C-C"PSC,P°PjPë, CĬPeC-
PĭCĤPëPNëPjP°P»Pë PĭP»P°C†PμP±Ps (16/4126, 0,4 %).
P PμC,CĤPsCĬPĭPμPeC,PëPIPSPëPNë P°PSP°P»C-P· C†CHPsPiPs
PrPsCĬP»C-PrP¶PμPSPSCĬ PĭPsPeP°P·P°PI PIPëC%Cr C†P°CĬC,PsC,Cr
CĬPμCĤC†PμPIPsC— PSPμPrPsCĬC,P°C,PSPsCĬC,C- Cr PĭP°C†C-C"PSC,C-PI, CĬPeC-
PĭCĤPëPNëPjP°P»Pë PrCrC,P°CĬC,PμCĤPëPr C- α-P±P»PsPeP°C,PsCĤ
PsPrPSPsC†P°CĬPSPs (12/1152, 1,0 %), PĭPsCĤC-PIPSCĬPSPs P· PĭP°C†C-C"PSC,P°PjPë,
CĬPeC- PĭCĤPëPNëPjP°P»Pë PrCrC,P°CĬC,PμCĤPëPr P±PμP· α-P±P»PsPeP°C,PsCĤP°
(18/2953, 0,6 %), PĭP»P°C†PμP±Ps C- α-P±P»PsPeP°C,PsCĤ (1/1399, <0,1 %) P°P±Ps
PĭP»P°C†PμP±Ps P±PμP· α-P±P»PsPeP°C,PsCĤP° (15/2727, 0,6 %). PμCĤPëC†PëPSPSPsPiPs
PIP·P°C" PjPsP·PiBĤ™ CĬP·PeCr PjC-P¶ P·P°CĬC,PsCĬCrPIP°PSPSCĬPj
PrCrC,P°CĬC,PμCĤPëPrCr (CĬPe PjPsPSPsC,PμCĤP°PĭC-C— P°P±Ps Cr
PePsPjP±C-PSP°C†C-C— P· α-P±P»PsPeP°C,PsCĤP°PjPë) C,P° PIPëPSPëPePSPμPSPSCĬPj
CĬPμCĤC†PμPIPsC— PSPμPrPsCĬC,P°C,PSPsCĬC,C- PICĬC,P°PSPsPIP»PμPSPs PSPμ
P±CrP»Ps (PrPëPI. CĤPsP·PrC-P» B«PhCĬPsP±P»PëPIPsCĬC,C-
P·P°CĬC,PsCĬCrPIP°PSPSCĬB»).

P P°Pe PĭPμCĤPμPrPjC-C...CrCĤPsPIPsC— P·P°P»PsP·Pë C-
PSPëP·CHPePsPrPëC,,PμCĤPμPSC†C-PNëPsPIP°PSC- PĭCrC...P»PëPSPë

Pj 4-CĤC-C†PSPsPjCr PrPsCĬP»C-PrP¶PμPSPSC-, PI CĬPePsPjCr PIPëPIC†P°P»Pë PrC-CĤ
PrCrC,P°CĬC,PμCĤPëPrCr PĭPsCĤC-PIPSCĬPSPs P· PĭP»P°C†PμP±Ps, Cr 8231 C†PsP»PsPIC-PeP°
PIC-PePsPj PIC-Pr 50 PrPs 75 CĤPsPeC-PI P· PĭPsPĭPμCĤPμPrPSC-PjPë PSPμPiP°C,PëPIPSPëPjPë
PrP°PSPëPjPë P±C-PsPĭCĬC-C— PSP° CĤP°Pe PĭPμCĤPμPrPjC-C...CrCĤPsPIPsC— P·P°P»PsP·Pë
C- PIPëC...C-PrPSPëPj CĤC-PIPSPμPj PSA PjC-P¶ 2,5 PSPi/PjP» C- 10,0 PSPi/PjP» Cr
C†PsP»PsPIC-PeC-PI PIC-PePsPj PIC-Pr 50 PrPs 60 CĤPsPeC-PI P°P±Ps 3 PSPi/PjP» C- 10,0
PSPi/PjP» Cr C†PsP»PsPIC-PeC-PI PIC-PePsPj PIC-Pr 60 CĤPsPeC-PI (PrPsCĬP»C-PrP¶PμPSPSCĬ
REDUCE) 6706 PĭP°C†C-C"PSC,P°Pj P±CrP»Ps PĭCĤPsPIPμPrPμPSPs PiPsP»PePsPICr
P±C-PsPĭCĬC-CĤ PĭCĤPsCĬC,P°C,Pë (PsP±PsPiBĤ™ CĬP·PePsPICr P·P° PĭPμCĤPIPëPSPSPëPj
PĭCĤPsC,PsPePsP»PsPj), PrP°PSC- CĬPePsC— P±CrP»Pë PIPëPePsCĤPëCĬC,P°PSC- PrP»CĬ
P°PSP°P»C-P·Cr PrPëC,,PμCĤPμPSC†C-CĤPIP°PSPSCĬ P·P° CĤPeP°P»PsCĤ P"»C-CĬPsPSP°. Pj
PrPsCĬP»C-PrP¶PμPSPSC- P±CrP»Ps PIPëCĬPIP»PμPSPs 1517 PĭP°C†C-C"PSC,C-PI P·
PrC-P°PiPSPsP·PsPj CĤP°Pe PĭCĤPsCĬC,P°C,Pë. P'C-P»CHCĤC-CĬC,CH PĭCrC...P»PëPS
PĭCĤPsCĬC,P°C,Pë (70 %), PIPëCĬPIP»PμPSPëC... P·P° PrPsPiPsPjPsPiPsCĤ P±C-PsPĭCĬC-C—, PI
PsP±PsC... PĭCĤCrPĭP°C... P»C-PeCrPIP°PSPSCĬ PjP°P»Pë PIPëCĬPsPePëPNë CĤC-PIPμPSCĤ
PrPëC,,PμCĤPμPSC†C-CĤPIP°PSPSCĬ (5BĤ"6 P±P°P»C-PI P·P° CĤPeP°P»PsCĤ P"»C-CĬPsPSP°).

Pj PĭCĤCrPĭC- PrCrC,P°CĬC,PμCĤPëPrCr P·P°CĤPμC"ĬC,CĤPsPIP°PSPs PIPëC%Cr
C†P°CĬC,PsC,Cr (n=29, 0,9 %) PSPëP·CHPePsPrPëC,,PμCĤPμPSC†C-PNëPsPIP°PSPsPiPs CĤP°PeCr
PĭCĤPsCĬC,P°C,Pë (8BĤ"10 P±P°P»C-PI P·P° CĤPeP°P»PsCĤ P"»C-CĬPsPSP°)
PĭPsCĤC-PIPSCĬPSPs P· PĭCĤCrPĭPsCĤ PĭP»P°C†PμP±Ps (n=19, 0,6 %) (CĤ=0,15). Pj
PĭPμCĤCĤC- 2 CĤPsPePë PrPsCĬP»C-PrP¶PμPSPSCĬ PeC-P»CHPeC-CĬC,CH
PĭP°C†C-C"PSC,C-PI P· CĤP°PePsPj PĭPμCĤPμPrPjC-C...CrCĤPsPIPsC— P·P°P»PsP·Pë P·
PĭPsPeP°P·PSPëPePsPj 8BĤ"10 P±P°P»C-PI P·P° CĤPeP°P»PsCĤ P"»C-CĬPsPSP° P±CrP»P°
PsPrPSP°PePsPIPsCĤ Cr PĭCĤCrPĭC- PrCrC,P°CĬC,PμCĤPëPrCr (n=17, 0,5 %) C- PI PĭCĤCrPĭC-
PĭP»P°C†PμP±Ps (n=18, 0,5 %). PμCĤPsC,CĬPiPsPj 3BĤ"4-PiPs CĤPsPeC-PI
PrPsCĬP»C-PrP¶PμPSPSCĬ P±C-P»CHCĤP° PeC-P»CHPeC-CĬC,CH PIPëPĭP°PrPeC-PI CĤP°PeCr
PĭPμCĤPμPrPjC-C...CrCĤPsPIPsC— P·P°P»PsP·Pë P· PĭPsPeP°P·PSPëPePsPj 8BĤ"10 P±P°P»C-PI
P·P° CĤPeP°P»PsCĤ P"»C-CĬPsPSP° P±CrP»Ps PrC-P°PiPSPsCĬC,PsPIP°PSPs Cr PĭCĤCrPĭC-
PrCrC,P°CĬC,PμCĤPëPrCr (n=12, 0,5 %) PĭPsCĤC-PIPSCĬPSPs P· PĭCĤCrPĭPsCĤ PĭP»P°C†PμP±Ps

(n=1, < 0,1 %) (C₇=0,0035). PkPμPjP°C” PrP°PSPëC... PíC₇Ps PIPiP»PëPI PSP° C₇PëP·PëPe C₇PsP·PIPëC,PeCr C₇P°PeCr PíC₇PsCíC,P°C,Pë Cr C₇PsP»PsPIC-PeC-PI, C₇IPeC-PíC₇PëPN₂PjP°P»Pë PrCrC,P°CíC,PμC₇PëPr PíPsPSP°Pr 4 C₇PsPePë. P’C-PrCíPsC,PsPe PíP°C†C-C”PSC,C-PI P· PrC-P°PiPSPsP·PsPj C₇P°PeCr PíPμC₇PμPrPjC-C...CrC₇PsPIPsC— P·P°P»PsP·Pë P· PíPsPeP°P·PSPëPePsPj 8b₇”10 P±P°P»C-PI P·P° CëPeP°P»PsC₇ P”P»C-CíPsPSP° P·P±PμC₇C-PiP°PICíC₇ PíPsCíC,C-PN₂PSPëPj Cr C₇C-P·PSC- PíPμC₇C-PsPrPë PrPsCíP»C-PrP¶PμPSPSC₇ (1b₇”2-PëPN₂ C₇PsPePë, 3b₇”4-PëPN₂ C₇PsPePë) Cr PíC₇CrPíC-PrCrC,P°CíC,PμC₇PëPrCr (0,5 % Cr PePsP¶PSPëPN₂ PíPμC₇C-PsPr C₇P°CíC), Cr C,PsPN₂ C₇P°CíC C₇IPe Cr PíC₇CrPíC- PíP»P°C†PμP±Ps PIC-PrCíPsC,PsPe PíP°C†C-C”PSC,C-PI C-P·PSPëP·CHPePsPrPëC,,PμC₇PμPSC†C-PN₂PsPIP°PSPëPj C₇P°PePsPj PíC₇PsCíC,P°C,Pë (8b₇”10 P±P°P»C-PI P·P° CëPeP°P»PsC₇ P”P»C-CíPsPSP°) P±CrPI PSPëP¶C₇PëPj Cr 3b₇”4-PëPN₂ C₇PsPePë, PSC-P¶ Cr 1b₇”2-PëPN₂ C₇PsPePë (< 0,1 % C- 0,5 % PIC-PrPíPsPIC-PrPSPs) (PrPëPI. C₇PsP·PrC-P» B«PhCíPsP±P»PëPIPsCíC,C- P·P°CíC,PsCíCíPIP°PSPSC₇IB»). PkPμ P±CrP»Ps PSC-C₇IPePsC— C₇C-P·PSPëC†C- PI C₇P°CíC,PsC,C- PIPëPíP°PrPeC-PI C₇P°PeCr PíPμC₇PμPrPjC-C...CrC₇PsPIPsC— P·P°P»PsP·Pë P· PíPsPeP°P·PSPëPePsPj 7b₇”10 P±P°P»C-PI P·P° CëPeP°P»PsC₇ P”P»C-CíPsPSP° (C₇=0,81).

Pj 4-C₇C-C₇PSPsPjCr PeP»C-PSC-C₇PSPsPjCr PrPsCíP»C-PrP¶PμPSPSC- P»C-PeCrPIP°PSPSC₇ PrPsP±C₇PsC₇IPeC-CíPSPsC— PiC-PíPμC₇PíP»P°P·C-C— PíPμC₇PμPrPjC-C...CrC₇PsPIPsC— P·P°P»PsP·Pë (Combat), PrPμ PíPμC₇PIPëPSPSPëPj PíC₇PsC,PsPePsP»PsPj PSPμ P±CrP»Ps PíPμC₇PμPrP±P°C†PμPSPs PsP±PsPIb₇™ C₇IP·PePsPICr P±C-PsPíCíC-C₇C- PICíC-PrC-P°PiPSPsP·Pë C₇P°PeCr PíC₇PsCíC,P°C,Pë P±CrP»Pë PICíC,P°PSPsPIP»PμPSC- PSP° P±C-PsPíCíC-C— P·P° PíPsPeP°P·P°PSPSC₇PjPë, C₇P°CíC,PsC,P° PIPëPíP°PrPeC-PI C₇P°PeCr PíPμC₇PμPrPjC-C...CrC₇PsPIPsC— P·P°P»PsP·Pë P· PíPsPeP°P·PSPëPePsPj 8b₇”10 P±P°P»C-PI P·P° CëPeP°P»PsC₇ P”P»C-CíPsPSP° P±CrP»P° 0,5 % (n=8) Cr PíC₇CrPíC-PrCrC,P°CíC,PμC₇PëPrCr, 0,7 % (n=11) b₇” Cr PíC₇CrPíC- C,P°PjCíCíP»PsP·PëPSCr C,P° 0,3 % (n=5) b₇” Cr PíC₇CrPíC- PePsPjP±C-PSPsPIP°PSPsC— C,PμC₇P°PíC-C—.

P—PIb₇™ C₇IP·PsPe PjC-P¶ P·P°CíC,PsCíCíPIP°PSPSC₇Pj PrCrC,P°CíC,PμC₇PëPrCr C,P° PIPëPSPëPePSPμPSPSC₇Pj PSPëP·CHPePsPrPëC,,PμC₇PμPSC†C-PN₂PsPIP°PSPsPiPs C₇P°PeCr PíPμC₇PμPrPjC-C...CrC₇PsPIPsC— P·P°P»PsP·Pë P·P°P»PëCëP°C”C,CHCíC₇ PSPμP·b₇™ C₇ICíPsPIP°PSPëPj.

P P°Pe PiC₇CíPrPSPsC— P·P°P»PsP·Pë Cí C₇PsP»PsPIC-PeC-PI

P”PIP° PIPëPíP°PrPsPe-PePsPSC,C₇PsP»CHPsPIP°PSC- PμPíC-PrPμPjC-PsP»PsPiC-C₇PSC-PrPsCíP»C-PrP¶PμPSPSC₇, P· C₇IPePëC... PsPrPSPμ PíC₇PsPIPμPrPμPSPs Cr PÝPëPh (n=339 PIPëPíP°PrPeC-PI C₇P°PeCr PíC₇CrPrPSPsC— P·P°P»PsP·Pë C- n=6780 Cr PíC₇CrPíC-PePsPSC,C₇PsP»C₇), P° C-PSCëPμ b₇” Cr P’PμP»PëPeC-PN₂ P’C₇PëC,P°PSC-C— (n=398 PIPëPíP°PrPeC-PI C₇P°PeCr PíC₇CrPrPSPsC— P·P°P»PsP·Pë C- n=3930 Cr PíC₇CrPíC-PePsPSC,C₇PsP»C₇) Cr P±P°P·P°C... PrP°PSPëC... PsC...PsC₇PsPSPë P·PrPsC₇PsPIb₇™ C₇IP, PSPμ PíPsPeP°P·P°P»Pë PSC-C₇IPePsPiPs P·P±C-P»CHCëPμPSPSC₇ C₇PëP·PëPeCr C₇PsP·PIPëC,PeCr C₇P°PeCr PíC₇CrPrPSPsC— P·P°P»PsP·Pë Cr C₇PsP»PsPIC-PeC-PI PíC₇Pë P·P°CíC,PsCíCíPIP°PSPSC- C-PSPiC-P±C-C,PsC₇C-PI 5α-C₇PμPrCrPeC,P°P·Pë. P PμP·CrP»CHC,P°C,Pë PíPμC₇CëPsPiPs PrPsCíP»C-PrP¶PμPSPSC₇ PSPμ PIPëC₇IPiPëP»Pë PíPsP·PëC,PëPIPsPiPs PIP·P°C”PjPsP·PIb₇™ C₇IP·PeCr P· C₇P°PePsPj PíC₇CrPrPSPsC— P·P°P»PsP·Pë (PIC-PrPSPsCíPSPëPN₂ C₇PëP·PëPe PrP»C₇ 31 C₇PsPeCr P·P°CíC,PsCíCíPIP°PSPSC₇ PrPs PICíC,P°PSPsPIP»PμPSPSC₇ PrC-P°PiPSPsP·Cr C₇P°PeCr PíC₇CrPrPSPsC— P·P°P»PsP·Pë PíPsC₇C-PIPSC₇IPSPs P· <1 C₇PsPeCr P·P°CíC,PsCíCíPIP°PSPSC₇: 0,70: 95 % P”P† 0,34, 1,45). Pj PrC₇CrPiPsPjCr PrPsCíP»C-PrP¶PμPSPSC- PsC†C-PSPμPSPëPN₂ PIC-PrPSPsCíPSPëPN₂ C₇PëP·PëPe

СҒP°PeCf PiCҒCfPrPSPSc— P·P°P»PsP·Pë, PiPsPIBҒ™ CҒP·P°PSPëPNë C-P·
P·P°CfC,PsCfCfPIP°PSPSCҒPj C-PSPiC-P±C-C,PsCҒC-PI 5α-СҒPμPrCfPeC,P°P·Pë
PiPsCҒC-PIPSCҒPSPs P· C,P°PePëPj PiCҒPë PIC-PrCfCfC,PSPScfC,C-
P·P°CfC,PsCfCfPIP°PSPSCҒ CfC,P°PSPsPIPëPI 1,08: 95 % P°P† 0,62, 1,87.

PμCҒPëC±PëPSPSPëPNë PIP·P°C°PjPsP·PIBҒ™ CҒP·PsPe PjC-PҒ PIPëPIP°PrPeP°PjPë CҒP°PeCf
PiCҒCfPrPSPSc— P·P°P»PsP·Pë Cf C±PsP»PsPIC-PeC-PI C,P° PrPsPIPiPsC,CҒPëPIP°P»PëPj
P·P°CfC,PsCfCfPIP°PSPSCҒPj PrCfC,P°CfC,PμCҒPëPrCf PSPμ PICfC,P°PSPsPIP»PμPSPs.

РҒP»C-PSC-C±PSC- C...P°CҒP°PeC,PμCҒPëCfC,PëPePë.

PμPsPeP°P·P°PSPSCҒ.

P>C-PeCfPIP°PSPSCҒ PiPsPjC-CҒPSPëC... C,P° C,CҒPҒPePëC... CfPëPjPiC,PsPjC-PI
PrPsP±CҒPsCҒPeC-CfPSPSc— PiC-PiPμCҒPiP»P°P·C-C— PiPμCҒPμPrPjC-C...CfCҒPsPIPsC—
P·P°P»PsP·Pë.

P—PjPμPSCëPμPSPSCҒ CҒPëP·PëPeCf PIPëPSPëPePSPμPSPSCҒ PiPsCfC,CҒPsC—
P·P°C,CҒPëPjPePë CfPμC±C- C,P° PSPμPsP±C...C-PrPSPScfC,C- C...C-CҒCfCҒPiC-C±PSPsPiPs
PIC,CҒCfC±P°PSPSCҒ Cf PiP°C†C-C°PSC,C-PI P· PiPsPjC-CҒPSPëPjPë C,P° C,CҒPҒPePëPjPë
CfPëPjPiC,PsPjP°PjPë PrPsP±CҒPsCҒPeC-CfPSPSc— PiC-PiPμCҒPiP»P°P·C-C—
PiPμCҒPμPrPjC-C...CfCҒPsPIPsC— P·P°P»PsP·Pë.

PμCҒPsC,PëPiPsPeP°P·P°PSPSCҒ.

P°CfC,P°C,,PsCҒCf PSPμ P·P°CfC,PsCfPsPICfCҒC,CH PrP»CҒ P»C-PeCfPIP°PSPSCҒ
PҒC-PSPsPe C- PrC-C,PμPNë (PrPëPI. CҒPsP·PrC-P» B«P—P°CfC,PsCfCfPIP°PSPSCҒ Cf
PiPμCҒC-PsPr PIP°PiC-C,PSPScfC,C- P°P±Ps PiPsPrCfPIP°PSPSCҒ PiCҒCfPrPrCҒB»).

P°CfC,P°C,,PsCҒCf PiCҒPsC,PëPiPsPeP°P·P°PSPëPNë C...PIPsCҒPëPj P· PiC-PrPIPëC%PμPSPsCҒ
C±CfC,P»PëPIC-CfC,CҒ PrPs PrCfC,P°CfC,PμCҒPëPrCf, C-PSCëPëC... C-PSPiC-P±C-C,PsCҒC-PI
5α-СҒPμPrCfPeC,P°P·Pë, C,P°PjCfCfP»PsP·PëPSCf (PIPeP»CҒC±P°CҒC±Pë
C,P°PjCfCfP»PsP·PëPSC-PSPrCfPePsPIP°PSPëPNë P°PSPiC-PsPSPμPICҒPsC,PëC±PSPëPNë
PSP°P±CҒCҒPe), C-PSCëPëC... PePsPjPiPsPSPμPSC,C-PI PiCҒPμPiP°CҒP°C,Cf P°P±Ps PrPs
CfPsC— C,P° P°CҒP°C...C-CfCf.

P°CfC,P°C,,PsCҒCf PiCҒPsC,PëPiPsPeP°P·P°PSPëPNë C...PIPsCҒPëPj, CҒPeC- PjP°CҒC,CH PI
P°PSP°PjPSPμP·C- PsCҒC,PsCfC,P°C,PëC±PSCf P°CҒC,PμCҒC-P°P»CHPSCf
PiC-PiPsC,PμPSP·C-CҒ.

P°CfC,P°C,,PsCҒCf PiCҒPsC,PëPiPsPeP°P·P°PSPëPNë C...PIPsCҒPëPj P· C,CҒPҒPePsCҒ
PiPμC±C-PSPePsPIPsCҒ PSPμPrPsCfC,P°C,PSC-CfC,CҒ.

***P°P·P°C°PjPsPrC-CҒ P· C-PSCëPëPjPë P»C-PeP°CҒCfCHPePëPjPë P·P°CfPsP±P°PjPë C,P°
C-PSCëC- PIPëPrPë PIP·P°C°PjPsPrC-PNë.***

P°PsCfP»C-PrPҒPμPSPSCҒ PIP·P°C°PjPsPrC-C— PePsPjP±C-PSPsPIP°PSPsPiPs

ΠίτῃPμΠίP°CῃP°C,Cῖ P· C-PSC€ΠέPjΠέ P»C-PeP°CῃCῖCῃPeΠέPjΠέ P·P°CῖPsP±P°PjΠέ
PSPμ ΠίCῃPsPIPSPPrΠέP»ΠέCῖCῖ. P''P°P»C- ΠίPsPrP°PSPs PSP°CῖPIPSCῖ
C-PSC,,PsCῃPjP°C†C-Cῃ ΠίCῃPs PsPeCῃPμPjC- PePsPjΠίPsPSPμPSC,Pέ
P»C-PeP°CῃCῖCῃPePsPiPs P·P°CῖPsP±Cῖ. P''CῖC,P°CῖC,PμCῃPέPr

P''P»Cῖ PsP·PSP°PNεPsPjP»PμPSPSCῖ P· C-PSC,,PsCῃPjP°C†C-C''Cῃ ΠίCῃPs
P·PSPέPΠPμPSPSCῖ CῃC-PIPSCῖ ΠίCῃPsCῖC,P°C,-CῖΠίPμC†ΠέC,,C-C†PSPsPiPs
P°PSC,PέΠίPμPSCῖ (PSA) ΠΙ CῖΠέCῃPsPIP°C,C†C- PeCῃPsPIC- ΠίC-Pr C†P°Cῖ
P»C-PeCῖPIP°PSPSCῖ PrCῖC,P°CῖC,PμCῃPέPrPsPj C,P° P·
CῃPμPePsPjPμPSPPrP°C†C-CῖPjΠέ C%oPsPrPs ΠIPέCῖPIP»PμPSPSCῖ CῃP°PeCῖ
ΠίPμCῃPμPrPjC-C...CῖCῃPsPIPsC— P·P°P»PsP·Πέ PrΠέΠΙ. CῃPsP·PrC-P»
B«PῃCῖPsP±P»ΠέPIPsCῖC,C- P·P°CῖC,PSCῖCῖPIP°PSPSCῖB».

P'ΠίP»ΠέΠΙ C-PSC€ΠέC... P»C-PeP°CῃCῖCῃPeΠέC... P·P°CῖPsP±C-ΠΙ PSP°
C,,P°CῃPjP°PePsPeC-PSPμC,PέPeCῖ PrCῖC,P°CῖC,PμCῃPέPrCῖ

P—P°CῖC,PSCῖCῖPIP°PSPSCῖ CῃP°P·PsPj P· C-PSPiC-P±C-C,PSCῃP°PjΠέ CYP3A4 C,P°/P°P±Ps P-
ΠίP»C-PePsΠίCῃPsC,PμC—PSCῖ

P''CῖC,P°CῖC,PμCῃPέPr ΠIPέPIPsPrΠέC,CῃCῖCῖ ΠίPμCῃPμPIP°PΠPSPs C€P»CῖC...PsPj
PjPμC,P°P±PsP»C-P·PjCῖ. P''PsCῖP»C-PrPΠPμPSPSCῖ in vitro ΠίPsPeP°P·CῖCῃC,Cῃ,
C%oPs PeP°C,P°P»C-P·P°C,PSCῃP°PjΠέ PjPμC,P°P±PsP»C-P·PjCῖ C'' CYP3A4 C- CYP3A5.
PῃC,,C-C†C-PNεPSC- PrPsCῖP»C-PrPΠPμPSPSCῖ ΠIP·P°C''PjPsPrC-C— P·
P°PeC,PέPIPSPέPjΠέ C-PSPiC-P±C-C,PSCῃP°PjΠέ CYP3A4 PSPμ
ΠίCῃPsPIPSPPrΠέP»ΠέCῖCῖ. PμCῃPsC,Pμ ΠΙ PrPsCῖP»C-PrPΠPμPSPSC-
ΠίPsΠίCῖP»CῖC†C-PNεPSPsC— C,,P°CῃPjP°PePsPeC-PSPμC,PέPeΠέ
PePsPSC†PμPSC,CῃP°C†C-C— PrCῖC,P°CῖC,PμCῃPέPrCῖ ΠΙ CῖΠέCῃPsPIP°C,C†C-
PeCῃPsPIC- P±CῖP»Πέ ΠΙ CῖPμCῃPμPrPSCῃPsPjCῖ ΠΙ 1,6Bῃ"1,8 CῃP°P·P°
ΠIPέC%oΠέPjΠέ Cῖ PSPμPIPμP»ΠέPePsC— PeC-P»CῃPePsCῖC,C- C,PέC...
ΠίP°C†C-C''PSC,C-ΠΙ, CῖΠeC- PsPrPSPsC†P°CῖPSPs P»C-PeCῖPIP°P»ΠέCῖCῖ
ΠIPμCῃP°ΠίP°PjC-P»PsPj P°P±Ps PrΠέP»C,C-P°P·PμPjPsPj (ΠίPsPjC-CῃPSC-
C-PSPiC-P±C-C,PSCῃPέ CYP3A4 C,P° C-PSPiC-P±C-C,PSCῃPέ P-
ΠίP»C-PePsΠίCῃPsC,PμC—PSCῖ), PSC-PΠ Cῖ C-PSC€ΠέC... ΠίP°C†C-C''PSC,C-ΠΙ.

PμCῃPέ PrPsPIPiPsCῖC,CῃPsPePsPIPsPjCῖ P·P°CῖC,PSCῖCῖPIP°PSPSC-
PePsPjP±C-PSP°C†C-C— PrCῖC,P°CῖC,PμCῃPέPrCῖ P· P»C-PeP°CῃCῖCῃPeΠέPjΠέ
P·P°CῖPsP±P°PjΠέ, CῖΠeC- C'' CῖΠέP»CῃPSPsPrC-CῃC†ΠέPjΠέ
C-PSPiC-P±C-C,PSCῃP°PjΠέ C,,PμCῃPjPμPSC,Cῖ CYP3A4 (PSP°ΠίCῃPέPeP»P°Pr,
CῃPέC,PSPSP°PIC-Cῃ, C-PSPPrΠέPSP°PIC-Cῃ, PSPμC,,P°P·PsPrPsPS,
C-C,CῃP°PePsPSP°P·PsP», PePμC,PSPePsPSP°P·PsP», CῖΠeC- ΠIPIPsPrΠέP»Πέ
ΠίPμCῃPsCῃP°P»CῃPSPs), PePsPSC†PμPSC,CῃP°C†C-Cῖ PrCῖC,P°CῖC,PμCῃPέPrCῖ ΠΙ
CῖΠέCῃPsPIP°C,C†C- PeCῃPsPIC- PjPsPΠPμ ΠίC-PrΠIPέC%oCῖPIP°C,ΠέCῖCῖ.
PμPsPrP°P»CῃC€Pμ C-PSPiC-P±CῖPIP°PSPSCῖ 5α-CῃPμPrCῖPeC,P°P·Πέ ΠίCῃPέ
ΠίC-PrCῖΠέP»PμPSC-PNε PrC-C— PrCῖC,P°CῖC,PμCῃPέPrCῖ C''
PjP°P»PsPNεPjPsPIC-CῃPSPέPj. PῃP»Pμ PjPsPΠP»ΠέPIPμ P·PjPμPSC€PμPSPSCῖ
C†P°CῖC,PSC,Pέ ΠIPIPμPrPμPSPSCῖ PrPsP· PrCῖC,P°CῖC,PμCῃPέPrCῖ Cῖ CῃP°P·C-
CῃPsP·ΠIPέC,PeCῖ ΠίPsP±C-C†PSPέC... PμC,,PμPeC,C-ΠΙ. Pj CῃP°P·C-
ΠίCῃPέΠiPSC-C†PμPSPSCῖ P°PeC,PέPIPSPSCῖC,C- C,,PμCῃPjPμPSC,Cῖ PrPsPIPiΠέPNε

PiPμC7C-PsPr PSp°PiC-PIPIPēPIPμPrPμPSPSCΠ PjPsP¶Pμ CÍC,P°C,Pē C%Pμ
PrPsPICεPēPj C- CÍCrPiCrC,PSCΠ C,PμC7P°PiC-Cl PjPsP¶Pμ Cr C,P°PePsPjCr
PIPēPiP°PrPeCr C,C7PēPIP°C,Pē PiPsPSP°Pr 6 PjC-CÍClC†C-PI PrPs C,PsPiPs, ClPe
P±CrPrPμ PrPsCÍClPiPSCrC,Ps PSPsPIPsC— C7C-PIPSPsIP°P¶PSPsC—
PePsPSC†PμPSC,C7P°C†C-C—.

P—P°CÍC,PsCÍCrPIP°PSPSCΠ 12 Pi C...PsP»PμCÍC,PēC7P°PjC-PSCr C†PμC7PμP· 1
PiPsPrPēPSCr PiC-CÍP»Cl P·P°CÍC,PsCÍCrPIP°PSPSCΠ PsPrPSPsC7P°P·PsPIPsC—
PrPsP·Pē 5 PjPi PrCrC,P°CÍC,PμC7PēPrCr PSPμ PIPiP»PēPIP°P»Ps PSP°
C„P°C7PjP°PePsPeC-PSPμC,PēPeCr PrCrC,P°CÍC,PμC7PēPrCr.

*P'PiP»PēPI PrCžC,P°CÍC,PμC7PēPrCž PSP° C„P°C7PjP°PePsPeC-PSPμC,PēPeCž C-PSCεPēC...
P»C-PeP°C7CÍCHPePēC... P·P°CÍPsP±C-PI*

PJ PSPμPIPμP»PēPePsPjCr PrPsCÍP»C-PrP¶PμPSPSC- (n=24) C,C7PēPIP°P»C-CÍC,Ch Cr
PrPIP° C,PēP¶PSC- P·P° CrC†P°CÍC,Ch P·PrPsC7PsPIPēC... C†PsP»PsPIC-PeC-PI-
PrPsP±C7PsPIPsP»CHC†C-PI PrCrC,P°CÍC,PμC7PēPr (0,5 PjPi PSP° PrPsP±Cr) PSPμ
PIPiP»PēPIP°PI PSP° C„P°C7PjP°PePsPeC-PSPμC,PēPeCr C,P°PjCÍCrP»PsP·PēPSCr
P°P±Ps C,PμC7P°P·PsP·PēPSCr. PJ C†CHPsPjCr PrPsCÍP»C-PrP¶PμPSPSC- C,P°PePsP¶
PSPμ P±CrP»Ps PIPēClPIP»PμPSPs PsP·PSP°Pe C„P°C7PjP°PePsPrPēPSP°PjC-C†PSPsC—
PIP·P°C”PjPsPrC-C—.

P”CrC,P°CÍC,PμC7PēPr PSPμ PIPiP»PēPIP°C” PSP° C„P°C7PjP°PePsPeC-PSPμC,PēPeCr
PIP°C7C„P°C7PēPSCr P°P±Ps PrPēPiPsPeCÍPēPSCr. PiPμ PIPeP°P·CrC” PSP° C,Pμ, C%Ps
PrCrC,P°CÍC,PμC7PēPr PSPμ C-PSPiC-P±CrC”/PSPμ C-PSPrCrPeCrC”
P°PeC,PēPIPSC-CÍC,Ch C„PμC7PjPμPSC,Cr CYP2C9 P°P±Ps P -
PiP»C-PePsPiC7PsC,PμC—PSCr- PiPμC7PμPSPsCÍPSPēPeP°. P”P°PSC-
PrPsCÍP»C-PrP¶PμPSCH PIP·P°C”PjPsPrC-C— *in vitro* PIPeP°P·CrCHC,Ch PSP° C,Pμ,
C%Ps PrCrC,P°CÍC,PμC7PēPr PSPμ C-PSPiC-P±CrC” C„PμC7PjPμPSC,Pē CYP1A2,
CYP2D6, CYP2C9, CYP2C19 P°P±Ps CYP3A4.

PjP°PjCÍCžP»PsP·PēPS

PhPrPSPsC†P°CÍPSPμ P·P°CÍC,PsCÍCrPIP°PSPSCΠ C,P°PjCÍCrP»PsP·PēPSCr
PiC-PrC7PsC...P»PsC7PēPrCr P· P»C-PeP°C7CÍCHPePēPjPē P·P°CÍPsP±P°PjPē, ClPeC-
PjPsP¶CrC,Ch P·PSPēP¶CrPIP°C,Pē P°C7C,PμC7C-P°P»CHPSPēPM C,PēCÍPe, Cr
C,PsPjCr C†PēCÍP»C- C7P°P·PsPj P·C- P·PSPμP±PsP»CHPIP°P»CHPSPēPjPē
P»C-PeP°C7CÍCHPePēPjPē P·P°CÍPsP±P°PjPē, C-PSPiC-P±C-C,PsC7P°PjPē 5-
C„PsCÍC„PsPrC-PμCÍC,PμC7P°P·Pē C,P° C-PSCεPēPjPē α-1-
P°PrC7PμPSPsP±P»PsPeP°C,PsC7P°PjPē PjPsP¶Pμ C,PμPsC7PμC,PēC†PSPs
PiC7PēP·PIPsPrPēC,Pē PrPs PiPsCÍPēP»PμPSPsC— PiC-PiPsC,PμPSP·PēPIPSPsC—
PrC-C—. PjPsPjCr P”CrC,P°C„PsC7CÍ PSPμ CÍP»C-Pr P·P°CÍC,PsCÍPsPICrPIP°C,Pē Cr
PePsPjP±C-PSP°C†C-C— P· C-PSCεPēPjPē α-1-P°PrC7PμPSPsP±P»PsPeP°C,PsC7P°PjPē.

PhPrPSPsC†P°CÍPSPμ P·P°CÍC,PsCÍCrPIP°PSPSCΠ C,P°PjCÍCrP»PsP·PēPSCr
PiC-PrC7PsC...P»PsC7PēPrCr C,P° PePμC,PsPePsPSP°P·PsP»Cr (CÍPēP»CHPSPsPiPs
C-PSPiC-P±C-C,PsC7P° CYP3A4) P·P±C-P»CHCεCrC” Pj_{max} C,P° AUC
C,P°PjCÍCrP»PsP·PēPSCr PiC-PrC7PsC...P»PsC7PēPrCr Cr 2,2 C,P° 2,8 C7P°P·P°

PIC-PrPiPsPIC-PrPSPs.

PŸCfPjC-CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCµ C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCfPsC...P»PsCfPëPrCf C,P° PiP°CfPsPeCfPµC,PëPSCf (CfPëP»CHbPSPsPiPs
C-PSPiC-P±C-C,PsCfP° CYP2D6) P·P±C-P»CHbC€CfC" PŸ_{max} C,P° AUC
C,P°PjCfCfP»PsP·PëPSCf PiC-PrCfPsC...P»PsCfPëPrCf Cf 1,3 C,P° 1,6 CfP°P·P°
PIC-PrPiPsPIC-PrPSPs. PhPSP°P»PsPiC-CfPSPµ P·P±C-P»CHbC€PµPSPSCµ
PsCfC-PeCfC"C,CHbCfCµ Cf PiP°CfC-C"PSC,C-PI P·C- CfP»P°P±PePëPj
PjPµC,P°P±PsP»C-P·PjPsPj CYP2D6 PiPsCfC-PIPSCµPSPs P· C,P°PePëPjPë P·
C-PSC,PµPSCfPëPIPSPëPj PjPµC,P°P±PsP»C-P·PjPsPj PiCfPë CfCfPjC-CfPSPsPjCf
P·P°CfC,PsCfCfPIP°PSPSC- P·C- CfPëP»CHbPSPëPjPë C-PSPiC-P±C-C,PsCfP°PjPë
CYP3A4.

P·C,,PµPeC, CfCfPjC-CfPSPsPiPs P·P°CfC,PsCfCfPIP°PSPSCµ PsP±PsC...
C-PSPiC-P±C-C,PsCfC-PI CYP3A4 C,P° C-PSPiC-P±C-C,PsCfC-PI CYP2D6 P·
C,P°PjCfCfP»PsP·PëPSPsPj PeP»C-PSC-CfPSPs PSPµ PrPsCfP»C-PrP¶CfPIP°PICfCµ,
PsPrPSP°Pe PiPsC,PµPSCfC-PNëPSPs PjPsP¶Pµ CfCfC,C,C"PiPs
P·P±C-P»CHbC€CfPIP°C,PëCfCµ PePsPSCfPµPSC,CfP°CfC-Cµ C,P°PjCfCfP»PsP·PëPSCf
(PrPëPI. CfPsP·PrC-P» B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSCµB»).

PhPrPSPsCfP°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCµ C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCfPsC...P»PsCfPëPrCf (0,4 PjPi) C- CfPëPjPµC,PëPrPëPSCf (400 PjPi PePsP¶PSC-
6 PiPsPrPëPS PiCfPsC,CµPiPsPj 6 PrPSC-PI) PiCfPëP·PIPsPrPëP»Ps PrPs
P·PSPëP¶PµPSPSCµ PeP»C-CfPµPSCfCf (26 %) C- P·P±C-P»CHbC€PµPSPSCµ AUC (44
%) C,P°PjCfCfP»PsP·PëPSCf PiC-PrCfPsC...P»PsCfPëPrCf. P>C-PeP°CfCfCHbPePëPNë
P·P°CfC-P± P"CfC,P°C,,PsCfCf CfP»C-Pr P· PsP±PµCfPµP¶PSC-CfC,Cf
P·P°CfC,PsCfPsPICfPIP°C,Pë Cf PePsPjP±C-PSP°CfC-C— P· CfPëPjPµC,PëPrPëPSPsPj.

P'PëCfPµCfPiPSPµ PrPsCfP»C-PrP¶PµPSPSCµ PIP·P°C"PjPsPrC-C—
C,P°PjCfCfP»PsP·PëPSCf PiC-PrCfPsC...P»PsCfPëPrCf C- PIP°CfC,,P°CfPëPSCf PSPµ
PiCfPsPIPsPrPëP»PsCfCµ. P PµP·CfP»CHbC,P°C,Pë PsP±PjPµP¶PµPSPëC...
PrPsCfP»C-PrP¶PµPSCb *in vitro* C,P° *in vivo* C" PSPµPrPsCfC,P°C,PSC-PjPë. P—
PsP±PµCfPµP¶PSC-CfC,Cf CfP»C-Pr PiCfPsPIPsPrPëC,Pë PsPrPSPsCfP°CfPSPµ
P»C-PeCfPIP°PSPSCµ PIP°CfC,,P°CfPëPSPsPj C- C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCfPsC...P»PsCfPëPrPsPj.

PkC-CµPePsC— PIP·P°C"PjPsPrC-C— PSPµ CfPiPsCfC,PµCfC-PiP°P»PsCfCµ, PePsP»Pë
C,P°PjCfCfP»PsP·PëPSCf PiC-PrCfPsC...P»PsCfPëPr PIPsPrPëP»Pë
PsPrPSPsCfP°CfPSPs P· P°C,PµPSPsP»PsP»PsPj P°P±Ps PµPSP°P»P°PiCfPëP»PsPj,
P°P±Ps PSC-C,,PµPrPëPiC-PSPsPj, P°P±Ps C,PµPsC,,C-P»C-PSPsPj. PhPrPSPsCfP°CfPSPµ
P·P°CfC,PsCfCfPIP°PSPSCµ C,,CfCfPsCfPµPjC-PrCf PiCfPëP·PIPsPrPëC,CHb PrPs
P·PSPëP¶PµPSPSCµ CfC-PIPSCµ C,P°PjCfCfP»PsP·PëPSCf PI CfPëCfPsPIP°C,CfC-
PeCfPsPIC-, P°P»Pµ, PsCfPeC-P»CHbPePë CfC- CfC-PIPSC- P·P°P»PëC€P°CfC,CHbCfCµ
Cf PjPµP¶P°C... PSPsCfPjP°P»CHbPSPsPiPs PrC-P°PiP°P·PsPSCf, PePsCfPµPeCfC-Cµ
PrPsP·Pë PSPµ PiPsC,CfC-P±PSP°.

P' CfPjPsPIP°C... *in vitro* PSC- PrC-P°P·PµPiP°Pj, PSC- PiCfPsPiCfP°PSPsP»PsP», PSC-
C,CfPëC...P»PsCfPjPµC,C-P°P·PëPr, PSC- C...P»PsCfPjP°PrPëPSPsPS, PSC-

P°PjC-C, CḡPëPīC, PëP»C-PS, PSC- PrPëPeP»PsC,, PμPSP°Pe, PSC-
 PiP»C-P±PμPSPeP»P°PjC-Pr, PSC- CḡPëPjPIP°CḡC, P°C, PëPS PSPμ P·PjC-PSCḡCḡC, CH
 PIC-P»CHPSCḡ C,, CḡP°PeC†C-Cḡ C, P°PjCḡCḡP»PsP·PëPSCḡ Cḡ PīP»P°P·PjC- PeCḡPsPIC-
 P»CḡPrPëPSPë. PḡP°PjCḡCḡP»PsP·PëPS C, P°PePsPḡ PSPμ P·PjC-PSCḡC” PIC-P»CHPSC-
 C,, CḡP°PeC†C-C— PrC-P°P·PμPīP°PjCḡ, PīCḡPsPīCḡP°PSPsP»PsP»Cḡ,
 C, CḡPëC...P»PsCḡPjPμC, C-P°P·PëPrCḡ C- C...P»PsCḡPjP°PrPëPSPsPSCḡ.

PḡC-CḡPePsC— PIP·P°C”PjPsPrC-C— PSP° CḡC-PIPSC- PīPμC†C-PSPePsPIPsPiPs
 PjPμC, P°P±PsP»C-P·PjCḡ PSPμ CḡPīPsCḡC, PμCḡC-PiP°P»PsCḡCḡ PīC-Pr C†P°Cḡ
 PrPsCḡP»C-PrPḡPμPSCḡ *in vitro* P·PjC-PeCḡPsCḡPsPjP°P»CHPSPëPjPë
 C,, CḡP°PeC†C-CḡPjPë PīPμC†C-PSPePë (PīPsPeP°P·PsPIPsCḡ C” CḡPëCḡC, PμPjP°
 PīPsPIBḡ™ CḡP·P°PSPëC... C-P·C†PëC, PsC...CḡPsPjPsPj P 450 C,, PμCḡPjPμPSC, C-PI,
 C%Ps PjPμC, P°P±PsP»C-P·CḡCḡC, CH P»C-PeP°CḡCḡCHPeC- P·P°CḡPsP±Pë) C-P·
 P·P°CḡC, PsCḡCḡPIP°PSPSCḡPj P°PjC-C, CḡPëPīC, PëP»C-PSCḡ,
 CḡP°P»CHP±CḡC, P°PjPsP»Cḡ C- PiP»C-P±PμPSPeP»P°PjC-PrCḡ. PḡCḡPsC, Pμ
 PrPëPeP»PsC,, PμPSP°Pe PjPsPḡPμ PīC-PrPIPëC%CḡPIP°C, Pë C€PIPëPrPeC-CḡC, CH
 PIPëPIPμPrPμPSPSCḡ C, P°PjCḡCḡP»PsP·PëPSCḡ.

PhCḡPsP±P»PëPIPsCḡC, C- P·P°CḡC, PsCḡCḡPIP°PSPSCḡ.

PḡPsPjP±C-PSPsPIP°PSCḡ C, PμCḡP°PīC-Cḡ PīCḡPëP·PSP°C†P°CḡC, CH PīC-CḡP»Cḡ
 CḡPμC, PμP»CHPSPsPiPs P°PSP°P»C-P·Cḡ CḡPīC-PIPIC-PrPSPsC€PμPSPSCḡ
 PePsCḡPëCḡC, CH/CḡPëP·PëPe Cḡ P·PIBḡ™ CḡP·PeCḡ P· PīPsC, PμPSC†C-PNḡPSPëPj
 P·P±C-P»CHC€PμPSPSCḡPj CḡPëP·PëPeCḡ PīPsP±C-C†PSPëC... CḡPμP°PeC†C-PNḡ
 (PIPeP»CḡC†P°CḡC†Pë CḡPμCḡC†PμPICḡ PSPμPrPsCḡC, P°C, PSC-CḡC, CH) C, P°
 PIPëPIC†PμPSPSCḡ PIP°CḡC-P°PSC, C-PI P°P»CHC, PμCḡPSP°C, PëPIPSPsPiPs
 P»C-PeCḡPIP°PSPSCḡ, PIPeP»CḡC†P°CḡC†Pë PjPsPSPsC, PμCḡP°PīC-Cḡ.

PμPsP±C-C†PSC- CḡPμP°PeC†C-C— P·P±PsPeCḡ CḡPμCḡC†PμPIPs-CḡCḡPrPëPSPSPsC—
 CḡPëCḡC, PμPjPë

P—P° PrP°PSPëPjPë PrPIPsC... 4-CḡC-C†PSPëC... PeP»C-PSC-C†PSPëC...
 PrPsCḡP»C-PrPḡPμPSCḡ, C†P°CḡC, PsC, P° PIPëPSPëPePSPμPSPSCḡ CḡPμCḡC†PμPIPsC—
 PSPμPrPsCḡC, P°C, PSPsCḡC, C- (PePsPjP±C-PSPsPIP°PSPëPNḡ C, PμCḡPjC-PS PrP»Cḡ PICḡC-C...
 PīPsPIC-PrPsPjP»PμPSCḡ, PīPsP»PsPIPsPëPj C†PëPSPsPj CḡPμCḡC†PμPIPsC—
 PSPμPrPsCḡC, P°C, PSPsCḡC, C- C, P° P·P°CḡC, C-PNḡPSPsC— CḡPμCḡC†PμPIPsC—
 PSPμPrPsCḡC, P°C, PSPsCḡC, C-) P±CḡP»P° PIPëC%PsCḡ Cḡ PsCḡC-P±, CḡPeC-
 P»C-PeCḡPIP°P»PëCḡCḡ PePsPjP±C-PSP°C†C-C”Cḡ PrCḡC, P°CḡC, PμCḡPëPrCḡ P· α-
 P±P»PsPeP°C, PsCḡPsPj, PīPsP»PsPIPsPëPj C†PëPSPsPj C, P°PjCḡCḡP»PsP·PëPSPsPj,
 PīPsCḡC-PIPSCḡPSPs P· PsCḡPsP±P°PjPë, CḡPeC- PSPμ P»C-PeCḡPIP°P»PëCḡCḡ C, P°PePsCḡ
 PePsPjP±C-PSP°C†C-C”Cḡ. PḡP°CḡC, PsC, P° CḡPμCḡC†PμPIPsC— PSPμPrPsCḡC, P°C, PSPsCḡC, C-
 P±CḡP»P° PSPëP·CHPePsCḡ (≤1 %) C, P° PIP°CḡC-P°P±PμP»CHPSPsCḡ Cḡ PjPμPḡP°C... C†PëC...
 PrPsCḡP»C-PrPḡPμPSCḡ. P”PëCḡPīCḡPsPīPsCḡC†C— Cḡ C†P°CḡC, PsC, C-
 PIPëPSPëPePSPμPSPSCḡ CḡPμCḡC†PμPIPs-CḡCḡPrPëPSPSPëC... PīPsP±C-C†PSPëC... CḡPIPëC%
 PSPμPjP°C” Cḡ PḡPsPrPSPsPjCḡ P· PrPsCḡP»C-PrPḡPμPSCḡ. PḡCḡPëC†PëPSPSPsPiPs
 PIP·P°C”PjPsP·PIBḡ™ CḡP·PeCḡ PjC-Pḡ P·P°CḡC, PsCḡCḡPIP°PSPSCḡPj PrCḡC, P°CḡC, PμCḡPëPrCḡ
 (PsPeCḡPμPjPs P°P±Ps Cḡ PePsPjP±C-PSP°C†C-C— P· α-P±P»PsPeP°C, PsCḡP°PjPë) C, P°
 PIPëPSPëPePSPμPSPSCḡPj CḡPμCḡC†PμPIPsC— PSPμPrPsCḡC, P°C, PSPsCḡC, C-

PICÍC,P°PSPsPIP»PμPSPs PSpμ P±CfP»Ps (PrPëPI. CḡPsP·PrC-P»
B«PαP°CḡPjP°PePsP»PsPiC-C±PSC- PIP»P°CÍC,PëPIPsCÍC,C-B»).

PμCḡPsPIPμPrPμPSPs PjPμC,P°P°PSP°P»C-P· 12 CḡP°PSPrPsPjC-P·PsPIP°PSPëC...,
PīP»P°C†PμP±Ps- P°P±Ps PīPsCḡC-PIPsCḡP»CHbPSPëC... PePsPSC,CḡPsP»CHbPsPIP°PSPëC...
PeP»C-PSC-C±PSPëC... PrPsCÍP»C-PrP¶PμPSCḡ (n=18802), CÍ CḡPePsPjCÍ
PsC†C-PSCḡPIP°P»Pë CḡPëP·PëPe CḡPsP·PIPëC,PeCÍ PīPsP±C-C±PSPëC... CḡPμP°PeC†C-PNë P·
P±PsPeCÍ

CÍPμCḡC†PμPIPs-CÍCÍPrPëPSPSPsC— CÍPëCÍC,PμPjPë PīCḡPë P·P°CÍC,PsCÍCÍPIP°PSPSC-
PrCÍC,P°CÍC,PμCḡPëPrCÍ (PīPsCḡC-PIPsCḡPSPs P· PePsPSC,CḡPsP»CHbPSPsCḡ PīCḡCÍPīPsCḡ).
PḡPμ P±CfP»Ps PICÍC,P°PSPsPIP»PμPSPs CÍC,C-PNëPePsPīPs CÍC,P°C,PëCÍC,PëC±PSPs
P·PSP°C±CÍC%PsPīPs P·P±C-P»CHbC€PμPSPSCḡ CḡPëP·PëPeCÍ CÍPμCḡC†PμPIPsC—
PSPμPrPsCÍC,P°C,PSPsCÍC,C- (RR 1,05; 95 % P”P† 0,71, 1,57), PīPsCÍC,CḡPsPīPs
C-PSC,,P°CḡPeC,CÍ PjC-PsPeP°CḡPrP° (RR 1,00; 95 % P”P† 0,77, 1,30) P°P±Ps
C-PSCÍCÍP»CHbC,CÍ (RR 1,20; 95 % P”P† 0,88, 1,64).

P P°Pe PīPμCḡPμPrPjC-C...CÍCḡPsPIPsC— P·P°P»PsP·Pë C,P° PīCÍC...P»PëPSPë PIPëCÍPsPePsPīPs
CÍC,CÍPīPμPSCḡ PīCḡP°PrP°C†C-C— P·P° P“C-CÍPsPSPsPj (PSPëP·CHbPePs-
PrPëC,,PμCḡPμPSC†C-PNëPsPIP°PSC-)

Pj PīCḡPsC†PμCÍC- 4-CḡC-C±PSPsPīPs PeP»C-PSC-C±PSPsPīPs PrPsCÍP»C-PrP¶PμPSPSCḡ P·P°
CÍC±P°CÍC,Cḡ > 8000 C±PsP»PsPIC-PeC-PI PIC-PePsPj PIC-Pr 50 PrPs 75 CḡPsPeC-PI P·
PīPsPīPμCḡPμPrPSCḡPsCḡ PSPμPīP°C,PëPIPsPSCḡ P±C-PsPīCÍC-C”Cḡ PSP° CḡP°Pe
PīPμCḡPμPrPjC-C...CÍCḡPsPIPsC— P·P°P»PsP·Pë C,P° C,,PsPSPsPIPëPj CḡC-PIPsPμPj PSA PjC-P¶
2,5 PSPi/PjP» C,P° 10,0 PSPi/PjP» (PrPsCÍP»C-PrP¶PμPSPSCḡ REDUCE) CÍ 1517
C±PsP»PsPIC-PeC-PI P±CfP»Ps PrC-P°PīPSPsCÍC,PsPIP°PSPs CḡP°Pe
PīPμCḡPμPrPjC-C...CÍCḡPsPIPsC— P·P°P»PsP·Pë. P’C-PrP·PSP°C±P°P»P°CÍCḡ PIPëC%P°
C±P°CÍC,PsC,P° PIPëPSPëPePSPμPSPSCḡ CḡP°PeCÍ PīPμCḡPμPrPjC-C...CÍCḡPsPIPsC—
P·P°P»PsP·Pë P· PrPëC,,PμCḡPμPSC†C-CḡPIP°PSPSCḡPj 8Bḡ“10 P±P°P»C-PI P·P° C€PeP°P»PsCḡ
P“P»C-CÍPsPSP° CÍ PīCḡCÍPīC- PrCÍC,P°CÍC,PμCḡPëPrCÍ (n=29, 0,9 %) PīPsCḡC-PIPsCḡPSPs
P· PīCḡCÍPīPsCḡ PīP»P°C†PμP±Ps (n=19, 0,6 %). PμCḡPëC±PëPSPSPsPīPs
PIP·P°C”PjPsP·PīBḡ™ CḡP·PeCÍ PjC-P¶ P·P°CÍC,PsCÍCÍPIP°PSPSCḡPj PrCÍC,P°CÍC,PμCḡPëPrCÍ
C,P° PIPëPSPëPePSPμPSPSCḡPj PSPëP·CHbPePsPrPëC,,PμCḡPμPSC†C-PNëPsPIP°PSPsPīPs
CḡP°PeCÍ PīPμCḡPμPrPjC-C...CÍCḡPsPIPsC— P·P°P»PsP·Pë PICÍC,P°PSPsPIP»PμPSPs PSpμ
P±CfP»Ps. PḡP»C-PSC-C±PSP° P·PSP°C±CÍC%C-CÍC,Cḡ C†PëC,,CḡPsPIPsPīPs
PrPëCÍP±P°P»P°PSCÍCÍ PSPμ PICÍC,P°PSPsPIP»PμPSP°.

PḡPsP»PsPIC-PePë, CḡPeC- P·P°CÍC,PsCÍPsPICÍCḡC,Cḡ P”CÍC,P°C,,PsCḡCÍ, PjP°CḡC,Cḡ
CḡPμPīCÍP»CḡCḡPSPs PīCḡPsC...PsPrPëC,Pë PsP±CÍC,PμP¶PμPSPSCḡ C%PsPrPs
PIPëP·PSP°C±PμPSPSCḡ CḡPëP·PëPeCÍ CḡPsP·PIPëC,PeCÍ CḡP°PeCÍ
PīPμCḡPμPrPjC-C...CÍCḡPsPIPsC— P·P°P»PsP·Pë, PIPeP»CḡC±P°CḡC±Pë C,PμCÍC, PSP°
PīCḡPsCÍC,P°C,-CÍPīPμC†PëC,,C-C±PSPëPNë P°PSC,PëPīPμPS.

Pj PrPsPrP°C,PePsPIPsPjCÍ PīPsCÍP»C-PrPsPIPSPsPjCÍ 2-CḡC-C±PSPsPjCÍ
CÍPīPsCÍC,PμCḡPμP¶PμPSPSC- PsCḡPëPīC-PSP°P»CHbPSPëC... PīP°C†C-C”PSC,C-PI PīCḡPë
P·P°CÍC,PsCÍCÍPIP°PSPSC- PrCÍC,P°CÍC,PμCḡPëPrCÍ P· PjPμC,PsCḡ C...C-PjC-C±PSPsC—
PīCḡPsC,,C-P»P°PeC,PëPePë (PrPsCÍP»C-PrP¶PμPSPSCḡ REDUCE) P±CfP»P°
PICÍC,P°PSPsPIP»PμPSP° PSPëP·CHbPeP° C±P°CÍC,PsC,P° PSPsPIPëC... PIPëPīP°PrPeC-PI
CḡP°PeCÍ PīPμCḡPμPrPjC-C...CÍCḡPsPIPsC— P·P°P»PsP·Pë (PīCḡCÍPīP°
PrCÍC,P°CÍC,PμCḡPëPrCÍ [n=14, 1,2 %]) C,P° PīCḡCÍPīP° PīP»P°C†PμP±Ps [n=7, 0,7 %]) P·
PIC-PrCÍCÍC,PSC-CÍC,Cḡ PSPsPIPëC... C-PrPμPSC,PëC,,C-PePsPIP°PSPëC... PIPëPīP°PrPeC-PI

СҗР°РєСр ПРмСҗРмРРРјС-С...СрСҗРсРІРсС— Р·Р°Р»РсР·Рө Р·
РРРөС,,РмСҗРмРсС†С-СҗРІР°РспсСІРј 8вҗ“10 Р±Р°Р»С-РІ Р·Р° С€РєР°Р°Р»РсСҗ
Р”Р»С-СІРсРсп°.

Р”РсРІРІсС,СҗРөРІР°Р»Рм РІсСІР»С-РРсРІРспм (РРс 18 СҗРсРєС-РІ)
СІРІсСІС,РмСҗРмР¶РмРспсСІ РІ°С†С-С”РсС,С-РІ С-Р· РєР»С-РсС-С†РспсРІс
РРсСІР»С-РРР¶РмРспсСІ С-Р· Р·Р°СІС,РсСІСрРІР°РспсСІРј С-РсС€РсРІс
С-РспІС-Р±С-С,РсСҗР° 5α-СҗРмРРрСрРєС,Р°Р·Рө (С,,С-Рсп°СІС,РмСҗРөРрСр) Р· РјРмС,РсСҗ
С...С-РјС-С†РспсС— РІСҗРсС,,С-Р»Р°РєС,РөРєРө Рспм РІсРєР°Р°Р·Р»Р»Рс
СІС,Р°С,РөСІС,РөС†Рспс Р·Рсп°С†С%РсС— СҗС-Р·РспөС†С- РјС-Р¶ РІСҗСрРІ°РјРө
С,,С-Рсп°СІС,РмСҗРөРрСр С,Р° РІР»Р°С†РмР±Рс Ср РІсРєР°Р°Р·РспөР°С...
Р·Р°РІР°Р»СҗРспсРІс РІөР¶РөРІР°РспсСІ (HR1,02, 95 % Р”Р† 0,97вҗ“1,08) Р°Р±Рс
РІөР¶РөРІР°РспсСІ РІС-СІР»СІ РРС-Р°РІспсСІС,СрРІР°РспсСІ СҗР°РєСр
РІмСҗРмРРРјС-С...СрСҗРсРІРсС— Р·Р°Р»РсР·Рө (HR1,01, 95 % Р”Р† 0,85вҗ“1,20).

Р’РІР»РөРІ Рсп° РІСҗРсСІС,Р°С,-СІРІмС†РөС,,С-С†РспөР№ Р°РсС,РөРІмРс (РсА)

РлРсРсС†РмРсС,СҗР°С†С-СІ РІСҗРсСІС,Р°С,-СІРІмС†РөС,,С-С†РспсРІс Р°РсС,РөРІмРсСр
РІмСҗРмРРРјС-С...СрСҗРсРІРсС— Р·Р°Р»РсР·Рө (РсА) С” РІР°Р¶РөРөРј
РєРсРјРІсРспмРсС,РсРј СІРєСҗРөРсС-РспІсРІсРІс РІСҗРсС†РмСІСр РРР»СІ
РІөСІРІР»РмРспсСІ СҗР°РєСр РІмСҗРмРРРјС-С...СрСҗРсРІРсС— Р·Р°Р»РсР·Рө.
Р”СрС,Р°СІС,РмСҗРөРр Р·РРР°С,РспөР№ Р·РспөР¶СрРІР°С,Рө СҗС-РІмРсСҗ
СІРөСҗРсРІР°С,РєРсРІсРІс РІСҗРсСІС,Р°С,-СІРІмС†РөС,,С-С†РспсРІс Р°РсС,РөРІмРсСр Ср
С...РІсСҗРөС... РІСҗРөР±Р»РөР·Рспс Рсп° 50 % С†РмСҗРмР· 6 РјС-СІСІС†С-РІ
Р»С-РєСрРІР°РспсСІ.

РмР°С†С-С”РсС,Рө, СІРєС- РІСҗРөР№РјРјР°СҗС,Сҗ Р”СрС,Р°С,,РсСҗСІ, РІсРІөРспсС-
РјР°С,Рө РспсРІөР№ РІөС...С-РРспөР№ СҗС-РІмРсСҗ РсА, РІСІС,Р°РспсРІР»РмРспөР№
С†РмСҗРмР· 6 РјС-СІСІС†С-РІ РІС-СІР»СІ Р»С-РєСрРІР°РспсСІ С†РөРј
РІСҗРмРІР°СҗР°С,РсРј. РќР°РРР»С- С†РмР№ СҗС-РІмРсСҗ
СҗРмРєРсРјРспРрСрС”С,СҗСІСІ РІмСҗРмРІС-СҗСІС,Рө СҗРмРІСрР»СІСҗРспс. Р’СрРҗСҗ-
СІРєРм РІС-РРС,РІмСҗРРР¶РмРсп Р·Р±С-Р»СҗС€РмРспсСІ СҗС-РІсСІ РсА РІС-РР
Рсп°Р№РспөР¶С†РсРІс СҗС-РІсСІ РІС-РР С†Р°СІ Р·Р°СІС,РсСІСрРІР°РспсСІ
Р»С-РєР°СҗСІСҗРєРсРІс Р·Р°СІРсР±Ср Р”СрС,Р°С,,РсСҗСІ РјРсР¶Рм Р±СрС,Рө
СІРІС-РРСРмРспсСІРј Рсп°СІРІспсСІС,С- СҗР°РєСр РІмСҗРмРРРјС-С...СрСҗРсРІРсС—
Р·Р°Р»РсР·Рө Р°Р±Рс РспмРРсС,СҗРөРјР°РспсСІ СҗРмР¶РөРјСр Р»С-РєСрРІР°РспсСІ
Р”СрС,Р°С,,РсСҗСІРсРј С- РІсС,СҗРмР±СрС” СҗРмС,РмР»СҗРспсРІс РІөРІС†РмРспсСІ,
Рсп°РІС-С,Сҗ СІРєС%Рс РІсРєР°Р°Р·РспөРө РсА Р·Рсп°С...РсРСІС,СҗСІСІ Ср
РјРмР¶Р°С... РспсСҗРө Ср С†РсР»РсРІС-РєС-РІ, СІРєС- Рспм Р»С-РєСрРІР°Р»РөСІСҗ
С-РспІС-Р±С-С,РсСҗР°РјРө 5α-СҗРмРРрСрРєС,Р°Р·Рө. РмСҗРө С-РсС,РмСҗРІСҗРмС,Р°С†С-С—
РІсРєРәР·РспөРє-РІ РсА Ср С...РІсСҗРөС..., СІРєС- Р»С-РєСрСҗС,СҗСІСІ
Р”СрС,Р°С,,РсСҗСІРсРј, СІР»С-РР Р·РІР°Р¶Р°С,Рө Рсп° РІсРІмСҗРмРРРсС-
РІсРєРәР·РспөРө РсА РРР»СІ РІсСҗС-РІсСІРспсСІ.

Р—Р°СІС,РсСІСрРІР°РспсСІ Р»С-РєР°СҗСІСҗРєРсРІс Р·Р°СІРсР±Ср Р”СрС,Р°С,,РсСҗСІ
Рспм РІРІР»РөРөРІР°С” Рсп° РІөРєРсСҗРөСІС,Р°РспсСІ СҗС-РІсСІ РІСҗРсСІС,Р°С,-
СІРІмС†РөС,,С-С†РспсРІс Р°РсС,РөРІмРсСр РРР»СІ РРС-Р°РІспсСІС,РөРөСҗРәРәРә
РІмСҗРмРРРјС-С...СрСҗРсРІРсС— Р·Р°РлРсР·Рө РІС-СІР»СІ РІСІС,Р°РспсРІР»РмРспсСІ
Р№РсРІс РспсРІсРІс РІөС...С-РРспсРІс СҗС-РІсСІ.

Р—Р°РІР°Р»СҗРспөР№ СҗС-РІмРсСҗ СІРөСҗРсРІР°С,РєРсРІсРІс РІСҗРсСІС,Р°С,-
СІРІмС†РөС,,С-С†РспсРІс Р°РсС,РөРІмРсСр РІсРІмСҗС,Р°С”С,СҗСІСІ РРс

PIPëC...C-PrPSPsPiPs CḡC-PIPSCḡ PiCḡPsC,CḡPiPsPj 6 PjC-CḡCḡCḡC-PI PiC-CḡP»Cḡ
PiCḡPëPiPëPSPμPSPSCḡ P»C-PeCḡPIP°PSPSCḡ.

PŸPiC-PIPIC-PrPSPsC€PμPSPSCḡ P¶ PIC-P»CHPSPsPiPs PiCḡPsCḡC,P°C,-
CḡPiPμCḡPëC,,C-CḡPSPsPiPs P°PSC,PëPiPμPSCḡ C- P·P°PiP°P»CHPSPsPiPs P№PsPiPs
CḡC-PIPSCḡ P·P°P»PëC€P°C”C,CHCḡCḡ CḡC,P°P»PëPj PSP°PIC-C,CH PiC-Pr CḡP°Cḡ
P·P°CḡC,PSCḡCḡPIP°PSPSCḡ P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ P”CḡC,P°C,,PsCḡCḡ.
PİPeC%oPs PrP»Cḡ PIPëP·PSP°CḡPμPSPSCḡ CḡP°PeCḡ PiPμCḡPμPrPjC-C...CḡCḡPsPiPsC—
P·P°P»PsP·Pë P»C-PeP°Cḡ PIPëCḡC-C€PëC,CH PIPëPePsCḡPëCḡC,P°C,Pë
PIC-PrCḡPsC,PePsPIPëP№ PiPsPeP°P·PSPëPe PIC-P»CHPSPsPiPs PiCḡPsCḡC,P°C,-
CḡPiPμCḡPëC,,C-CḡPSPsPiPs P°PSC,PëPiPμPSCḡ Cḡ C...PIPsCḡPsPiPs, CḡPePëP№
P·P°CḡC,PSCḡCḡPICḡC” P»C-PeP°CḡCḡCHPePëP№ P·P°CḡC-P± P”CḡC,P°C,,PsCḡCḡ,
PSC-CḡPePsPiPs PePsCḡPμPiCḡPIP°PSPSCḡ PiPsPeP°P·PSPëPeP° PIC-P»CHPSPsPiPs
PiCḡPsCḡC,P°C,-CḡPiPμCḡPëC,,C-CḡPSPsPiPs P°PSC,PëPiPμPSCḡ PiCḡPsPiPsPrPëC,Pë PSPμ
PiPsC,CḡC-P±PSPs.

PμPμCḡPμPr PiPsCḡP°C,PePsPj PeCḡCḡCḡCḡ P»C-PeCḡPIP°PSPSCḡ P”CḡC,P°C,,PsCḡCḡPsPj C,P°
PiPμCḡC-PsPrPëCḡPSPs PiC-Pr CḡP°Cḡ P»C-PeCḡPIP°PSPSCḡ PiP°CḡC-C”PSC,P°Pj C-P·
PrPsP±CḡPsCḡPeC-CḡPSPsCḡ PiC-PiPμCḡPiP»P°P·C-C”Cḡ PiPμCḡPμPrPjC-C...CḡCḡPsPiPsC—
P·P°P»PsP·Pë CḡP»C-Pr CḡPsP±PëC,Pë PiP°P»CHCḡPμPiPμ CḡPμPeC,P°P»CHPSPμ
PsP±CḡC,PμP¶PμPSPSCḡ, P° C,P°PePsP¶ PIPëPePsCḡPëCḡC,PSCḡCḡPIP°C,Pë C-PSC€C-
PjPμC,PsPrPë PIPëCḡPIP»PμPSPSCḡ CḡP°PeCḡ PiPμCḡPμPrPjC-C...CḡCḡPsPiPsC— P·P°P»PsP·Pë.

PḡPëCḡPePsPIP° PSPμPrPsCḡC,P°C,PSC-CḡC,CH

P»C-PeCḡPIP°PSPSCḡ C...PIPsCḡPëC... P· C,CḡP¶PePsCḡ PSPëCḡPePsPiPsCḡ
PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ (PeP»C-CḡPμPSCḡ PeCḡPμP°C,PëPSC-PSCḡ <10 PjP»/C...PI)
PiPsC,CḡC-P±PSPs PiCḡPsPiPsPrPëC,Pë P· PsP±PμCḡPμP¶PSC-CḡC,Cḡ, PsCḡPeC-P»CHPePë
C,,P°CḡPjP°PePsPeC-PSPμC,PëPeP° PrCḡC,P°CḡC,PμCḡPëPrCḡ Cḡ C,P°PePëC... C...PIPsCḡPëC...
PSPμ PIPëPICḡP°P»P°CḡCḡ.

PḡCḡC,PμCḡC-P°P»CHPSP° PiC-PiPsC,PμPSP·C-Cḡ

PμPsPrC-P±PSPs PrPs C-PSC€PëC... α1-P°PrCḡPμPSPsP±P»PsPeP°C,PSCḡC-PI,
PsCḡC,PSCḡC,P°C,PëCḡPSP° PiC-PiPsC,PμPSP·C-Cḡ PjPsP¶Pμ PIPëPSPëPePSCḡC,Pë Cḡ
PiP°CḡC-C”PSC,C-PI, CḡPeC- P»C-PeCḡPIP°P»PëCḡCḡ C,P°PjCḡCḡP»PsP·PëPSPsPj, C- Cḡ
CḡC-PrPeC-CḡPSPëC... PIPëPiP°PrPeP°C... PjPsP¶Pμ PiCḡPëP·PIPμCḡC,Pë PrPs CḡPëPSPePsPiPμ.

PμCḡPë PiPμCḡC€PëC... PsP·PSP°PeP°C... PsCḡC,PSCḡC,P°C,PëCḡPSPsC— PiC-PiPsC,PμPSP·C-C—
(P·P°PiP°PjPsCḡPsCḡPμPSPSCḡ, CḡP»P°P±PeC-CḡC,CH) PiP°CḡC-C”PSC,C-PI, CḡPeC-
CḡPsP·PiPsCḡP°P»Pë P»C-PeCḡPIP°PSPSCḡ P”CḡC,P°C,,PsCḡCḡPsPj, CḡP»C-Pr
PiPμCḡPμPIPμCḡC,Pë Cḡ PiPsP»PsP¶PμPSPSCḡ CḡPëPrCḡCḡPë P°P±Ps P»PμP¶P°CḡPë, PiPsPePë
CḡPëPjPiC,PsPjPë PSPμ PjPëPSCḡC,CH.

PḡPμPsP±C...C-PrPSPs PrPsC,CḡPëPjCḡPIP°C,PëCḡCḡ PsP±PμCḡPμP¶PSPsCḡC,C- PiCḡPë
CḡCḡPjC-CḡPSPsPjCḡ P·P°CḡC,PSCḡCḡPIP°PSPSC- α-P°PrCḡPμPSPsP±P»PsPeP°C,PSCḡC-PI,
PIPeP»CḡCḡP°CḡCḡPë C,P°PjCḡCḡP»PsP·PëPS, C,P° C-PSPiC-P±C-C,PSCḡC-PI 5-
C,,PsCḡC,,PsPrC-PμCḡC,PμCḡP°P·Pë. α-P°PrCḡPμPSPsP±P»PsPeP°C,PSCḡPë C,P°
C-PSPiC-P±C-C,PSCḡPë 5-C,,PsCḡC,,PsPrC-PμCḡC,PμCḡP°P·Pë C”
PIP°P·PsPrPëP»P°C,P°C,PSCḡP°PjPë C,P° PjPsP¶CḡC,CH P·PSPëP¶CḡPIP°C,Pë

PŸCřPjC-CřPSPµ P·P°CřC,PsCřCřPIP°PSPSCř C,P°PjCřCřP»PsP·PëPSCř
 PiC-PrCřPsC...P»PsCřPëPrCř P·C- CřPëP»CHbPSPëPjPë C-PSPiC-P±C-C,PsCřP°PjPë PŸYP3A4
 (PSP°PiCřPëPeP»P°Pr, C-P· PePµC,PsPePsPSP°P·PsP»PsPj) P°P±Ps бђ“ Cř PjPµPSC€C-PN₂
 PjC-CřC- бђ“ P·C- CřPëP»CHbPSPëPjPë C-PSPiC-P±C-C,PsCřP°PjPë CYP2D6
 (PSP°PiCřPëPeP»P°Pr, C-P· PiP°CřPsPeCřPµC,PëPSPsPj) PjPsP¶Pµ P·P±C-P»CHbC€CřPIP°C,Pë
 PePsPSC†PµPSC,CřP°C†C-Cř C,P°PjCřCřP»PsP·PëPSCř (PrPëPI, CřPsP·PrC-P»

B«P'P·P°C"PjPsPrC-CI P· C-PSC€PëPjPë P»C-PeP°CĤCĬCHPePëPjPë P·P°CĬPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C"PjPsPrC-PMëB»). PŷPsPjCr PSPµ CĤPµPePsPjPµPSPPrCrC"C,CHCĬCI P·P°CĬC,PsCĬPsPICrPIP°C,Pë C,P°PjCĬCrP»PsP·PëPS PİP°C†C-C"PSC,P°Pj, CIµPeC- P»C-PeCřCĤC,CHCĬCI CĬPëP»CHPSPëPjPë C-PSPiC-P±C-C,PsCĤP°PjPë PŷYP3A4, C,P° CĤPµPePsPjPµPSPPrPsPIP°PSPs P· PsP±PµCĤPµP¶PSC-CĬC,CH P·P°CĬC,PsCĬPsPICrPIP°C,Pë C,P°PjCĬCrP»PsP·PëPS PİP°C†C-C"PSC,P°Pj, CIµPeC- P»C-PeCřCĤC,CHCĬCI PİPsPjC-CĤPSPëPjPë C-PSPiC-P±C-C,PsCĤP°PjPë PŷYP3A4 (PSP°PİCĤPëPeP»P°Pr, PµCĤPëC,CĤPsPjC-C†PëPSPsPj), CĬPëP»CHPSPëPjPë P°P±Ps PİPsPjC-CĤPSPëPjPë C-PSPiC-P±C-C,PsCĤP°PjPë CYP2D6, PePsPjP±C-PSP°C†C-C"CĤ PsP±PsC... PŷYP3A4 C,P° CYP2D6 C-PSPiC-P±C-C,PsCĤC-PI P°P±Ps PİP°C†C-C"PSC,P°Pj P·C- CĬP»P°P±PePëPj PjPµC,P°P±PsP»C-P·PjPsPj CYP2D6.

PµPµC±C-PSPePsPIP° PSPµPrPsCĬC,P°C,PSC-CĬC,CH

P'PİP»PëPI PİPµC±C-PSPePsPIPSc— PSPµPrPsCĬC,P°C,PSPScĬC,C- PSP° C,,P°CĤPjP°PePsPeC-PSPµC,PëPeCř PrCrC,P°CĬC,PµCĤPëPrCr PSPµ PIPëPIC†P°PICĬCI. PŞPµCĤPµP· P°PeC,PëPIPSPëPNë PjPµC,P°P±PsP»C-P·Pj PrCrC,P°CĬC,PµCĤPëPrCr C,P° 3BĤ"5- C,PëP¶PSPµPIPëPNë PİPµCĤC-PsPr PNëPsPiPs PSP°PİC-PIIPëPIPµPrPµPSPSCİ P»C-PeCřPIP°PSPSCİ PrCrC,P°CĬC,PµCĤPëPrPsPj C...PIPScĤPëC... P· P»PµPiPePsCĤ P°P±Ps PİPsPjC-CĤPSPScĤ PİPµC±C-PSPePsPIPScĤ PSPµPrPsCĬC,P°C,PSC-CĬC,CH CĬP»C-Pr PİCĤPsIPsPrPëC,Pë P· PsP±PµCĤPµP¶PSC-CĬC,CH (PrPëPI. CĤPsP·PrC-P»Pë B«PαP°CĤPjP°PePsP»PsPiC-C†PSC- PIP»P°CĬC,PëPIPsCĬC,C-B», B«PµCĤPsC,PëPİPsPeP°P·P°PSPSCİB» C,P° B«PŷPİPsCĬC-P± P·P°CĬC,PsCĬCrPIP°PSPSCİ C,P° PrPsP·PëB»).

P"PsPİPsPjC-P¶PSC- CĤPµC±PsPIPëPSPë

P>C-PeP°CĤCĬCHPePëPNë P·P°CĬC-P± PjC-CĬC,PëC,CH P±P°CĤPIPSPëPe P¶PsPIC,PëPNë B«CĬPsPSCİC†PSPëPNë P·P°C...C-PrB» (E 110), C%oPs PjPsP¶Pµ CĬPİCĤPëC†PëPSPëC,Pë P°P»PµCĤPiC-C†PSC- CĤPµP°PeC†C-C—.

P"P°PSPëPNë P»C-PeP°CĤCĬCHPePëPNë P·P°CĬC-P± PjC-CĬC,PëC,CH P»PµC†PëC,PëPS, PsC,CĤPëPjP°PSPëPNë P·C- CĬPsC"PIPSc— PsP»C-C—. PJ CĤP°P·C- PICĬC,P°PSPsPIP»PµPSPSCİ P°P»PµCĤPiC-C— PSP° P°CĤP°C...C-CĬ P°P±Ps CĬPsCĤ PSPµ P·P°CĬC,PsCĬPsPICrPIP°C,Pë PrP°PSPëPNë P»C-PeP°CĤCĬCHPePëPNë P·P°CĬC-P± (PrPëPI. CĤPsP·PrC-P» B«PµCĤPsC,PëPİPsPeP°P·P°PSPSCİB»).

P P°Pe PiCĤCrPrPSPSc— P·P°P»PsP·Pë Cr C†PsP»PsPIC-PeC-PI

PµPsPIC-PrPsPjP»CIµP»PsCĬCI PİCĤPs CĤC-PrPeC-CĬPSC- PIPëPİP°PrPePë CĤP°PeCř PiCĤCrPrPSPSc— P·P°P»PsP·Pë Cr C†PsP»PsPIC-PeC-PI PİC-Pr C†P°CĬ PeP»C-PSC-C†PSPëC... PrPsCĬP»C-PrP¶PµPSCĤ C,P° Cr PİPsCĬC,PjP°CĤPePµC,PëPSPiPsPIPëPNë PİPµCĤC-PsPr. PµCĤPë C†CHPsPjCr PµPİC-PrPµPjC-PsP»PsPiC-C†PSC- PrPsCĬP»C-PrP¶PµPSPSCİ PİPeP°P·CřCĤC,CH PSP° PIC-PrCĬCrC,PSC-CĬC,CH PİC-PrPIPëC%oPµPSPSCİ CĤPëP·PëPeCř CĤPsP·PIPëC,PeCř CĤP°PeCř PiCĤCrPrPSPSc— P·P°P»PsP·Pë Cr C†PsP»PsPIC-PeC-PI PİCĤPë P·P°CĬC,PsCĬCrPIP°PSPSC- C-PSPiC-P±C-C,PsCĤC-PI 5α-CĤPµPrCrPeC,P°P·Pë. P>C-PeP°CĤC- PİPsPIPëPSPSC- PİPsPİPµCĤPµPrPëC,Pë CĬPIPSc—C... PİP°C†C-C"PSC,C-PI PİCĤPs PSPµPsP±C...C-PrPSC-CĬC,CH PSPµPiP°PNëPSPs PİPsPIC-PrPsPjP»CIµC,Pë PİCĤPs P±CřPrCH-

$\text{C}\ddot{\text{C}}\text{P}\text{eC}-\text{P}\cdot\text{PjC}-\text{PSP}\ddot{\text{e}}\text{ Cr C},\text{PeP}^{\circ}\text{PSP}\ddot{\text{e}}\text{PSC}-\text{PiC}\ddot{\text{H}}\text{CrPrPSPsC}-\text{P}\cdot\text{P}^{\circ}\text{P}\gg\text{PsP}\cdot\text{P}\ddot{\text{e}}, \text{PSP}^{\circ}\text{PiC}\ddot{\text{H}}\text{P}\ddot{\text{e}}\text{PeP}\gg\text{P}^{\circ}\text{Pr}$
 $\text{PiC}\ddot{\text{H}}\text{Ps PiP}\ddot{\text{e}}\text{PrC}-\text{P}\gg\text{P}_{\mu}\text{PSPSC}\ddot{\text{C}}\text{ C}-\text{P}\cdot\text{C}\ddot{\text{I}}\text{PsC}\ddot{\text{I}}\text{PeP}^{\circ}\text{ P}^{\circ}\text{P}\pm\text{Ps PiC}\ddot{\text{H}}\text{P}\ddot{\text{e}}\text{PiCrC}\dots\text{P}\gg\text{C}-\text{C}\ddot{\text{I}}\text{C},\text{C}\ddot{\text{H}}.$

$$P-P^{\circ}C\dot{I}C, P_sC\dot{I}C\dot{\alpha}PIP^{\circ}PSPSC\dot{I}C\dot{\alpha}P\ddot{i}P_{\mu}C\dot{I}C-P_sPrPIP^{\circ}P\dot{i}C-C, PSP_sC\dot{I}C, C-P^{\circ}P\pm P_sP\dot{i}P_sPrC\dot{\alpha}PIP^{\circ}PSPSC\dot{I}C\dot{\alpha}P\dot{i}C\dot{I}C\dot{\alpha}PrPrC\dot{I}.$$

P"CrC,P°C,,PsC₇Cl₇ PiC₇PsC,PëPiPsPeP°P·P°PSPëPN₂ PrP»C₇ P»C-PeCrPIP°PSPSC₇ P₇Cl-PSPsPe.
P"PsC₇P»C-PrP₇P₇PSPSC₇ P· PIPëPIC₇P₇PSPSC₇ PIPiP»PëPIC₇ P»C-PeP°C₇Cl₇CH₇PePsPiPs
P·P°C₇PsP±C₇ PSP° PIP°PiC-C,PSC-C₇C,CH₇, P»P°PeC,P°C₇C-C₇ C,P°
C,,P₇C₇C,PëP»CH₇PSC-C₇C,CH₇ PSP₇ PiC₇PsPIPsPrPëP»Pë. P"P°P»C- PSP°PrP°C"C,CH₇Cl₇C₇
C-PSC,,PsC₇PjP°C₇C-C₇ Cl₇ PiC₇Ps P·P°C₇C,P₇C₇Cl₇PIP°PSPSC₇ PePsP₇P₇PSPsPiPs
PePsPjPiPsPSP₇PSC,P° PsPeC₇P₇PjPs.

Р_αР_μС₇С, Р_өР_»С_НР_{SC}-С_ГС, С_Н

$P''CrC, P^{\circ}ClC, P_{\mu}CH_3P\ddot{e}P_{\mu} PIPiP \gg P\ddot{e}PIP^{\circ}C''$ $PSP^{\circ} C \dots P^{\circ}CH_3P^{\circ}PeC, P_{\mu}CH_3P\ddot{e}ClC, P\ddot{e}PeP\ddot{e}$
 $P_{\mu}ClIPeCrP \gg ClIC, Cr (P \cdot PjP_{\mu}PSC\epsilon P_{\mu}PSPSCII PeC - P \gg CH_3PePsClC, C-$
 $ClPiP_{\mu}CH_3PjP^{\circ}C, PsP \cdot PsC - PrC - PI, PsP \pm B\mathcal{T}^m C'' PjCr P_{\mu}ClIPeCrP \gg ClIC, Cr C, P^{\circ}$
 $CH_3CrC \dots PsPjPsClC, C- ClPiP_{\mu}CH_3PjP^{\circ}C, PsP \cdot PsC - PrC - PI). PkP_{\mu} PIP\ddot{e}PeP \gg CH_3\ddagger P_{\mu}PSP\ddot{e}P_{\mu}$
 $CH_3P\ddot{e}P \cdot P\ddot{e}Pe P \cdot PSP\ddot{e}P_{\mu} P_{\mu}PSPSCII C\ddagger PsP \gg PsPIC - C\ddagger PsC - C_{\mu} P_{\mu}CH_3, P\ddot{e}P \gg CH_3PSPsClC, C-.$

PhC†C-PSPEP° PIPiP»PèPICr C,P°PjC†C†P»PsP·PèPSCr PiC-PrC†PSC...P»PsC†PèPrC† PSP°
PeC-P»CHbPeC-C†C,CH P°P±Ps C,,CrPSPeC†C-CH C†PiPµC†PjP°C,PsP·PsC—PrC-PI PSPµ
PiC†PSPiPsPrPèP»P°C†C†.

P'P°PiC-C,PSC-CΓC,CH

$\text{PiPe C- C-PSCeC- C-PSPIC-P}\pm\text{C-C, PsC}\mathfrak{H}\text{P}\ddot{\text{e}}\ 5\alpha\text{-C}\mathfrak{H}\text{P}\mu\text{PrCrPeC, P}^\circ\text{P}\cdot\text{P}\ddot{\text{e}}, \text{PrCrC, P}^\circ\text{C}\acute{\text{I}}\text{C, P}\mu\text{C}\mathfrak{H}\text{P}\ddot{\text{e}}\text{Pr}$
 $\text{PiP}\mu\text{C}\mathfrak{H}\text{P}\mu\text{C}\mathfrak{E}\text{PePsPrP}\mathfrak{H}\text{P}^\circ\text{C}'' \text{ PiP}\mu\text{C}\mathfrak{H}\text{P}\mu\text{C, PIPsC}\mathfrak{H}\text{P}\mu\text{PSPSC}\mathfrak{H} \text{ C, P}\mu\text{C}\acute{\text{I}}\text{C, PsC}\acute{\text{I}}\text{C, P}\mu\text{C}\mathfrak{H}\text{PsPSCr} \text{ Cr}$
 $\text{PrP}\ddot{\text{e}}\text{PiC-PrC}\mathfrak{H}\text{PsC, P}\mu\text{C}\acute{\text{I}}\text{C, PsC}\acute{\text{I}}\text{C, P}\mu\text{C}\mathfrak{H}\text{PsPS, C}\%_{\text{Ps}} \text{ PjPsP}\mathfrak{H}\text{P}\mu \text{ PiP}^\circ\text{P}\gg\text{CH}\mathfrak{H}\text{PjCrPIP}^\circ\text{C, P}\ddot{\text{e}}$
 $\text{C}\mathfrak{H}\text{PsP}\cdot\text{PIP}\ddot{\text{e}}\text{C, PsPe P}\cdot\text{PsPIPSC-C}\mathfrak{E}\text{PSC-C... C}\acute{\text{I}}\text{C, P}^\circ\text{C, P}\mu\text{PIP}\ddot{\text{e}}\text{C... PsC}\mathfrak{H}\text{PiP}^\circ\text{PSC-PI Cr P}\ddot{\text{I}}\text{P}\gg\text{PsPrP}^\circ$
 $\text{C}\mathfrak{H}\text{PsP}\gg\text{PsPIC-C}\mathfrak{H}\text{PsC- C}\acute{\text{I}}\text{C, P}^\circ\text{C, C-}. \text{P}\acute{\text{K}}\text{P}\mu\text{P}\cdot\text{PSP}^\circ\text{C}\mathfrak{H}\text{PSCr} \text{ PeC-P}\gg\text{CH}\mathfrak{H}\text{PeC-C}\acute{\text{I}}\text{C, CH}$
 $\text{PrCrC, P}^\circ\text{C}\acute{\text{I}}\text{C, P}\mu\text{C}\mathfrak{H}\text{P}\ddot{\text{e}}\text{PrCr} \text{ P}\pm\text{CrP}\gg\text{Ps PIP}\ddot{\text{e}}\text{C}\mathfrak{H}\text{PIP}\gg\text{P}\mu\text{PSPs PI P}\mu\text{C}\mathfrak{H}\text{PeCrP}\gg\text{C}\mathfrak{H}\text{C, C- PiC}\mathfrak{H}\text{P}\ddot{\text{e}}$
 $\text{PiC}\mathfrak{H}\text{PsPIP}\mu\text{PrP}\mu\text{PSPSC- PrPsC}\acute{\text{I}}\text{P}\gg\text{C-PrP}\mathfrak{H}\text{P}\mu\text{PSPSC}\mathfrak{H}. \text{P}\acute{\text{K}}\text{P}\mu\text{PIC-PrPsPjPs, C}\mathfrak{H}\text{P}\ddot{\text{e}} \text{ PIP}\ddot{\text{I}}\text{P}\gg\text{P}\ddot{\text{e}}\text{PIP}^\circ\text{C}''$
 $\text{PrCrC, P}^\circ\text{C}\acute{\text{I}}\text{C, P}\mu\text{C}\mathfrak{H}\text{P}\ddot{\text{e}}\text{Pr, C}\%_{\text{Ps}} \text{ PiPsC, C}\mathfrak{H}\text{P}^\circ\text{PiP}\ddot{\text{e}}\text{PI PrPs PsC}\mathfrak{H}\text{PiP}^\circ\text{PSC-P}\cdot\text{PjCr P}\mathfrak{H}\text{C-PSPeP}\ddot{\text{e}} \text{ P}\cdot\text{C-}$
 $\text{C}\acute{\text{I}}\text{C-Pj}\mathfrak{B}\mathfrak{H}^{\text{TM}} \text{ C}\mathfrak{H}\text{Pj C}\mathfrak{H}\text{PsP}\gg\text{PsPIC-PeP}^\circ, \text{C}\mathfrak{H}\text{PeP}\ddot{\text{e}}\text{P}\mathfrak{N}\mathfrak{e} \text{ P}\gg\text{C-PeCrC}''\text{C, CHC}\acute{\text{I}}\text{C}\mathfrak{H} \text{ P}''\text{CrC, P}^\circ\text{C,, PsC}\mathfrak{H}\text{C}\acute{\text{I}}\text{PsPj,}$
 $\text{PSP}^\circ \text{ P}\ddot{\text{I}}\text{P}\gg\text{C-Pr C}\mathfrak{H}\text{PsP}\gg\text{PsPIC-C}\mathfrak{H}\text{PsC- C}\acute{\text{I}}\text{C, P}^\circ\text{C, C-}.$

$\text{P}\ddot{\text{I}}\text{e C- Cr C}\ddot{\text{H}}\text{P}^{\circ}\text{P-C- P}\cdot\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C,PsC}\dot{\text{I}}\text{C}\dot{\text{r}}\text{PIP}^{\circ}\text{PSPSC}\dot{\text{I}}\text{ C-PSC}\text{€P}\ddot{\text{e}}\text{C... C-PSPiC-P}\pm\text{C-C,PsC}\ddot{\text{H}}\text{C-PI } 5\alpha\text{-}$
 $\text{C}\ddot{\text{H}}\text{P}\mu\text{PrCrPeC,P}^{\circ}\text{P}\cdot\ddot{\text{e}},\text{C}\ddot{\text{H}}\text{P}\mu\text{PePsPjP}\mu\text{PSPrCrC}''\text{C,CHC}\dot{\text{I}}\text{C}\dot{\text{I}}\text{ PePsC}\ddot{\text{H}}\text{P}\ddot{\text{e}}\text{C}\dot{\text{I}}\text{C,CrPIP}^{\circ}\text{C,P}\ddot{\text{e}}\text{C}\dot{\text{I}}\text{CH}$
 $\text{PiC}\ddot{\text{H}}\text{P}\mu\text{P}\cdot\text{P}\mu\text{C}\ddot{\text{H}}\text{PIP}^{\circ}\text{C,P}\ddot{\text{e}}\text{PIP}\text{Sj PiC-Pr C}\ddot{\text{H}}\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C}\dot{\text{I}}\text{C,P}^{\circ}\text{C,P}\mu\text{PIPsPiPs P}^{\circ}\text{PeC,Cr, C}\dot{\text{I}}\text{PeC}\%_{\text{oo}}\text{Ps}$
 $\text{P}\text{¶C-PSPeP}^{\circ}\text{PIP}^{\circ}\text{PiC-C,PSP}^{\circ},\text{P}^{\circ}\text{C}\ddot{\text{H}}\text{PsP}\gg\text{PsPIC-Pe P}\cdot\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C,PsC}\dot{\text{I}}\text{PsPICrC}''$
 $\text{P}\gg\text{C-PeP}^{\circ}\text{C}\ddot{\text{H}}\text{C}\dot{\text{I}}\text{CHPePeP}\ddot{\text{e}}\text{P}\text{N}\ddot{\text{e}}\text{ P}\cdot\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C-P}\pm\text{P}''\text{CrC,P}^{\circ}\text{C,,PsC}\ddot{\text{H}}\text{C}\dot{\text{I}},\text{P}\cdot\text{PjP}\mu\text{C,PsC}\ddot{\text{H}}$
 $\text{P}\cdot\text{P}^{\circ}\text{PiPsP}\pm\text{C-PiP}^{\circ}\text{PSPSC}\dot{\text{I}}\text{ PiPsC,C}\ddot{\text{H}}\text{P}^{\circ}\text{PiP}\gg\text{C}\dot{\text{I}}\text{PSPSC}\ddot{\text{H}}\text{C}\dot{\text{I}}\text{C-PjB}\ddot{\text{H}}^{\text{TM}}\text{C}\dot{\text{I}}\text{PrPs PsC}\ddot{\text{H}}\text{PiP}^{\circ}\text{PSC-P}\cdot\text{PjCr}$
 $\text{P}\text{¶C-PSPeP}\ddot{\text{e}}.$

PkPμPjP°C" PrPsPeP°P·C-PI C,PsPiPs, C%oPs PIPiPμPrPμPSPSCl C,P°PjCíCíP»PsP·PëPSCí
PiC-PrCíPjPsC...P»PsCíPëPrCr PIP°PiC-C,PSPëPj CíP°PjPeP°Pj C%oCíCíC-PI C,P° PeCíPjPsP»C-PI
Cí PrPsP·P°C..., C%oPs PìPμCíPμPIPëC%oCíCíC,Ch C,PμCíP°PìPμPIC,PëC±PSC-,
PSPμPiP°C,PëPIPSPs PIPìP»PëPIP°C" PSP° PìP»C-Pr.

РμРμСҢС-РsРr РiРsРrСrРiР°РsРsСiРi РiСҢСrРrРrСҢ

РќРμРiС-РrРsРjРs, С±Рө РiСҢРsРsРөРeР°СҢС,СҢ РrСrС,Р°СҢС,РμСҢРөРr С,Р°
С,Р°РјСҢСrР»РsР·РөРs Сr РiСҢСrРrРsРμ РjРsР»РsРeРs Р¶С-РsРeРө.

*Р—РrР°С,РsС-СҢС,СҢ РiРiР»РөРiР°С,Рө РsР° С€РiРөРrРeС-СҢС,СҢ СҢРμР°РeС†С-С— РiСҢРө
РeРμСҢСзРiР°РsРsС- Р°РiС,РsС,СҢР°РsСҢРiРsСҢС,РsРj Р°Р±Рs С-РsС€РөРjРө
РjРμС...Р°РsС-Р·РjР°РjРө.*

Р"РsСҢР»С-РrР¶РμРsРsСi Р· РiРөРiС±РμРsРsСi РiРiР»РөРiСr Р»С-РeР°СҢСҢСҢРeРsРiРs
Р·Р°СҢРs±Сr Р"СrС,Р°СҢ,РsСҢСҢ РsР° Р·РrР°С,РsС-СҢС,СҢ РeРμСҢСrРiР°С,Рө
Р°РiС,РsС,СҢР°РsСҢРiРsСҢС,РsРj Р°Р±Рs С-РsС€РөРjРө РjРμС...Р°РsС-Р·РjР°РjРө РsРμ
РiСҢРsРiРsРrРөР»РөСҢС. РҗРrРsР°Рe РiР°С†С-С"РsС,С-Рi РiРsС,СҢС-Р±РsРs
РiСҢРsС-РsС,РsСҢРjСrРiР°С,Рө РiСҢРs РjРsР¶Р»Р»РөРiРμ РiРөРsРөРeРsРμРsРsСi
СҢРөРjРiС,РsРjС-Рi, РiРsРiБҢ™ СiР·Р°РsРөС... Р· РsСҢС,РsСҢС,Р°С,РөС±РsРsСҢ
Р°СҢС,РμСҢС-Р°Р»СҢРsРsСҢ РiС-РiРsС,РμРsР·С-С"СҢ, Р·РsРeСҢРμРjР° РiСҢРs
Р·Р°РiР°РjРsСҢС±РμРsРsСi, РiСҢРө Р·Р°СҢС,РsСҢСrРiР°РsРsС- Р"СrС,Р°СҢ,РsСҢСҢСr.

РҮРiРsСҢС-Р± Р·Р°СҢС,РsСҢСзРiР°РsРsСi С,Р° РrРsР·Рө.

Р"РsСҢРsСҢР»С- (РiРeР»СҢС±Р°СҢС±Рө С...РiРsСҢРөС... Р»С-С,РsСҢРsРiРs РiС-РeСr)

Р РμРeРsРjРμРsРrРsРiР°РsР° РrРsР·Р° Р"СrС,Р°СҢ,РsСҢСҢСr БҢ“ 1 РeР°РiСҢСrР»Р° (0,5 РjРi/0,4
РjРi) РsР° РrРsР±Сr. РμСҢРμiР°СҢР°С, РiСҢРөРμРjР°СҢС,СҢ РiРμСҢРsСҢР°»СҢРsРs
С±РμСҢРμ· 30 С...РiРөР»РөРs РiС-СҢР»СҢ СҢРiРsР¶РiРiР°РiР°РsРsСi С-Р¶С- Рi РsРrРөРs С-
С,РsРμ Р¶Рμ С±Р°СҢ. РҗР°РiСҢСrР»Сr СҢР»С-Рr РeРsРiС,Р°С,Рө С†С-Р»РsСҢ, РsРμ
РiС-РrРeСҢРөРiР°С,Рө С,Р° РsРμ СҢРsР·Р¶РiРiР°РiР°С,Рө, РsСҢРeС-Р»СҢРeРө РiСҢРө
РeРsРsС,Р°РeС,С- С-Р· РiРjС-СҢС,РsРj РeР°РiСҢСrР»Рө РjРsР¶Р»Р»РөРiРμ
РiРsРrСҢР°Р·РsРμРsРsСi СҢР»РөР·РsРiРs— РsР±РsР»РsРsРөРө СҢРsС,Р° С,Р° РiР»РsС,РeРө.

Р"СrС,Р°СҢ,РsСҢСҢ РjРsР¶РsР° Р·Р°СҢС,РsСҢРsРiСrРiР°С,Рө РrР»СҢ Р·Р°РјС-С%РμРsРsСi
РeРsРjР±С-РsРiР°РsРsС— С,РμСҢР°РiС-С— РrСrС,Р°СҢС,РμСҢРөРrРsРj С,Р°
С,Р°РјСҢСrР»РsР·РөРsСr РiС-РrСҢРsС...Р»РsСҢРөРrРsРj Р· РjРμС,РsСҢ РiРsР»РμРiС€РμРsРsСi
Р»С-РeСrРiР°РsРsСi.

Р—Р°РјС-РsР° Р"СrС,Р°СҢ,РsСҢСҢРsРj РrСrС,Р°СҢС,РμСҢРөРrСr Р°Р±Рs
С,Р°РјСҢСrР»РsР·РөРsСr РiС-РrСҢРsС...Р»РsСҢРөРrСr РiСҢРө РjРsРsРsС,РμСҢР°РiС-С—
РjРsР¶Р»Р»РөРiР°, СiРeС%Рs С†Рμ РeР»С-РsС-С±РsРs РsР±Т'СҢСrРsС,РsРiР°РsРs.

РќРөСҢРeРsРiР° РsРμРrРsСҢС,Р°С,РsС-СҢС,СҢ

Р°Р°СҢРjР°РeРsРeС-РsРμС,РөРeР° РiСҢРμРiР°СҢР°С,Сr Сr С...РiРsСҢРөС... Р·
РsРөСҢРeРsРiРsСҢ РsРμРrРsСҢС,Р°С,РsС-СҢС,СҢ РsРμ РiРөРiС±Р°Р»Р°СҢСҢ.
Р—РjС-РsСҢРiР°С,Рө РrРsР·Рi РiСҢРμРiР°СҢР°С,Сr РrР»СҢ Р»С-РeСrРiР°РsРsСi С,Р°РeРөС...
С...РiРsСҢРөС... РsРμ РiРsС,СҢС-Р±РsРs (РrРөРi. СҢРsР·РrС-Р»Рө
Б«Р°Р°СҢРjР°РeРsРeС-РsРμС,РөРeР°Б» С,Р° Б«РҗСҢРsР±Р»РөРiРsСҢС,С-
Р·Р°СҢС,РsСҢСrРiР°РsРsСiБ»).

РμРμС±С-РsРeРsРiР° РsРμРrРsСҢС,Р°С,РsС-СҢС,СҢ

PkP°PrC...PsPrPëP»Pë PiPsPIC-PrPsPjP»PµPSPSCΠ C%oPsPrPs PiPsCfC,CḡPsPiPs
 PiPµCḡPµPrPsP·CfPIP°PSPSCΠ C,P°PjCfCfP»PsP·PëPSCf PiC-PrCḡPsC...P»PsCḡPëPrPsPj Cf
 PrPsP·C- 5 PjPi, PI CḡPµP·CfP»CHbC,P°C,C- CΠPePsPiPs CfPiPsCfC,PµCḡC-PiP°P»P°CfCHb
 PiPsCfC,CḡP° P°CḡC,PµCḡC-P°P»CHbPSP° PiC-PiPsC,PµPSP·C-CΠ (CfPëCfC,Psp»C-C‡PSPëPNë
 P°CḡC,PµCḡC-P°P»CHbPSPëPNë C,PëCfPe 70 PjPj/Hg), P±P»CḡPIP°PSPSCΠ C,P° PrC-P°CḡPµCΠ,
 CΠPeC- P»C-PëCfPIP°P»Pë C-PSC,,CfP·C-C”Cḡ CḡC-PrPëPSPë, PiC-CfP»CΠ C‡PsPiPs
 PiP°C†C-C”PSC, PIC-PrC‡CfPI PiPsP»PµPiCεPµPSPSCΠ Cf C,PsPNë CfP°PjPëPNë PrPµPSCb. Pj
 CḡP°P·C- PiPsCfC,CḡPsC— P°CḡC,PµCḡC-P°P»CHbPSPsC— PiC-PiPsC,PµPSP·C-C—, CΠPeP°
 PIPëPSPëPeP°C” PiC-CfP»CΠ PiPµCḡPµPrPsP·CfPIP°PSPSCΠ C,P°PjCfCfP»PsP·PëPSCf
 PiC-PrCḡPsC...P»PsCḡPëPrPsPj, CfP»C-Pr P·P°P±PµP·PiPµC‡PëC,Pë PiC-PrC,CḡPëPjPeCf
 PrC-CΠP»CHbPSPsCfC,C- CfPµCḡC†PµPIPs-CfCfPrPëPSPSPsC— CfPëCfC,PµPjPë.

$P_{\mu}P^{\circ}C^{\dagger}C-C^{\circ}PSC$, $C^{\dagger}PI C$, $P^{\circ}PePsPjC^{\dagger}C^{\dagger}C$, $P^{\circ}PSC-C^{\dagger}P^{\circ}C-Pr$ $PiC_{\eta}P_{\eta}PN_{\eta}PSC_{\eta}C$, P_{η}
 $PiPsC_{\eta}P_{\eta}P.PsPSC$, $P^{\circ}P^{\circ}CH_{\eta}PSP_{\mu}$ $PiPsP^{\circ}PsP_{\eta}P_{\mu}PSPSC_{\eta}$, $C\%PsP_{\pm}PIC-PrPSPsPIP_{\eta}C$, P_{η}
 $P^{\circ}C_{\eta}C$, $P_{\mu}C_{\eta}C-P^{\circ}P^{\circ}CH_{\eta}PSP_{\eta}PN_{\eta}C$, $P_{\eta}C^{\dagger}P_{\eta}C-PSPsC_{\eta}PjP^{\circ}P^{\circ}C-P.C^{\dagger}PIP^{\circ}C$, $P_{\eta}C^{\dagger}P^{\circ}C^{\dagger}C$, PsC , $C^{\dagger}$
 $C^{\dagger}P_{\mu}C_{\eta}C^{\dagger}P_{\mu}PIP_{\eta}C...$ $C^{\dagger}P_{\eta}PsC_{\eta}PsC^{\dagger}P_{\mu}PSC_{\eta}$. $PiPeC\%Ps$ $C^{\dagger}P_{\mu}PSP_{\mu}$ $PrPsPiPsPjPsP_{\eta}P_{\mu}$,
 $PSP_{\mu}PsP_{\pm}C...C-PrPSPs$ $PiC_{\eta}P_{\eta}P.PSP^{\circ}C^{\dagger}P_{\eta}C$, P_{η} $PiP^{\circ}P^{\circ}PjPsP.P^{\circ}PjC-PSPS_{\eta}P_{\eta}P_{\eta}$, P° $C^{\dagger}$ $C_{\eta}P^{\circ}P.C-$
 $PSP_{\mu}PsP_{\pm}C...C-PrPSPsC^{\dagger}C$, $C-$ η $C^{\dagger}C^{\dagger}PrP_{\eta}PSPsP.PiC^{\dagger}P_{\eta}C^{\dagger}PIP^{\circ}P^{\circ}CH_{\eta}PSC- P.P^{\circ}C^{\dagger}PsP_{\pm}P_{\eta}$.
 $P_{\mu}PsC$, $C_{\eta}C-P_{\pm}PSPs$ $C^{\dagger}C$, $P_{\mu}P_{\eta}P_{\eta}C$, P_{η} $P.P^{\circ}C$, $C^{\dagger}PSPeC^{\dagger}C-C^{\circ}C_{\eta}$ $PSP_{\eta}C_{\eta}PsPeC-$
 $PiC_{\eta}PsPiPsPrP_{\eta}C$, P_{η} $P.P^{\circ}PiP^{\circ}P^{\circ}CH_{\eta}PSPsPiC-PrC$, $C_{\eta}P_{\eta}PjC^{\dagger}PIP^{\circ}P^{\circ}CH_{\eta}PSC^{\dagger}C$, $P_{\mu}C_{\eta}P^{\circ}PiC-C_{\eta}$.
 $P^{\circ}C-P^{\circ}P^{\circ}C-P$ $PjPsP_{\eta}P_{\mu}$ $PIP_{\eta}C_{\eta}PIP_{\eta}C$, $P_{\eta}C^{\dagger}C_{\eta}$ $PSP_{\mu}P_{\mu}C$, $P_{\mu}PeC$, $P_{\eta}PIPSP_{\eta}Pj$, $PsC^{\dagger}PeC-P^{\circ}CH_{\eta}PeP_{\eta}$
 C , $P^{\circ}PjC^{\dagger}C^{\dagger}P^{\circ}PsP.P_{\eta}PSC^{\dagger}PiC-PrC_{\eta}PsC...P^{\circ}PsC_{\eta}P_{\eta}Pr$ $PjP^{\circ}PN_{\eta}P_{\eta}P_{\mu}$ $PiPsPIPSC-C^{\dagger}C$, C_{η}
 $P.Pi_{\eta}C^{\dagger}C_{\eta}P.C^{\dagger}C^{\circ}C$, $CH_{\eta}C^{\dagger}C_{\eta}$ $P.P_{\pm}C-P^{\circ}PeP^{\circ}PjP_{\eta}$ $PiP^{\circ}P^{\circ}PjP_{\eta}$ $PeC_{\eta}PsPIC-$.

$P_{\mu}C_{\eta}P_{\eta}$ $PiP_{\mu}C_{\eta}P_{\mu}PrPsP.C^{\dagger}PIP^{\circ}PSPSC-$, $C\%PsP_{\pm}$ $P.P^{\circ}PiPsP_{\pm}C-PiC$, P_{η} $P^{\circ}P_{\pm}C^{\dagger}PsC_{\eta}P_{\pm}C^{\dagger}C-C-$,
 $C^{\dagger}$ $PiP^{\circ}C^{\dagger}C-C^{\circ}PSC$, P° $PSP_{\mu}PsP_{\pm}C...C-PrPSPs$ $PIP_{\eta}PeP^{\circ}P_{\eta}PeP^{\circ}C$, P_{η} $P_{\pm}P^{\circ}CH_{\eta}PIP^{\circ}PSPSC_{\eta}$.
 $PiPeC\%Ps$ $PiC_{\eta}P_{\eta}PN_{\eta}PSC_{\eta}C$, Ps $PIP_{\mu}P^{\circ}P_{\eta}PeC-$ $PrPsP.P_{\eta}$ $PiC_{\eta}P_{\mu}PiP^{\circ}C_{\eta}P^{\circ}C$, $C^{\dagger}$,
 $PSP_{\mu}PsP_{\pm}C...C-PrPSPs$ $PiC_{\eta}PsPiP_{\mu}C^{\dagger}C$, P_{η} $PiC_{\eta}PsPjP_{\eta}PIP^{\circ}PSPSC_{\eta}$ $C_{\eta}P^{\circ}C^{\dagger}PSPeP^{\circ}$, $PrP^{\circ}C$, P_{η}
 $P^{\circ}PeC$, $P_{\eta}PIPSP_{\eta}PSP_{\mu}$ $PiC^{\dagger}PiC-P^{\circ}P^{\circ}C_{\eta}$ C , P° $PiC_{\eta}PsPSPsC^{\dagger}PSP_{\mu}$, $PSP^{\circ}PiC_{\eta}P_{\eta}PeP^{\circ}P^{\circ}Pr$
 $C^{\dagger}C^{\dagger}P^{\circ}CH_{\eta}C$, $P^{\circ}C$, $PSP^{\circ}C$, $C_{\eta}C-C_{\eta}$.

$P_{\mu}PsP_{\pm}C-C^{\dagger}PSC- C_{\eta}P_{\mu}P^{\circ}PeC^{\dagger}C-C-$.

$P^{\dagger}PSC$, $PsC_{\eta}PjP^{\circ}C^{\dagger}C-C_{\eta}$ $PiC_{\eta}Ps$ $PiPsP_{\pm}C-C^{\dagger}PSC-$ $C_{\eta}P_{\mu}P^{\circ}PeC^{\dagger}C-C-$ $PePsP_{\eta}PSPsPiPs$
 $PePsPjPiPsPSP_{\mu}PSC$, P° $PsPeC_{\eta}P_{\mu}PjPs$ ($PrC^{\dagger}C$, $P^{\circ}C^{\dagger}C$, $P_{\mu}C_{\eta}P_{\eta}Pr$ C , P° C , $P^{\circ}PjC^{\dagger}C^{\dagger}P^{\circ}PsP.P_{\eta}PS$)
 C , $P^{\circ}PePsP_{\eta}$ $PSP^{\circ}PIP_{\mu}PrP_{\mu}PSPs$ $PSP_{\eta}P_{\eta}C^{\dagger}P_{\mu}$. $P_{\eta}P_{\mu}$ $PiC_{\eta}Ps$ $PiC^{\dagger}C-$ $PiPsP_{\pm}C-C^{\dagger}PSC-$
 $C_{\eta}P_{\mu}P^{\circ}PeC^{\dagger}C-C-$, $C\%Ps$ $PIC-PrPjC-C^{\dagger}P^{\circ}P^{\circ}P_{\eta}$ $PiC_{\eta}P_{\eta}$ $P.P^{\circ}C^{\dagger}C$, $PsC^{\dagger}C^{\dagger}PIP^{\circ}PSPSC-$
 $PePsP_{\eta}PSPsPiPs$ $PePsPjPiPsPSP_{\mu}PSC$, P° $PsPeC_{\eta}P_{\mu}PjPs$, $PiPsPIC-PrPsPjP^{\circ}C_{\eta}P^{\circ}P_{\eta}$ $PiC_{\eta}P_{\eta}$
 $P.P^{\circ}C^{\dagger}C$, $PsC^{\dagger}C^{\dagger}PIP^{\circ}PSPSC-$ $PePsPjP_{\pm}C-PSP^{\circ}C^{\dagger}C-C-$ $PrC^{\dagger}C$, $P^{\circ}C^{\dagger}C$, $P_{\mu}C_{\eta}P_{\eta}Pr$
 C , $P^{\circ}PjC^{\dagger}C^{\dagger}P^{\circ}PsP.P_{\eta}PS$, C , $PsPjC^{\dagger}C-PSC$, $PsC_{\eta}PjP^{\circ}C^{\dagger}C-C_{\eta}$ $PiC_{\eta}Ps$ $PiPsP_{\pm}C-C^{\dagger}PSC-$
 $C_{\eta}P_{\mu}P^{\circ}PeC^{\dagger}C-C-$ $PiC_{\eta}P_{\eta}$ $P.P^{\circ}C^{\dagger}C$, $PsC^{\dagger}C^{\dagger}PIP^{\circ}PSPSC-$ $PsPeC_{\eta}P_{\mu}PjP_{\eta}C...$
 $PePsPjPiPsPSP_{\mu}PSC$, $C-PI$ $P^{\circ}C^{\dagger}C$, $P^{\circ}C$, $PsC_{\eta}C^{\dagger}C^{\dagger}C$, $P^{\circ}PePsP_{\eta}$ $PIPeP^{\circ}CH_{\eta}C^{\dagger}P_{\mu}PSPs$ PI $PrP^{\circ}PSC^{\dagger}$
 $C-PSC^{\dagger}C$, $C_{\eta}C^{\dagger}PeC^{\dagger}C-C_{\eta}$.

$P-P^{\circ}$ $PrP^{\circ}PSP_{\eta}PjP_{\eta}$ $4-C_{\eta}C-C^{\dagger}PSPsPiPs$ $PrPsC^{\dagger}P^{\circ}C-PrP_{\eta}P_{\mu}PSPSC_{\eta}$ $CombAT$, $PIC-PrC^{\dagger}PsC$, $PsPe$
 $PiPsP_{\pm}C-C^{\dagger}PSP_{\eta}C...$ $C_{\eta}P_{\mu}P^{\circ}PeC^{\dagger}C-PN_{\eta}$, $PIP_{\eta}P.PSP^{\circ}C^{\dagger}P_{\mu}PSP_{\eta}C...$ $PrPsC^{\dagger}P^{\circ}C-PrPSP_{\eta}PeP^{\circ}PjP_{\eta}$
 $PiC_{\eta}PsC$, $C_{\eta}PiPsPj$ $PiP_{\mu}C_{\eta}C_{\eta}PsPiPs$, $PrC_{\eta}C^{\dagger}PiPsPiPs$, C , $C_{\eta}P_{\mu}C$, $CH_{\eta}PsPiPs$ C , P°
 $C^{\dagger}P_{\mu}C$, $PIP_{\mu}C_{\eta}C$, $PsPiPs$ $C_{\eta}PsPeC-PI$ $P^{\circ}C-PeC^{\dagger}PIP^{\circ}PSPSC_{\eta}$, $P.PjC-PSC_{\eta}PIP^{\circ}PiC^{\dagger}C_{\eta}$:
 $PIC-PrPiPsPIC-PrPSPs$ 22% , 6% , 4% C , P° 2% $PiC_{\eta}P_{\eta}$ $PePsPjP_{\pm}C-PSPsPIP^{\circ}PSC-PN_{\eta}$
 C , $P_{\mu}C_{\eta}P^{\circ}PiC-C-$ $PrC^{\dagger}C$, $P^{\circ}C^{\dagger}C$, $P_{\mu}C_{\eta}P_{\eta}Pr$ C , $P^{\circ}PjC^{\dagger}C^{\dagger}P^{\circ}PsP.P_{\eta}PS$; 15% , 6% , 3% C , P° 2%
 $PiC_{\eta}P_{\eta}$ $PjPsPSPsC$, $P_{\mu}C_{\eta}P^{\circ}PiC-C-$ $PrC^{\dagger}C$, $P^{\circ}C^{\dagger}C$, $P_{\mu}C_{\eta}P_{\eta}PrPsPj$; 13% , 5% , 2% , C , P° 2% $PiC_{\eta}P_{\eta}$
 $PjPsPSPsC$, $P_{\mu}C_{\eta}P^{\circ}PiC-C-$ C , $P^{\circ}PjC^{\dagger}C^{\dagger}P^{\circ}PsP.P_{\eta}PS$ Pj . $P^{\circ}PeC\%P_{\eta}PN_{\eta}$ $PIC-PrC^{\dagger}PsC$, $PsPe$
 $PiPsP_{\pm}C-C^{\dagger}PSP_{\eta}C...$ $C_{\eta}P_{\mu}P^{\circ}PeC^{\dagger}C-PN_{\eta}$ $C^{\dagger}$ $PiC_{\eta}C^{\dagger}PiC-$, $C_{\eta}PeP^{\circ}$ PsC , $C_{\eta}P_{\eta}PjC^{\dagger}PIP^{\circ}P^{\circ}$
 $PePsPjP_{\pm}C-PSPsPIP^{\circ}PSC^{\dagger}C$, $P_{\mu}C_{\eta}P^{\circ}PiC-C_{\eta}$, $PiC_{\eta}PsC$, $C_{\eta}PiPsPj$ $PiP_{\mu}C_{\eta}C_{\eta}PsPiPs$ $C_{\eta}PsPeC^{\dagger}$
 $P^{\circ}C-PeC^{\dagger}PIP^{\circ}PSPSC_{\eta}$ $P.C^{\dagger}PjPsPIP^{\circ}P_{\mu}PSP_{\eta}PN_{\eta}$ $PIP_{\eta}C\%P_{\eta}PjP_{\eta}$ $PiPsPeP^{\circ}P.PSP_{\eta}PeP^{\circ}PjP_{\eta}$
 $C_{\eta}P_{\mu}PiC_{\eta}PsPrC^{\dagger}PeC$, $P_{\eta}PIPSP_{\eta}C...$ $PiPsC_{\eta}C^{\dagger}C_{\eta}P_{\mu}PSC_{\eta}$, P° $C^{\dagger}P^{\circ}PjP_{\mu}$: $PiPsC_{\eta}C^{\dagger}C_{\eta}P_{\mu}PSPSC_{\eta}$
 $P_{\mu}C_{\eta}PeC^{\dagger}P^{\circ}C_{\eta}C^{\dagger}C-C-$, $C_{\eta}PeC-$ $C^{\dagger}PiPsC^{\dagger}C$, $P_{\mu}C_{\eta}C-PiP^{\circ}P^{\circ}P_{\eta}C^{\dagger}C_{\eta}$ $C^{\dagger}$ $PiC_{\eta}C^{\dagger}PiC-$.

$P_{\mu}PsP_{\pm}C-C^{\dagger}PSC-$ $C_{\eta}P_{\mu}P^{\circ}PeC^{\dagger}C-C-$, $C\%Ps$ $PIP_{\eta}PSP_{\eta}PeP^{\circ}P^{\circ}P_{\eta}$ P_{η} $C^{\dagger}P^{\circ}C^{\dagger}C$, PsC , PsC_{η} $\geq 1\%$
 $PiC_{\eta}PsC$, $C_{\eta}PiPsPj$ $PiP_{\mu}C_{\eta}C_{\eta}PsPiPs$ $C_{\eta}PsPeC^{\dagger}$ $P.P^{\circ}C^{\dagger}C$, $PsC^{\dagger}C^{\dagger}PIP^{\circ}PSPSC_{\eta}$, $P.P^{\circ}$ $PrP^{\circ}PSP_{\eta}PjP_{\eta}$
 $PrPsC^{\dagger}P^{\circ}C-PrPSP_{\eta}C^{\dagger}CH_{\eta}PeP_{\eta}C...$ $P^{\circ}PSP^{\circ}P^{\circ}C-P.C-PI$ $CombAT$, $REDUCE$, P° C , $P^{\circ}PePsP_{\eta}$
 $PeP^{\circ}C-PSC-C^{\dagger}PSP_{\eta}C...$ $PrPsC^{\dagger}P^{\circ}C-PrP_{\eta}P_{\mu}PSC_{\eta}$ $PjPsPSPsC$, $P_{\mu}C_{\eta}P^{\circ}PiC-PN_{\eta}$

PePsPjPiPsPSPμPSC,P°PjPë P"CrC,P°C,,PsCḡCḡCḡ, PSP°PIPμPrPμPSC- PI C,P°P±P»PëC†C-.

P†PSC,,PsCḡPjP°C†C-Cḡ C%PsPrPs PiPsP±C-C†PSPëC... CḡPμP°PeC†C-PNë
C,P°PjCḡCḡP»PsP·PëPSCḡ P±P°P·CḡC" C,ChCḡCḡ PSP° PrP°PSPëC..., C%Ps PrPsCḡC,CḡPiPSC-
PSP° PIC-PrPiPsPIC-PrPSPëC... PjPμPrPëC†PSPëC... CḡPμCḡCḡCḡCḡP°C.... P§P°CḡC,PsC,P°
C—C... PIPëPSPëPePSPμPSPSCḡ PjPsPḡPμ P·CḡPsCḡC,P°C,Pë PiCḡPë PsPrPSPsC†P°CḡPSPsPjCḡ
P·P°CḡC,PsCḡCḡPIP°PSPSC- PrCḡC,P°CḡC,PμCḡPëPrCḡ C,P° C,P°PjCḡCḡP»PsP·PëPSCḡ.

P§P°CḡC,PsC,P° PIPëPSPëPePSPμPSPSCḡ PiPsP±C-C†PSPëC... CḡPμP°PeC†C-PNë,
PIPëCḡPIP»PμPSPëC... Cr PeP»C-PSC-C†PSPëC... PrPsCḡP»C-PrPḡPμPSPSCḡC...: C†P°CḡC,Ps
(≥1/100 вḡ" <1/10), PSPμC†P°CḡC,Ps (≥1/1000 вḡ" <1/100), CḡC-PrPePs (≥1/10000 вḡ" <1/1000),
PrCḡPḡPμ CḡC-PrPePs (<1/10000). PμPsP±C-C†PSC- CḡPμP°PeC†C-C—,
PeP»P°CḡPëC,,C-PePsPIP°PSC- P·P° PeP»P°CḡP°PjPë CḡPëCḡC,PμPj PsCḡPiP°PSC-PI,
PiCḡPμPrCḡC,P°PIP»PμPSPs Cr PiPsCḡCḡPrPeCḡ P·PSPëPḡPμPSPSCḡ C—C... CḡC,CḡPiPμPSCḡ
C,CḡPḡPePsCḡC,C-.

PḡP»P°Cḡ CḡPëCḡC,PμPjPë PsCḡPiP°PSC-PI	PμPsP±C-C†PSC- CḡPμP°PeC†C-C—	P"CrC,P°CḡC,PμCḡPëPr C,P°PjCḡCḡP»PsP·PëPS"	P"CrC,P°CḡC,PμCḡPëPr	PjP°PjCḡCḡP»PsP·PëPS
P— P±PsPeCḡ PSPμCḡPIPpsPpsC— CḡPëCḡC,PμPjPë	PSPμPiCḡPëC,PsPjPSC-CḡC,Ch P·P°PiP°PjPsCḡPsC†PμPSPSCḡ PiPsP»PsPIPSPëPNë P±C-P»Ch	- C†P°CḡC,Ps -	-	CḡC-PrPePs C†P°CḡC,Ps PSPμC†P°CḡC,Ps
P— P±PsPeCḡ CḡPμCḡC†Cḡ	B CḡPμCḡC†PμPIP° PSPμPrPsCḡC,P°C,PSC-CḡC,Ch (P·P±C-CḡPSPμ PiPsPSCḡC,C,Cḡ ¹) PiPsCḡPëP»PμPSPμ CḡPμCḡC†PμP±PëC,C,Cḡ	PSPμC†P°CḡC,Ps -	PSPμC†P°CḡC,Ps ^d -	- PSPμC†P°CḡC,Ps PSPμC†P°CḡC,Ps
P— P±PsPeCḡ CḡCḡPrPëPSPSPsC— CḡPëCḡC,PμPjPë	PiPsCḡC,CḡCḡP°P»ChPSP° PiC-PiPμC,PμPSP·C-Cḡ	-	-	PSPμC†P°CḡC,Ps
P— P±PsPeCḡ PrPëC...P°P»ChPSPsC— CḡPëCḡC,PμPjPë, PsCḡPiP°PSC-PI PiCḡCḡPrPSPsC— PeP»C-C,PëPë C- CḡPμCḡPμPrPsCḡC,C-PSPSCḡ	CḡPëPSC-C,	-	-	PSPμC†P°CḡC,Ps
P— P±PsPeCḡ CḡP»CḡPSPePsPiPs- PePëCḡPePsPiPsPiPs C,CḡP°PeC,Cḡ	P·P°PiPsCḡ PrC-P°CḡPμCḡ PSCḡPrPsC,P° P±P»CḡPIP°PSPSCḡ	- - - -	- - - -	PSPμC†P°CḡC,Ps PSPμC†P°CḡC,Ps PSPμC†P°CḡC,Ps PSPμC†P°CḡC,Ps
P— P±PsPeCḡ CḡPeC-CḡPë C,P° PiC-PrCḡPeC-CḡPSPëC... C,PeP°PSPëPS	P°PSPiC-PsPSPμPiCḡPsC,PëC†PSPëPNë- PSP°P±CḡCḡPe CḡPëPSPrCḡPsPj PḡC,C-PiPμPSCḡP° вḡ" P"ḡPḡPsPSCḡPsPSP° PeCḡPsPiPëPiḡḡ CḡPSPeP° PiPëCḡPëPiP°PSPSCḡ CḡPiPμCḡP±C-Pḡ	- - - - - -	- - - - -	CḡC-PrPePs PrCḡPḡPμ CḡC-PrPePs PSPμC†P°CḡC,Ps PSPμC†P°CḡC,Ps PSPμC†P°CḡC,Ps
P— P±PsPeCḡ CḡPμPiCḡPsPrCḡPeC,PëPI-PSPsC— CḡPëCḡC,PμPjPë C- PiCḡCḡPrPSPëC... P·P°P»PsP·	PiCḡC-P°PiC-P·Pj C-PjPiPsC,PμPSC†C-Cḡ ³ PiPsCḡCḡCḡPμPSPSCḡ ³ (P·PSPëPḡPμPSPSCḡ) P»C-P±C-PrPs PiPsCḡCḡCḡPμPSPSCḡ ^{3°} PμCḡPeCḡP»CḡC†C-C— P·P°C...PiPsCḡCḡPiP°PSPSCḡ PiCḡCḡPrPSPëC... P·P°P»PsP· ²	C†P°CḡC,Ps C†P°CḡC,Ps C†P°CḡC,Ps C†P°CḡC,Ps C†P°CḡC,Ps C†P°CḡC,Ps	C†P°CḡC,Ps ^b C†P°CḡC,Ps ^b C†P°CḡC,Ps ^b C†P°CḡC,Ps ^b C†P°CḡC,Ps ^b C†P°CḡC,Ps ^b	- - - C†P°CḡC,Ps -
P—P°PiP°P»ChPSC- CḡPsP·P»P°PrPë	P°CḡC,PμPSC-Cḡ	-	-	PSPμC†P°CḡC,Ps

^a P"CrC,P°CḡC,PμCḡPëPr C,P°PjCḡCḡP»PsP·PëPS: Cr PrPsCḡP»C-PrPḡPμPSPSC- CombAT
C†P°CḡC,PsC,P° C†PëC... PiPsP±C-C†PSPëC... CḡPμP°PeC†C-PNë P·PSPëPḡCḡC" C,ChCḡCḡ P·
PePsPḡPSPëPj PSP°CḡC,CḡPiPSPëPj CḡPsPePsPj P· 1-PiPs PrPs 4-PiPs.

^b P— PrPsCḡP»C-PrPḡPμPSCḡ PjPsPSPsC,PμCḡP°PiC-C— PrPsP±CḡPsCḡPeC-CḡPSPsC—
PiC-PiPμCḡPiP»P°P·C-C— PiPμCḡPμPrPjC-C...CḡCḡPsPiPsC— P·P°P»PsP·Pë
PrCḡC,P°CḡC,PμCḡPëPrPsPj.

^c P — PsCÍPSPsPIPSsC — C-PSC,,PsCĤPjP°C†C-C — P· P±PμP·PīPμPePē
C,P°PjCÍCÍP»PsP·PēPSCÍ PrP»CĬ PeCĤP°C — PS P•PŸ.

^d P''PsCÍP»C-PrP¶PμPSPSCĬ REDUCE.

¹ P — P±C-CĤPSPμ PīPsPSCĬC,C,CĬ B«CÍPμCĤC†PμPIP°
PSPμPrPsCÍC,P°C,PSC-CÍC,CĤB» PIPeP»CĤC†P°C'' P·P°CÍC,C-PNēPSCÍ
CÍPμCĤC†PμPICÍ PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ, CÍPμCĤC†PμPICÍ
PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ, PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ P»C-PIPsPiPs
C€P»CÍPSPsC†PeP°, PiPsCÍC,CĤCÍ CÍPμCĤC†PμPICÍ PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ,
PeP°CĤPrC-PsPiPμPSPSPēPNē C€PsPe, PiPsCÍC,CĤCÍ PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ
P»C-PIPsPiPs C€P»CÍPSPsC†PeP°, PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ PīCĤP°PIPsPiPs
C€P»CÍPSPsC†PeP°, PiPsCÍC,CĤCÍ PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ PīCĤP°PIPsPiPs
C€P»CÍPSPsC†PeP°, PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ C€P»CÍPSPsC†PeP°,
PeP°CĤPrC-PsPīCÍP»CĤPjPsPSP°P»CĤPSCÍ PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ,
P·P°CÍC,C-PNēPSCÍ PeP°CĤPrC-PsPīP°C,C-CĤ.

² P'PeP»CĤC†P°CĤC†Pē PiC-PīPμCĤPμCÍC,PμP·C-CĤ C,P° P·P±C-P»CĤC€PμPSPSCĬ
PīCĤCÍPrPSPēC... P·P°P»PsP·.

³ PīPsP±C-C†PSC- CĤPμP°PeC†C-C —, PīPsPIBĤ™ CĬP·P°PSC- P· PīPsCĤCÍC€PμPSPSCĬPj
CÍPμPeCÍCÍP°P»CĤPSPsC — C,,CÍPSPeC†C-C —, P°CÍPsC†C-CĤCĤC,CĤCÍCĬ P·
P»C-PeCÍPIP°PSPSCĬPj PrCÍC,P°CÍC,PμCĤPēPrPsPj (PIPeP»CĤC†P°CĤC†Pē
PjPsPSPsC,PμCĤP°PiC-CĤ C,P° PePsPjP±C-PSP°C†C-CĤ P· C,P°PjCÍCÍP»PsP·PēPSPsPj). PīC-
PīPsP±C-C†PSC- CĤPμP°PeC†C-C — PjPsP¶CÍC,CĤ C,CĤPēPIP°C,Pē PīC-CÍP»CĬ
PīCĤPēPīPēPSPμPSPSCĬ P»C-PeCÍPIP°PSPSCĬ. P'PīP»PēPI PrCÍC,P°CÍC,PμCĤPēPrCÍ PSP°
C — C... C,CĤPēPIP°P»C-CÍC,CĤ PSPμPIC-PrPsPjP°.

^ P'PeP»CĤC†P°CĤC†Pē P·PjPμPSC€PμPSPSCĬ PsP±BĤ™ C''PjCÍ CÍPīPμCĤPjPē.

P''P°PSC- PīPsCÍC,PjP°CĤPePμC,PēPSPiPsPIPēC... PrPsCÍP»C-PrP¶PμPSCĤ

Pj PīPsCÍC,PjP°CĤPePμC,PēPSPiPsPIPsPjCÍ CÍPīPsCÍC,PμCĤPμP¶PμPSPSC- PīPsP±C-C†PSC-
CĤPμP°PeC†C-C — C,,C-PeCÍCÍPIP°P»PēCÍCĬ P·C- CÍPīPsPSC,P°PSPSPēC...
PīPsPIC-PrPsPjP»PμPSCĤ, C,PsPjCÍ C,PsC†PSP° C†P°CÍC,PsC,P° C,P°PePēC... CĤPμP°PeC†C-PNē
PSPμPIC-PrPsPjP°.

PĤPsPSPsC,PμCĤP°PiC-CĬ PrCÍC,P°CÍC,PμCĤPēPrPsPj

P — P±PsPeCž C-PjCžPSPSPsC — CÍPēCÍC,PμPjPē

PŠP°CÍC,PsC,P° PSPμPIC-PrPsPjP°: P°P»PμCĤPiC-C†PSC- CĤPμP°PeC†C-C —,
PIPeP»CĤC†P°CĤC†Pē PIPēCÍPēPīP°PSPSCĬ, CÍPIPμCĤP±C-P¶, PeCĤPsPīPēPIBĤ™ CĬPSPeCÍ,
P»PsPeP°P»C-P·PsPIP°PSPēPNē PSP°P±CĤCĬPe C,P° P°PSPiC-PsPSPμPICĤPsC,PēC†PSPēPNē
PSP°P±CĤCĬPe.

P — P±PsPeCž PīCÍPēC...C-PePē

PŠP°CÍC,PsC,P° PSPμPIC-PrPsPjP°: PrPμPīCĤPμCÍC-CĬ.

$P - P \pm PsPeC \acute{e} C \epsilon PeC - C \bar{H} P \ddot{e} C, P^{\circ} PiC - PrC \epsilon PeC - C \bar{H} PSPsC - PeP \gg C - C, PePsPIP \ddot{e} PSP \ddot{e}$

P C-PrPePs: P°P»PsPiPµC†C-Cl (PiPsP»PsPIPSPëPj C‡PëPSPsPj, PIC,C‡P°C,P° PIPsP»PsC†C†Cl PSP° C,C-P»C-), PiC-PiPµC‡C,C‡PëC...PsP.

$P - P \pm PsPeC \acute{e} C \bar{H} P \mu PiC \bar{H} PsPrC \acute{e} PeC, P \ddot{e} PIPSPsC - C \bar{I} P \ddot{e} C \bar{I} C, P \mu PjP \ddot{e} C, P^{\circ} PiC \bar{H} C \acute{e} PrPSP \ddot{e} C \dots P \cdot P^{\circ} P \gg PsP.$

PS°C†C,PsC,P° PSPµPIC-PrPsPjP°: C,PµC†C,PëPeC†P»ClC‡PSPëPNë P±C-P»CH C,P° PSP°P±C‡ClPe.

PµPsPSPsC,PµC‡P°PiC-Cl C,P°PjC†C†P»PsP·PëPSPsPj

P—P° PrP°PSPëPjPë PiPsC†C,PjP°C‡PePµC,PëPSPiPsPiPs C†PiPsC†C,PµC‡PµP¶PµPSPSCl PiC-Pr C‡P°C† PsPiPµC‡P°C†C— P· PiC‡PëPIPsPrC† PeP°C,P°C‡P°PeC,Pë C,P° PiP»P°C†PePsPjPë C† PrPµClPePëC... PiP°C†C—C’PSC,C-PI, ClPeC— C‡P°PSC—CεPµ PsC,C‡PëPjC†PIP°P»Pë α1-P°PrC‡PµPSPsP±P»PsPeP°C,PsC‡Pë, PIPeP»C‡C‡P°C‡C‡Pë C,P°PjC†C†P»PsP·PëPS, P±C†PI PIC-PrP·PSP°C‡PµPSPëPNë C-PSC,C‡P°PsPiPµC‡P°C†C—PNëPSPëPNë C†PëPSPrC‡PsPj P°C,PsPSC—C‡PSPsC— C‡P°PNëPrC†P¶PePë (P†PŸP̃P, PIP°C‡C—P°PSC, C†PëPSPrC‡PsPjC† PIC†P·CHPePsC— P·C—PSPëC†C-) (PrPëPI. C‡PsP·PrC—P» B«PhC†PsP±P»PëPIPsC†C,C— P·P°C†C,PsC†C†PIP°PSPSClB»).

PµC-Pr C‡P°C† PiC—C†P»ClC‡PµC”C†C,C‡P°C†C—PNëPSPsPiPs P·P°C†C,PsC†C†PIP°PSPSCl P±C†P»Pë PrPsPrP°C,PePsPIC— PiPsPIC-PrPsPjP»PµPSPSCl PiC‡Ps PIPëPiP°PrPePë C„C—P±C‡PëP»ClC†C— PiPµC‡PµPrC†PµC‡PrCH, P°C‡PëC,PjC—C—, C,P°C...C—PeP°C‡PrC—C—, PrPëC†PiPSPsPµ, PSPsC†PsPIPëC... PeC‡PsPIPsC,PµC‡, PiPsC‡C†CεPµPSCH P·PsC‡C†, PI C., C‡. C† PIPëPiP»ClPrC— P·PSPëP¶PµPSPSCl PNëPsPiPs PiPsC†C,C‡PsC,Pë, PjC†P»CHC,PëC„PsC‡PjPSPsC— PµC‡PëC,PµPjPë, PµPeC†C„PsP»C—P°C,PëPIPsPiPs PrPµC‡PjP°C,PëC,C† C,P° C†C†C...PsC†C,C— C†P»PëP·PsPIPsC— PsP±PsP»PsSPEPë C‡PsC,PsPIPsC— PiPsC‡PsP¶PSPëPSPë, P°C†PsC†C—PNëPsPIP°PSC— C—P· P·P°C†C,PsC†C†PIP°PSPSClPj C,P°PjC†C†P»PsP·PëPSC†.

P†PSCεC— PrP°PSC—

PJ C...PsPrC— PeP»C—PSC—C‡PSPsPiPs PrPsC†P»C—PrP¶PµPSPSCl (PrPsC†P»C—PrP¶PµPSPSCl REDUCE) C† C‡PsP»PsPIC—PeC—PI, ClPeC— P»C—PeC†PIP°P»PëC†Cl PrC†C,P°C†C,PµC‡PëPrPsPj, PIC-PrP·PSP°C‡P°P»P°C†CH PIPëC%P° C‡P°C†C,PsC,P° PIPëPSPëPePSPµPSPSCl C‡P°PeC† PiPµC‡PµPrPjC—C...C†C‡PsPIPsC— P·P°P»PsP·Pë (P·P° CεPeP°P»PsCH P”P»C—C†PsPSP° B‡” 8B‡”10) PiPsC‡C—PIPSClPSPs P· PiC‡C†PiPsCH PiP»P°C†PµP±Ps (PrPëPI. C‡PsP·PrC—P»Pë B«PαP°C‡PjP°PePsP»PsPiC—C‡PSC— PIP»P°C†C,PëPIPsC†C,C—B» C,P° B«PhC†PsP±P»PëPIPsC†C,C— P·P°C†C,PsC†C†PIP°PSPSClB»). PµC‡PëC‡PëPSPSPsPiPs P·PiB‡™ ClP·PeC† PjC—P¶ P·P°C†C,PsC†C†PIP°PSPSClPj PrC†C,P°C†C,PµC‡PëPrC† C,P° PIPëPSPëPePSPµPSPSClPj C‡P°PeC† PiPµC‡PµPrPjC—C...C†C‡PsPIPsC— P·P°P»PsP·Pë PIPëC†PsPePsC— PiC‡P°PrP°C†C— P·P° P”P»C—C†PsPSPsPj PIC†C,P°PSPsPIP»PµPSPs PSPµ P±C†P»Ps.

P—P° PrP°PSPëPjPë PeP»C—PSC—C‡PSPëC... PrPsC†P»C—PrP¶PµPSCH C,P° PiPsC†C,PjP°C‡PePµC,PëPSPiPsPIPëC... C†PiPsC†C,PµC‡PµP¶PµPSCH P±C†P»Pë PiPsPIC-PrPsPjP»PµPSPSCl PiC‡Ps PIPëPiP°PrPePë C‡P°PeC† PiC‡C†PrPSPsC— P·P°P»PsP·Pë C† C‡PsP»PsPIC—PeC—PI (PrPëPI. C‡PsP·PrC—P» B«PhC†PsP±P»PëPIPsC†C,C— P·P°C†C,PsC†C†PIP°PSPSClB»).

PŸPµCḡPjC-PS PïCḡPëPrP°C,PSPsCÍC,C-.

3 CḡPsPePë.

PJPjPsPIPë P•P±PµCḡC-PiP°PSPSCII.

P—P±PµCḡC-PiP°C,Pë PI PsCḡPëPiC-PSP°P»CHḡPSC-PNë CÍPïP°PePsPIC†C- PïCḡPë C,PµPjPïPµCḡP°C,CÍCḡC- PSPµ PIPëC‰Pµ 25 B°PŸ.

P—P±PµCḡC-PiP°C,Pë CÍ PSPµPrPsCÍC,CÍPïPSPsPjCÍ PrP»CII PrC-C,PµPNë PjC-CÍC†C-.

PJPïP°PePsPIPëP°.

PµPs 6 PeP°PïCÍCÍP» C,PIPµCḡPrPëC... CÍ P±P»C-CÍC,PµCḡC-, PïPs 5 P±P»C-CÍC,PµCḡC-PI CÍ PïP°C†C†C-. PµPs 9 PeP°PïCÍCÍP» C,PIPµCḡPrPëC... CÍ P±P»C-CÍC,PµCḡC-, PïPs 10 P±P»C-CÍC,PµCḡC-PI CÍ PïP°C†C†C-.

PљP°C,PµPiPsCḡC-CII PIC-PrPïCÍCÍPëCÍ. P—P° CḡPµC†PµPïC,PsPj.

P’PëCḡPsP±PSPëPe.

PŸPḡP“ PḡPḡPḡPJPḡPḡPљPŸPJP P†PḡP“, PŸ.Pḡ.PJ., P†CÍPïP°PSC-CII/

SAG MANUFACTURING, S.L.U., Spain.

PḡC-CÍC†PµP•PSP°C...PsPrP¶PµPSPSCII PIPëCḡPsP±PSPëPeP° C,P° P°PrCḡPµCÍP° PjC-CÍC†CII PïCḡPsPIP°PrP¶PµPSPSCII PNëPsPiPs PrC-CIIP»CHḡPSPsCÍC,C-.

PљP°CḡCḡPµC,PµCḡP° PḡP°C†C-PsPSP°P» 1 PљPj 36, PŸP°PS PḡPiCÍCÍC,C-PS PrPµP»CHḡ P“PIP°PrP°P»C-PëCÍ, 28750 PḡP°PrCḡPëPr P†CÍPïP°PSC-CII / Carretera Nacional 1 Km 36, San Agustin del Guadalix, 28750 Madrid Spain.