

P—PhPŸP'P•P P''P-P•PĶPh

**PĶP°PeP°P• PĤC-PSC-CÍC,PµCĤCÍC,PIP° PsC...PsCĤPsPSPë P•PrPsCĤPsPI'CII
PJPeCĤP°C—PSPë**

===== B„- =====

P PµC''CÍC,CĤP°C†C-PN₂PSPµ PİPsCÍPIC-PrC‡PµPSPSCII

B„- UA/16524/01/03

P†PĶPŸPŸP PJPĤPıP†Pİ

**PrP»CII PJPµPrPëC‡PSPsPiPs P•P°CÍC,PsCÍCıPIP°PSPSCII P»C-PeP°CĤCÍCĤPePsPiPs
P•P°CÍPsP±Cı**

PᄁP»CıPePsPSP°P•PsP»-PŸPµPIP°

(Fluconazole-Teva)

PŸPeP»P°Pr:

PrC-CĤC‡P° CĤPµC‡PsPIPëPSP°: C„P»CıPePsPSP°P•PsP»;

1 PeP°PİCÍCıP»° C,PIPµCĤPrP° PjC-CÍC,PëC,CH C„P»CıPePsPSP°P•PsP»Cı 150 PjPi;

PrPsPİPsPjC-P¶PSC- CĤPµC‡PsPIPëPSPë:

*PIPJc-CÍC, PeP°PİCÍCıP»Pë: P»P°PeC,PsP•Pë PjPsPSPsPiC-PrCĤP°C,, PeCĤPsC...PjP°P»CH
PeCıPeCıCĤCıPrP•CİPSPëPNë, PeCĤPµPjPSC-CĤ PrC-PsPeCÍPëPr PePsP»PsC—PrPSPëPNë
P±PµP•PIPsPrPSPëPNë, PSP°C,CĤC-CĤ P»P°CıCĤPëP»CÍCıP»CHC„P°C,, PjP°PİPSC-CĤ
CÍC,PµP°CĤP°C,,;*

*PeP°PİCÍCıP»CHPSP° PsP±PsP»PsPSPeP°: C,PëC,P°PSCı PrC-PsPeCÍPëPr (P• 171),
PrC-P°PjP°PSC,PsPIPëPNë CÍPëPSC-PNë FCF (P• 133), P¶PµP»P°C,PëPS.*

P»C-PeP°CĤCÍCĤPeP° C„PsCĤPjP°. PĤP°PİCÍCıP»Pë C,PIPµCĤPrC-.

*PhCÍPSPsPIpsc- C„C-P•PëPePs-C...C-PjC-C‡PSC- PIP»P°CÍC,PëPIPsCÍC,C-: C,PIPµCĤPrC-
P¶PµP»P°C,PëPSPsPIC- PeP°PİCÍCıP»Pë, PSP°PİPsPIPsPµPSC- P±C-P»PëPj P°P±Ps
P¶PsPIC,CıPIP°C,Ps-P±C-P»PëPj PsPrPSPsCĤC-PrPSPëPj PİPsCĤPsCëPePsPj, P•
PSPµPİCĤPsP•PsCĤPsCĤ PeCĤPëCëPµC‡PePsCĤ C,P° PePsCĤPİCıCÍPsPj P±P»P°PePëC,PSPsPiPs
PePsP»CHPsCĤCı.*

**PᄁP°CĤPjP°PePsC,PµCĤP°PİPµPIC,PëC‡PSP° PİCĤCıPİP°. PµCĤPsC,PëPİCĤPëP±PePsPIC-
PİCĤPµPİP°CĤP°C,Pë PrP»CII CÍPëCÍC,PµPjPSPsPiPs P•P°CÍC,PsCÍCıPIP°PSPSCII,**

РiPсC...C-PrPSC- C, CтjPëP°P·PsP»Cf. РлPsPr PһPÿPГ J02A C01.

PαP°CтjPjP°PePsP»PsPiC-C‡PSC- PIP»P°CfC, PëPIPsCfC, C-.

PαP°CтjPjP°PePsPrPëPSP°PjC-PeP°.

РһPμC...P°PSC-P·Pj PrC-C—.

PαP»CfPePsPSP°P·PsP» втj “ PïCтjPsC, PëPiCтjPëP±PePsPIPëPNë P·P°CfC-P± PeP»P°CfCf C, CтjPëP°P·PsP»C-PI. PμPμCтjPIPëPSPSPëPj PjPμC...P°PSC-P·PjPsPj PNëPsPiPs PrC-C— C” C-PSPiC-P±CfPIP°PSPSCf PïCтjPëP±PePsPIPsPiPs 14-α-P»P°PSPsCfC, PμCтjPsP»-PrPμPjPμC, PëP»CтjPIP°PSPSCf, PsPiPsCfPμCтjPμPrPePsPIP°PSPsPiPs C†PëC, PsC...CтjPsPjPsPj P 450, C%Ps C” PSPμPIC-Pr’C”PjPSPëPj PμC, P°PïPsPj P±C-PsCfPëPSC, PμP·Cf PïCтjPëP±PePsPIPsPiPs PμCтjPiPsCfC, PμCтjPsP»Cf. PһPeCfPjCfP»CтjPIP°PSPSCf 14-α-PjPμC, PëP»-CfC, PμCтjPsP»C-PI PePsCтjPμP»CтC” P·PïPsPrP°P»CҺCëPsCҺ PIC, CтjP°C, PsCҺ PμCтjPiPsCfC, PμCтjPsP»Cf PjPμPjP±CтjP°PSPsCҺ PïCтjPëP±PePsPIPs— PeP»C-C, PëPSPë C, P° PjPsP¶Pμ PIC-PrPïPsPIC-PrP°C, Pë P·P° PïCтjPsC, PëPiCтjPëP±PePsPICf P°PeC, PëPIPSC-CfC, CҺ C,, P»CfPePsPSP°P·PsP»Cf. PαP»CfPePsPSP°P·PsP» C” P±C-P»CҺCë CfPμP»PμPeC, PëPIPSPëPj PrPs PïCтjPëP±PePsPIPëC... C,, PμCтjPjPμPSC, C-PI C†PëC, PsC...CтjPsPjCf P 450, PSC-P¶ PrPs CтjC-P·PSPëC... CfPëCfC, PμPj C,, PμCтjPjPμPSC, C-PI C†PëC, PsC...CтjPsPjCf P 450 CfCfP°PIC†C-PI.

P—P°CfC, PsCfCfPIP°PSPSCf C,, P»CfPePsPSP°P·PsP»Cf 50 PjPi PSP° PrPsP±Cf PïCтjPsC, CfPiPsPj 28 PrPSC-PI PSPμ PIPiP»PëPIP°P»Ps PSP° PePsPSC†PμPSC, CтjP°C†C-CҺ C, PμCfC, PsCfC, PμCтjPsPSCf Cf PïP»P°P·PjC- PeCтjPsPIC- Cf C‡PsP»PsPIC-PeC-PI P°P±Ps PSP° PePsPSC†PμPSC, CтjP°C†C-CҺ CfC, PμCтjPsC—PrC-PI Cf P¶C-PSPsPe CтjPμPïCтjPsPrCfPeC, PëPIPSPsPiPs PIC-PeCf. PαP»CfPePsPSP°P·PsP» Cf PrPsP·P°C... 200втj“400 PjPi PSP° PrPsP±Cf PSPμ PïCтjPsCfPIP»CfPI PeP»C-PSC-C‡PSPs P·PSP°C‡CfC%PsPiPs PIPiP»PëPICf PSP° CтjC-PIPμPSCH PμPSPrPsPiPμPSPSPëC... CfC, PμCтjPsC—PrC-PI P°P±Ps PSP° PIC-PrPïPsPIC-PrCҺ PSP° CfC, PëPjCfP»CfC†C-CҺ P°PrCтjPμPSPsPePsCтjC, PëPePsC, CтjPsPïPSPsPiPs PiPsCтjPjPsPSCf (PһPлPÿP”) Cf P·PrPsCтjPsPIPëC... PrPsP±CтjPsPIPsP»CҺC†C-PI C‡PsP»PsPIC-C‡PsC— CfC, P°C, C-.

P”PsCfP»C-PrP¶PμPSPSCf PIP·P°C”PjPsPrC-C— P·P°PSC, PëPiC-CтjPëPSPsPj PïCтjPsPrPμPjPsPSCfC, CтjCfPIP°P»Pë, C%Ps P·P°CfC, PsCfCfPIP°PSPSCf 50 PjPi C,, P»CfPePsPSP°P·PsP»Cf CтjP°P·PsPIPs P°P±Ps P±P°PiP°C, PsCтjP°P·PsPIPs PSPμ PIPiP»PëPIP°C” PSP° PjPμC, P°P±PsP»C-P·Pj P°PSC, PëPiC-CтjPëPSCf.

PšCfC, P»PëPIC-CfC, CҺ in vitro

P†n vitro C,, P»CfPePsPSP°P·PsP» PrPμPjPsPSCfC, CтjCfC” PïCтjPsC, PëPiCтjPëP±PePsPICf P°PeC, PëPIPSC-CfC, CҺ CfC, PsCfPsPIPs P±C-P»CҺCëPsCfC, C- PeP»C-PSC-C‡PSPs PïPsCëPëCтjPμPSPëC... PIPëPrC-PI *Candida* (PIPeP»CтC‡P°CтC‡Pë *C. albicans*, *C. parapsilosis*, *C. tropicalis*). *C. glabrata* PrPμPjPsPSCfC, CтjCfC” P·PSPëP¶PμPSCf C‡CfC, P»PëPIC-CfC, CҺ PrPs C,, P»CfPePsPSP°P·PsP»Cf, C, PsPrC- CfPe *C. krusei* C, P° *C. auris* CтjPμP·PëCfC, PμPSC, PSC- PrPs C,, P»CfPePsPSP°P·PsP»Cf. PһC-PSC-PjP°P»CҺPSP° C-PSPiC-P±CfCтC‡P° PePsPSC†PμPSC, CтjP°C†C-Cf (PһP†Pл) C, P° PμPïC-PrPμPjC-PsP»PsPiC-C‡PSPμ PïCтjP°PSPëC‡PSPμ P·PSP°C‡PμPSPSCf (ECOFF) C,, P»CfPePsPSP°P·PsP»Cf PrP»Cf C. *guilliermondii* PIPëC%C-, PSC-P¶ PrP»Cf C. *albicans*.

PαP»CfPePsPSP°P·PsP» *in vitro* C, P°PePsP¶ PïCтjPsCfPIP»CfC” P°PeC, PëPIPSC-CfC, CҺ

ПісC, Пє Cryptococcus neoformans C, P° Cryptococcus gattii C, P° Pe CГP°PjPs, CИPe C-
ПісC, Пє PμPSPPrPμPjC-C±PSPeC... ПісC, Пє P±PePsPIPeC... C,, PsCГPj Blastomyces dermatitidis,
Coccidioides immitis, Histoplasma capsulatum C, P° Paracoccidioides brasiliensis.

P·P·C°PjPsP·PI·CИP·PsPe C,, P°CГPjP°PePsPeC-PSPμC, PēC±PSPeC... C-
C,, P°CГPjP°PePsPrPēPSP°PjC-C±PSPeC... PIP»P°CГC, PēPIPsCГC, PμPNē

P—P° CГPμP·CГP»CHC, P°C, P°PjPē PrPsCГP»C-PrPИPμPSCн PSP° C, PIP°CГPēPSP°C...
C-CГPSCГC° PePsCГPμP»CИCГC-CИ PjC-PИ ПіPsPeP°P·PSPePeP°PjPē PнPГPн C, P°
PμC,, PμPeC, PēPIPsC-CГC, Cн ПісC, Пє PμPeCГPiPμCГPēPjPμPSC, P°P»CHPSPeC...
PjPsPrPμP»PμPNē PjC-PePsP·C-PI, CГPiсCГPēC±PēPSPμPSPeC... PIPePrP°PjPē Candida.
P°C-PrPiPsPIC-PrPSPs PrPs CГPμP·CГP»CHC, P°C, C-PI PeP»C-PSC-C±PSPeC...
PrPsCГP»C-PrPИPμPSCн PIPeCИPIP»PμPSPs PjP°PNēPИPμ 1:1 P»C-PSC-PNēPSPμ
CГPiс-PIPIC-PrPSPsCєPμPSPSCИ PjC-PИ AUC C, P° PrPsP·PsCн C,, P»CГPePsPSP°P·PsP»CГ.
PкP°CИPIPsPēPNē C, P°PePsPИ ПісC, ПєPjPēPNē, P°P»Pμ PSPμPrPsCГC, P°C, PSC-PNē P·PI·CИP·PsPe
PjC-PИ AUC P°P±Ps PrPsP·PsCн C, P° ПіPsP·PēC, PēPIPsPsCн PeP»C-PSC-C±PSPsCн
PIC-PrPiPsPIC-PrPrCн PSP° P»C-PeCГPIP°PSPSCИ PsCГP°P»CHPSPsPiPs PeP°PSPPrPēPrPsP·CГ
C, P° PjPμPSCєPsCн PjC-CГPsCн вГ° PeP°PSPPrPēPrPμPjC-C—. PъP°PePsPИ P»C-PeCГPIP°PSPSCИ
C° PjPμPSCє PμC,, PμPeC, PēPIPsPēPj CГ CГP°P·C- C-PSC,, PμPeCГC-PNē,
CГPiсCГPēC±PēPSPμPSPeC... CєC, P°PjP°PjPē P· PIPeC%PsCн PнPГPн C,, P»CГPePsPSP°P·PsP»CГ.

PнPμC...P°PSC-P·Pj CГPμP·PēCГC, PμPSC, PSPsCГC, C-

P°PēPr Candida PjP°C° CГCИPr PjPμC...P°PSC-P·PjC-PI CГPμP·PēCГC, PμPSC, PSPsCГC, C- PrPs
P°P·PsP»CHPSPeC... ПісC, ПєPісC, ПєP±PePsPIPeC... P·P°CГPsP±C-PI. P°CГPēP±PePsPIC-
CєC, P°PjPē, CИPeC- CГPsP·PIPēPSCГP»Pē PsPrPēPS P°P±Ps P±C-P»CHCєPμ CГPēC...
PjPμC...P°PSC-P·PjC-PI CГPμP·PēCГC, PμPSC, PSPsCГC, C-, PIC-PrPsPjC- CИPe C, P°PeC-, C%Ps
C...P°CГP°PeC, PμCГPēP·CГCн, CHCГCИ PIPeCГPsPePsCн PнPГPн PrPs
C,, P»CГPePsPSP°P·PsP»CГ, C%Ps PSPμCГPiсCГPēCИC, P»PēPIPs PIPiP»PēPIP°C° PSP°
PμC,, PμPeC, PēPIPsC-CГC, CH in vivo C, P° PI PeP»C-PSC-C±PSPeC... CГPjPsPIP°C....

Pj P·P°P·PIPeC±P°PNē C±CГC, P»PēPIPēC... PIPePrC-PI Candida PjPμC...P°PSC-P·Pj
CГPsP·PIPeC, PeCГ CГPμP·PēCГC, PμPSC, PSPsCГC, C-, CИPePēPNēB PSP°PNēC±P°CГC, C-CєPμ
PIPēPSPePeP°C°, ПіPsPI·CИP·P°PSPēPNē C-P· C,, PμCГPjPμPSC, P°PjPē-PjC-CєPμPSCИPjPē
P°P·PsP»C-PI, CИPeC- PIC-PrPiPsPIC-PrP°Cн, CH P·P° P±C-PsCГPēPSC, PμP·
PμCГPiPsCГC, PμCГPēPSCГ. P PμP·PēCГC, PμPSC, PSC-CГC, CH PjPsPИPμ P±CГC, Pē
CГPiсCГPēC±PēPSPμPSP° PjCГC, P°CГC-C°Cн, P·P±C-P»CHCєPμPSPSCИPj
PIPēCГPsP±P»PμPSPSCИ C,, PμCГPjPμPSC, CГ, PμC,, P»CHPeCГPSPēPjPē PjPμC...P°PSC-P·PjP°PjPē
P°P±Ps CГPsP·PIPeC, PePsPj PePsPjPiPμPSCГP°C, PsCГPSPeC... CєP»CИC...C-PI.

PμPsPIC-PrPsPjP»CИP»Pē ПісC, Пє PIPēPiP°PrPePē CГCГPiPμCГC-PSC,, PμPeCГC-C— PIPePrP°PjPē
Candida, C-PSCєPēPjPē, PSC-PИ C. albicans, CИPeC- PjP°Cн, CH ПісC, ПєCГPsPrPSCГ
P·PSPePИPμPSCГ C±CГC, P»PēPIC-CГC, CH (C. glabrata) P°P±Ps CГPμP·PēCГC, PμPSC, PSC- PrPs
C,, P»CГPePsPSP°P·PsP»CГ (PSP°PiсCГPēPeP»P°Pr C. krusei C, P° C. auris). PъP°PeC-
C-PSC,, PμPeCГC-C— PjPsPИCГC, CH ПіPsC, CГPμP±CГPIP°C, Pē P°P»CHC, PμCГPSP°C, PēPIPsC—
ПісC, ПєPісC, ПєP±PePsIPsC— C, PμCГP°PiсC—. PнPμC...P°PSC-P·PjPē
CГPμP·PēCГC, PμPSC, PSPsCГC, C- PSPμ P±CГP»Pē ПіPsIPsC-CГC, Cн P·CИCГPsPIP°PSC- CГ
PrPμCИPePēC... PIPePrC-PI Candida P· PIP»P°CГPSPsCн CГC, C-PNēPeC-CГC, Cн (C. krusei)
P°P±Ps PSPsPIPeC... (C. auris).

PнPsPSC, CГPsP»CHPSC- C, PsC±PePē (PIC-PrPiPsPIC-PrPSPs PrPs CГPμPePsPjPμPSPPrP°CГC-PNē
P,, PICГPsPiPμPNēCГCHPePsPiPs PePsPjC-C, PμC, CГ P· PrPsCГP»C-PrPИPμPSCн

РiPsPrC-P±PSPëPjPë PïCтPë PIPSCrC,чґC-CєPSCнPsPIPμPSPSPsPjCr C-
PïPμCтPsCтP°P»CHPSPsPjCr P·P°CтC,PsCтCrPIP°PSPSC-.

PhP±CтPsCтP±CтC-Cl. PαP»CrPePsPSP°P·PsP» PrPsP±CтPμ P°P±CтPsCтP±CrC”C,чґCтCl
PïCтPë PïPμCтPsCтP°P»CHPSPsPjCr P·P°CтC,PsCтCrPIP°PSPSC-, P° CтC-PIPμPSCн
PïCтPμPïP°CтP°C,Cr Cr PïP»P°P·PjC- PeCтPsPIC- C- CтPëCтC,PμPjPSP°
P±C-PsPrPsCтC,CrPïPSC-CтC,чґ PïPμCтPμPIPëC%CrCтC,чґ 90 % CтC-PIPSCл
C,,P»CrPePsPSP°P·PsP»Cr Cr PïP»P°P·PjC- PeCтPsPIC-, C%Ps PrPsCтClPiP°C”C,чґCтCl
PïCтPë PIPSCrC,чґC-CєPSCнPsPIPμPSPSPsPjCr PIPμPrPμPSPSC- PïCтPμPïP°CтP°C,Cr.
PhPrPSPsC±P°CтPSPμ PIP¶PëPIP°PSPSCл C-P¶C- PSPμ PIPïP»PëPIP°C” PSP°
PICтPjPsPeC,CrPIP°PSPSCл PïCтPμPïP°CтP°C,Cr PïCтPë P№PsPiPs
PïPμCтPsCтP°P»CHPSPsPjCr P·P°CтC,PsCтCrPIP°PSPSC-. PμC-PePsPIP°
PePsPSCтPμPSC,CтP°CтC-Cl Cr PïP»P°P·PjC- PeCтPsPIC- PrPsCтClPiP°C”C,чґCтCl
C±PμCтPμP· 0,5вґ”1,5 PiPsPrPëPSPë PïC-CтP»Cl PïCтPëP№PsPjCr PïCтPμPïP°CтP°C,Cr
PSP°C,C%PμCтPμCтPμ. P№PsPSCтPμPSC,CтP°CтC-Cl Cr PïP»P°P·PjC-
PïCтPsPïPsCтCтC-P№PSP° PrPs PrPsP·Pë. P C-PIPSPsPIP°P¶PSP° 90 %
PePsPSCтPμPSC,CтP°CтC-Cl PrPsCтClPiP°C”C,чґCтCl PSP° 4вґ”5 PrPsP±Cr PïCтPë
P±P°PiP°C,PsCтP°P·PsPIPsPjCr P·P°CтC,PsCтCrPIP°PSPSC- PïCтPμPïP°CтP°C,Cr PI
CтPμP¶PëPjC- PsPrPëPS CтP°P· PSP° PrPsP±Cr. P C-PIPSPsPIP°P¶PSP°
PePsPSCтPμPSC,CтP°CтC-Cl PSP° CтC-PIPSC- 90 % PrPsCтClPiP°C”C,чґCтCl PSP°
PrCтCrPiPëP№ PrPμPSCн P»C-PeCrPIP°PSPSCл PïCтPë P·P°CтC,PsCтCrPIP°PSPSC- Cr
PïPμCтCєPëP№ PrPμPSCн PSP°PIP°PSC,P°P¶CrPIP°P»CHPSPsC— PrPsP·Pë, C%Ps
PIPrPIC-CтC- PïPμCтPμPIPëC%CrC” P·PIPëC±P°P№PSCr PrPsP±PsPICr PrPsP·Cr.

P PsP·PïPsPrC-P». PhP±'C”Pj CтPsP·PïPsPrC-P»Cr PïCтPëP±P»PëP·PSPs PrPsCтC-PIPSCнC”
P·P°PiP°P»CHPSPsPjCr PIPjC-CтC,Cr CтC-PrPëPSPë PI PsCтPiP°PSC-P·PjC-.
P—PI'CлP·CrPIP°PSPSCл P· P±C-P»PeP°PjPë PïP»P°P·PjPë PeCтPsPIC- PSPëP·CHPePμ
(11вґ”12 %).

PαP»CrPePsPSP°P·PsP» PrPsP±CтPμ PïCтPsPSPëPeP°C” PI CrCтC- PrPsCтP»C-PrP¶CrPIP°PSC-
CтC-PrPëPSPë PsCтPiP°PSC-P·PjCr. P C-PIPμPSCн C,,P»CrPePsPSP°P·PsP»Cr Cr CтP»PëPSC-
C,P° PjPsPeCтPsC,PëPSPSC- C” PïPsPrC-P±PSPëPj PrPs PePsPSCтPμPSC,CтP°CтC-C— Cr
PïP»P°P·PjC- PeCтPsPIC-. PJ PïP°CтC-C”PSC,C-PI C-P· PïCтPëP±PePsPIPëPj
PjPμPSC-PSPiC-C,PsPj CтC-PIPμPSCн C,,P»CrPePsPSP°P·PsP»Cr Cr
CтPiPëPSPSPsPjPsP·PePsPIC-P№ CтC-PrPëPSC- PrPsCтClPiP°C” 80 %
PePsPSCтPμPSC,CтP°CтC-C— Cr PïP»P°P·PjC- PeCтPsPIC-.

P’PëCтPsPeC- PePsPSCтPμPSC,CтP°CтC-C— C,,P»CrPePsPSP°P·PsP»Cr Cr CєPeC-CтC-, C%Ps
PïPμCтPμPIPëC%CrCтC,чґ CтPëCтPsPIP°C,PePsPIC-, PrPsCтClPiP°CтC,чґCтCl Cr
CтPsPiPsPIPsPjCr CєP°CтC-, PμPïC-PrPμCтPjC-CтC-, PrPμCтPjC- C,P° PμPePeCтPëPSPSPsPjCr
PïPsC,C-. PαP»CrPePsPSP°P·PsP» PSP°PePsPïPëC±CrC”C,чґCтCl Cr CтPsPiPsPIPsPjCr
CєP°CтC-. PμCтPë P·P°CтC,PsCтCrPIP°PSPSC- PrPsP·Pë 50 PjPi 1 CтP°P· PSP° PrPsP±Cr
PePsPSCтPμPSC,CтP°CтC-Cl C,,P»CrPePsPSP°P·PsP»Cr PïC-CтP»Cl 12 PrPSC-PI
P»C-PeCrPIP°PSPSCл CтC,P°PSPsPIPëP»P° 73 PjPePi/Pi, P° C±PμCтPμP· 7 PrPSC-PI PïC-CтP»Cl
P·P°PIPμCтCєPμPSPSCл P»C-PeCrPIP°PSPSCл PePsPSCтPμPSC,CтP°CтC-Cl PICтPμ C%Pμ
CтC,P°PSPsPIPëP»P° 5,8 PjPePi/Pi. PμCтPë P·P°CтC,PsCтCrPIP°PSPSC- PrPsP·Pë 150 PjPi
1 CтP°P· PSP° C,PëP¶PrPμPSCн PePsPSCтPμPSC,CтP°CтC-Cl C,,P»CrPePsPSP°P·PsP»Cr Cr
CтPsPiPsPIPsPjCr CєP°CтC- PSP° 7-P№ PrPμPSCн P»C-PeCrPIP°PSPSCл CтC,P°PSPsPIPëP»P°
23,4 PjPePi/Pi; C±PμCтPμP· 7 PrPSC-PI PïC-CтP»Cl P·P°CтC,PsCтCrPIP°PSPSCл
PSP°CтC,CrPïPSPsC— PrPsP·Pë PePsPSCтPμPSC,CтP°CтC-Cl PICтPμ C%Pμ
CтC,P°PSPsPIPëP»P° 7,1 PjPePi/Pi.

РлPsPSC†PμPSC,ЧҫP°C†C-Cl C,,P»CfPePsPSP°P·PsP»Cf PI PSC-PiC,ClC... PiC-CfP»Cl
4 PjC-CfClC†C-PI P·P°CfC,PsCfCfPIP°PSPSCl 150 PjPi 1 ЧҫP°P·PSP° C,PeP¶PrPμPSCн
CfC,P°PSPsPIPeP»P° 4,05 PjPePi/Pi Cf P·PrPsЧҫPsPIPeC... PrPsP±ЧҫPsPIPsP»ЧҫC†C-PI C,P°
1,8 PjPePi/Pi Cf PiP°C†C-C”PSC,C-PI C-P·P·P°C...PIPsЧҫЧҫPIP°PSPSClPjPe PSC-PiC,C-PI;
C,,P»CfPePsPSP°P·PsP» PIPeP·PSP°C†P°PICfCl Cf P·ЧҫP°P·PeP°C... PSC-PiC,C-PI C†PμЧҫPμP· 6
PjC-CfClC†C-PI PiC-CfP»Cl P·P°PIPμЧҫC€PμPSPSCl C,PμЧҫP°PiC-C—.

P’C-PsC,ЧҫP°PSCfC,,PsCҫPjP°C†C-Cl. PαP»CfPePsPSP°P·PsP»
PjPμC,P°P±PsP»C-P·CfC”C,ЧҫCfCl PSpμP·PSP°C†PSPsЧҫ PjC-ЧҫPsЧҫ. PμЧҫPe
PIPIPμPrPμPSPSC- PrPsP·Pe, PjC-C†PμPSPsC— ЧҫP°PrC-PsP°PeC,PePIPSPePjPe
C-P·PsC,PsPiP°PjPe, P»PeC€Pμ 11 % C,,P»CfPePsPSP°P·PsP»Cf PμPeCfPeЧҫPμC,CfC”C,ЧҫCfCl
P· CfPμC†PμЧҫ Cf P·PjC-PSPμPSPsPjCf PIPePiP»ClPrC-. PαP»CfPePsPSP°P·PsP» C”
PiPsPjC-ЧҫPSPePj C-PSPiC-P±C-C,PsCҫPsPj C-P·PsC,,PμЧҫPjPμPSC,C-PI CYP2Pҫ9 C,P° CYP3Pҫ4,
P° C,P°PePsP¶ PiPsC,CfP¶PSPePj C-PSPiC-P±C-C,PsCҫPsPj C-P·PsC,,PμЧҫPjPμPSC,Cf CYP2Pҫ19.

P’PePIPμPrPμPSPSCl. PμPμЧҫC-PsPr PSP°PiC-PIPIPePIPμPrPμPSPSCl
C,,P»CfPePsPSP°P·PsP»Cf C-P·PiP»P°P·PjPe PeЧҫPsPIC- CfC,P°PSPsPIPeC,Чҫ P±P»PeP·ЧҫPePs
30 PiPsPrPePS. P’C-P»ЧҫC€P° C†P°CfC,PePSP° PiЧҫPμPiP°ЧҫP°C,Cf PIPePIPsPrPeC,ЧҫCfCl
PSPeЧҫPeP°PjPe, PiЧҫPeC†PsPjCf 80 % PIPIPμPrPμPSPsC— PrPsP·Pe
PIPeClPIP»ClC”C,ЧҫCfCl Cf CfPμC†C- PI PSpμP·PjC-PSPμPSPsPjCf CfC,P°PSC-.
PлP»C-ЧҫPμPSCf C,,P»CfPePsPSP°P·PsP»Cf PiЧҫPsPiPsЧҫC†C-PнPSPePн PrPs
PeP»C-ЧҫPμPSCfCf PeЧҫPμP°C,PePSC-PSCf. PiPeЧҫPeCfP»ЧҫЧҫC†PeC...
PjPμC,P°P±PsP»C-C,C-PI PSpμ PIPeClPIP»PμPSPs.

PҫЧҫPePIP°P»PePн PiPμЧҫC-PsPr PSP°PiC-PIPIPePIPμPrPμPSPSCl PiЧҫPμPiP°ЧҫP°C,Cf P·
PiP»P°P·PjPe PeЧҫPsPIC- PrP°C” PjPsP¶P»PePIC-CfC,Чҫ ЧҫP°P·PsPIPsPiPs
P·P°CfC,PsCfCfPIP°PSPSCl PiЧҫPμPiP°ЧҫP°C,Cf PiЧҫPe PIP°PiC-PSP°P»ЧҫPSPsPjCf
PeP°PSPPrPePrPsP·C-, P° C,P°PePsP¶ P·P°CfC,PsCfCfPIP°PSPSCl PiЧҫPμPiP°ЧҫP°C,Cf 1 ЧҫP°P·
PSP° C,PeP¶PrPμPSCн PiЧҫPe C-PSC€PeC... PiPsPeP°P·P°PSPSClC....

PαP°ЧҫPjP°PePsPeC-PSPμC,PePeP° PiЧҫPe PiPsЧҫCfC€PμPSPSC- C,,CfPSPeC†C-C— PSPeЧҫPsPe

Pj PiP°C†C-C”PSC,C-PI C-P· C,ClP¶PePsЧҫ PSPeЧҫPePsPIPsЧҫ PSpμPrPsCfC,P°C,PSC-CfC,Чҫ
(PĖPлPα < 20 PjP»/C...PI) PiPμЧҫC-PsPr PSP°PiC-PIPIPePIPμPrPμPSPSCl
P·P±C-P»ЧҫC€CfC”C,ЧҫCfCl P· 30 PrPs 98 PiPsPrPePS, C°Ps PIC-PrPiPsPIC-PrPSPs
PiPsC,ЧҫPμP±CfC” P·PSPeP¶PμPSPSCl PrPsP·Pe. PαP»CfPePsPSP°P·PsP»
PIPePIPsPrPeC,ЧҫCfCl P·P° PrPsPiPsPjPsPiPsЧҫ PiPμPjPsPrC-P°P»C-P·Cf C,P° PjPμPSC€PsЧҫ
PjC-ЧҫPsЧҫ вҫ” C€P»ClC...PsPj PiPμЧҫPeC,PsPSPμP°P»ЧҫPSPsPiPs PrC-P°P»C-P·Cf.
PҫPμP°PSCf PiPμPjPsPrC-P°P»C-P·Cf C,ЧҫPePIP°P»C-CfC,Чҫ 3 PiPsPrPePSPe P·PSPeP¶CfC”
ЧҫC-PIPμPSCн C,,P»CfPePsPSP°P·PsP»Cf Cf PiP»P°P·PjC- PeЧҫPsPIC- PiЧҫPeP±P»PeP·PSPs
PSP° 50 %.

PαP°ЧҫPjP°PePsPeC-PSPμC,PePeP° Cf PiPμЧҫC-PsPr P»P°PeC,P°C†C-C—

РлPsPSC†PμPSC,ЧҫP°C†C-C— C,,P»CfPePsPSP°P·PsP»Cf Cf PiP»P°P·PjC- PeЧҫPsPIC- C-
PjP°C,PμЧҫPePSCfЧҫPePsPjCf PjPsP»PsC†C- PIPiЧҫPsPrPsPIP¶ 48 PiPsPrPePS PiC-CfP»Cl
PiЧҫPePнPsPjCf PsPrPSPsЧҫP°P·PsPIPsC— PrPsP·Pe 150 PjPi C,,P»CfPePsPSP°P·PsP»Cf
PsC†C-PSCнPIP°P»Pe Cf C...PsPrC- C,,P°ЧҫPjP°PePsPeC-PSPμC,PeC†PSPsPiPs
PrPsCfP»C-PrP¶PμPSPSCl P· CfC†P°CfC,Чҫ PrPμCfClC,Pe P¶C-PSPsPe Cf PiPμЧҫC-PsPrC-
P»P°PeC,P°C†C-C—, ClPeC- C,PePjC†P°CfPsPIPs P°P±Ps PiPsCfC,C-PнPSPs
PiЧҫPePiPePSPeP»Pe PiPsPrCfPIP°C,Pe CfPIPsC—C... PSPμPjPsPIP»ClC, PiЧҫCfPrPrЧҫ. Pj
PjP°C,PμЧҫPePSCfЧҫPePsPjCf PjPsP»PsC†C- C,,P»CfPePsPSP°P·PsP» PIPeClPIPeP»Pe Cf

P"PsCÍPIC-Pr P·P°CÍ'C,PsCÍ'CrPIP°PSPSCÍ C„P»CÍPePsPSP°P·PsP»CÍ PrP»CÍ
P»C-PeCÍPIP°PSPSCÍ PSPsPIPsPSP°CÍPsPrP¶PµPSPëC... PsP±PjPµP¶CÍ'C"C,CHCÍ'CÍ
C„P°CÍPjP°PePsPeC-PSPµC,PëC±PSPëPjPë PrPsCÍ'P»C-PrP¶PµPSPSCÍPjPë 12
PSPµPrPsPSPsC€PµPSPëC... PrC-C,PµPNë C-P·C,PµCÍPjC-PSPsPj PiPµCÍ'C,P°C†C-C—
PiCÍPëP±P»PëP·PSPs 28 C,PëP¶PSC-PI. PŸPµCÍPµPrPSC-PNë PIC-Pe PrPëC,PëPSPë PiCÍPë
PIPIPµPrPµPSPSC- PiPµCÍ'C€PsC— PrPsP·Pë CÍ'C,P°PSPsPIPëPI 24 PiPsPrPëPSPë
(PrC-P°PiP°P·PsPS
9БҢ“36 PiPsPrPëPS), CÍPµCÍPµPrPSCÍ PjP°CÍ'P° C,C-P»P° PiCÍPë PSP°CÍPsPrP¶PµPSPSC-
CÍ'C,P°PSPsPIPëP»P° 0,9 PePi (PrC-P°PiP°P·PsPS 0,75БҢ“1,10 PePi). P"P»CÍ
7 PiP°C†C-C"PSC,C-PI PiCÍPµC,PsPePsP» PrPsCÍ'P»C-PrP¶PµPSPSCÍ P±CÍ'P»Ps
PIPëPePsPSP°PSPs. PҢP°PeCÍ'PëPjCÍPj 5 PIPSCÍ'C,ЧҢC-C€PSCҢPsPIPµPSPSPëC...
C-PS'C"PeC†C-PNë C„P»CÍPePsPSP°P·PsP»CÍ Cr PrPsP·C- 6 PjPi/PePi PIIPsPrPëP»Pë PePsP¶PSC-
72 PiPsPrPëPSPë. PŸPµCÍPµPrPSC-PNë PiPµCÍ'C-PsPr PSP°PiC-PIIPëPIPµPrPµPSPSCÍ

$C\dot{I}C, P^{\circ}PSPsPI\ddot{P}PI$ 74 $PiPsPr\ddot{P}PSP\ddot{P}$ (44вґ“185) $C\dot{r} P\ddot{I}P\mu C\dot{H}C\ddot{E}P\ddot{E}PN_{\ddot{e}}$ $PrP\mu PSCH$, $PiPsC, C-Pj$
 $P\cdot PjP\mu PSC\ddot{E}P\ddot{E}PIC\dot{I}C\dot{I} PrPs$ 53 $PiPsPr\ddot{P}PS$ (30вґ“131) $PSP^{\circ} 7-PN_{\ddot{e}}$ $PrP\mu PSCH$ $C, P^{\circ} PrPs$
 47 (27вґ“68) $PSP^{\circ} 13-PN_{\ddot{e}}$ $PrP\mu PSCH$. $P\ddot{u}P\gg PsC\%P^{\circ} P\dot{I}C-Pr PeC\dot{H}P\ddot{E}PIPsC\dot{H}$ ($PjPePi*PiPsPr/PjP\gg$)
 $C\dot{I}C, P^{\circ}PSPsPI\ddot{P}P\gg P^{\circ} 271$ (173вґ“385) $C\dot{r} P\ddot{I}P\mu C\dot{H}C\ddot{E}P\ddot{E}PN_{\ddot{e}}$ $PrP\mu PSCH$,
 $P\cdot P\pm C-P\gg CHC\ddot{E}C\dot{r}PIP^{\circ}P\gg C\dot{I}C\dot{I} PrPs$ 490 (292вґ“734) $PSP^{\circ} 7-PN_{\ddot{e}}$ $PrP\mu PSCH$, $PiPsC, C-Pj$
 $P\cdot PSP\ddot{P}\cdot P\ddot{E}P\gg P^{\circ}C\dot{I}C\dot{I} PrPs$ 360 (167вґ“566) $PSP^{\circ} 13-PN_{\ddot{e}}$ $PrP\mu PSCH$. $PhP\pm'C^{\circ}Pj$
 $C\dot{H}PsP\cdot PiPsPrC-P\gg C\dot{r}$ ($PjP\gg/PePi$) $C\dot{I}C, P^{\circ}PSPsPI\ddot{P}PI$ 1183 (1070вґ“1470) $C\dot{r} P\ddot{I}P\mu C\dot{H}C\ddot{E}P\ddot{E}PN_{\ddot{e}}$
 $PrP\mu PSCH$, $P\cdot P\pm C-P\gg CHC\ddot{E}C\dot{r}PIP^{\circ}PIC\dot{I}C\dot{I} PrPs$
 1184 (510вґ“2130) $PSP^{\circ} 7-PN_{\ddot{e}}$ $PrP\mu PSCH$ $C, P^{\circ} PrPs$ 1328 (1040вґ“1680) $PSP^{\circ} 13-PN_{\ddot{e}}$ $PrP\mu PSCH$
 $PIC-PrPiPsPIC-PrPSPs$.

$P\ddot{x}P^{\circ}C\dot{H}PjP^{\circ}PePsPeC-PSP\mu C, P\ddot{e}PeP^{\circ} C\dot{r} P\ddot{I}P^{\circ}C\dot{I}C-C^{\circ}PSC, C-PI P\gg C-C, PSCHPsPiPs PIC-PeC\dot{r}$

$Pj PrPsC\dot{I}P\gg C-PrP\ddot{I}P\mu PSPSC-$, $C\dot{I}PeP\mu P\dot{I}C\dot{H}PsPIPsPr\ddot{P}P\gg P\ddot{e} P\cdot C\dot{r}C\dot{I}P^{\circ}C\dot{I}C, C\dot{H}$ 22
 $P\ddot{I}P^{\circ}C\dot{I}C-C^{\circ}PSC, C-PI$ ($PIC-PePsPj PIC-Pr$ 65 $C\dot{H}PsPeC-PI$) $C,, P\gg C\dot{r}PePsPSP^{\circ}P\cdot PsP\gg$
 $P\cdot P^{\circ}C\dot{I}C, PsC\dot{I}PsPIC\dot{r}PIP^{\circ}P\gg P\ddot{e} P\ddot{I}P\mu C\dot{H}PsC\dot{H}P^{\circ}P\gg CHPSPs$ $C\dot{r} PrPsP\cdot C-$ 50 $PjPi$. 10
 $P\ddot{I}P^{\circ}C\dot{I}C-C^{\circ}PSC, C-PI PsPrPSPsC\dot{I}P^{\circ}C\dot{I}PSPs P\cdot P^{\circ}C\dot{I}C, PsC\dot{I}PsPIC\dot{r}PIP^{\circ}P\gg P\ddot{e} PrC-C\dot{r}C\dot{H}P\mu C, P\ddot{e}PeP\ddot{e}$.
 $C_{max} C\dot{I}C, P^{\circ}PSPsPI\ddot{P}P\gg P^{\circ} 1,54 PjPePi/PjP\gg C, P^{\circ} PrPsC\dot{I}C\dot{I}PiP^{\circ}P\gg P^{\circ}C\dot{I}C\dot{I} P\dot{I}C\dot{H}PsC, C\dot{I}PiPsPj$
 1,3 $PiPsPr\ddot{P}PSP\ddot{P} P\dot{I}C-C\dot{I}P\gg C\dot{I} P\cdot P^{\circ}C\dot{I}C, PsC\dot{I}C\dot{r}PIP^{\circ}PSPSC\dot{I} C,, P\gg C\dot{r}PePsPSP^{\circ}P\cdot PsP\gg C\dot{r}$.
 $P\ddot{Y}P\mu C\dot{H}P\mu PrPSC\dot{I} AUC C\dot{I}C, P^{\circ}PSPsPI\ddot{P}P\gg P^{\circ} 76,4 B\pm 20,3 PjPePi*PiPsPr/PjP\gg$.
 $P\ddot{Y}P\mu C\dot{H}P\mu PrPSC-PN_{\ddot{e}} P\ddot{I}P\mu C\dot{H}C-PsPr PSP^{\circ}P\dot{I}C-PIPI\ddot{P}PIP\mu PrP\mu PSPSC\dot{I} вґ“ 46,2 PiPsPr\ddot{P}PSP\ddot{P}$.
 $P\dot{I}C- C,, P^{\circ}C\dot{H}PjP^{\circ}PePsPeC-PSP\mu C, P\ddot{e}C\dot{I}PSC- P\ddot{I}PsPeP^{\circ}P\cdot PSP\ddot{E}PeP\ddot{e} C^{\circ} PIP\ddot{e}C\%P\ddot{e}PjP\ddot{e}$
 $PiPsC\dot{H}C-PIPSC\dot{I}PSPs P\cdot P^{\circ}PSP^{\circ}P\gg PsPiC-C\dot{I}PSP\ddot{E}PjP\ddot{e} C\dot{r} P\cdot PrPsC\dot{H}PsPIP\ddot{e}C...$
 $PrPsP\pm C\dot{H}PsPIPsP\gg CHC\dot{I}C-PI PjPsP\gg PsPrC\ddot{E}PsPiPs PIC-PeC\dot{r}$. $PhPrPSPsC\dot{I}P^{\circ}C\dot{I}PSP\mu$
 $P\cdot P^{\circ}C\dot{I}C, PsC\dot{I}C\dot{r}PIP^{\circ}PSPSC\dot{I} PrC-C\dot{r}C\dot{H}P\mu C, P\ddot{e}PeC-PI PSP\mu PjP^{\circ}P\gg Ps P\cdot PSP^{\circ}C\dot{I}PSPsPiPs$
 $PIP\ddot{I}P\gg P\ddot{E}PIC\dot{r} PSP^{\circ} C_{max} C, P^{\circ} AUC$. $P\ddot{Y}P^{\circ}PePsP\ddot{I} PeP\gg C-C\dot{H}P\mu PSC\dot{I} PeC\dot{H}P\mu P^{\circ}C, P\ddot{e}PSC-PSC\dot{r}$ (74
 $PjP\gg/C...PI$), $PIC-PrC\dot{I}PsC, PsPe C,, P\gg C\dot{r}PePsPSP^{\circ}P\cdot PsP\gg C\dot{r}$, $C\%Ps P\mu PeC\dot{I}PeC\dot{H}P\mu C, C\dot{r}PIP^{\circ}PIC\dot{I}C\dot{I}$
 $C-P\cdot C\dot{I}P\mu C\dot{I}P\mu C\dot{H} C\dot{r} PSP\mu P\cdot PjC-PSP\mu PSPsPjC\dot{r} PIP\ddot{E}PiP\gg C\dot{I}PrC-$ (0вґ“24 $PiPsPr\ddot{P}PSP\ddot{P}$, 22 %) $C\dot{r}$
 $C, P^{\circ} PSP\ddot{E}C\dot{H}PePsPI\ddot{P}PN_{\ddot{e}} PeP\gg C-C\dot{H}P\mu PSC\dot{I} C,, P\gg C\dot{r}PePsPSP^{\circ}P\cdot PsP\gg C\dot{r}$ (0,124 $PjP\gg/C...PI/PePi$) $C\dot{r}$
 $P\ddot{I}P^{\circ}C\dot{I}C-C^{\circ}PSC, C-PI PrP^{\circ}PSPsC- PIC-PePsPIPsC- P\dot{I}C\dot{H}C\dot{r}PiP\ddot{e} P\pm C\dot{r}P\gg P\ddot{e} PSP\ddot{E}P\ddot{I}C\dot{I}P\ddot{e}PjP\ddot{e}$,
 $PSC-P\ddot{I} P^{\circ}PSP^{\circ}P\gg PsPiC-C\dot{I}PSC- P\ddot{I}PsPeP^{\circ}P\cdot PSP\ddot{E}PeP\ddot{e} C\dot{r} PjPsP\gg PsPrC\ddot{E}P\ddot{e}C...$
 $PrPsP\pm C\dot{H}PsPIPsP\gg CHC\dot{I}C-PI$. $P\ddot{Y}PsPjC\dot{r} P\cdot PjC-PSP\ddot{E} C,, P^{\circ}C\dot{H}PjP^{\circ}PePsPeC-PSP\mu C, P\ddot{e}PeP\ddot{e} C\dot{r}$
 $P\ddot{I}P^{\circ}C\dot{I}C-C^{\circ}PSC, C-PI P\gg C-C, PSCHPsPiPs PIC-PeC\dot{r}$, $PsC\dot{I}P\mu PIP\ddot{E}PrPSPs$, $P\cdot P^{\circ}P\gg P\mu P\ddot{I}P^{\circ}C, CH$
 $PIC-Pr P\ddot{I}P^{\circ}C\dot{H}P^{\circ}PjP\mu C, C\dot{H}C-PI C,, C\dot{r}PSPeC\dot{I}C-PN_{\ddot{e}} PSP\ddot{E}C\dot{H}PsPe$.

$P\ddot{L}P\gg C-PSC-C\dot{I}PSC- C...P^{\circ}C\dot{H}P^{\circ}PeC, P\mu C\dot{H}P\ddot{E}C\dot{I}C, P\ddot{e}PeP\ddot{e}$.

$P\mu PsPeP^{\circ}P\cdot P^{\circ}PSPSC\dot{I}$.

$P^{\circ}PsC\dot{I}C, C\dot{H}P\ddot{E}PN_{\ddot{e}} PIP^{\circ}PiC-PSP^{\circ}P\gg CHPSP\ddot{E}PN_{\ddot{e}} PeP^{\circ}PSPPr\ddot{P}PrPsP\cdot, PePsP\gg P\ddot{e} PjC-C\dot{I}C\dot{I}P\mu PIP^{\circ}$
 $C, P\mu C\dot{H}P^{\circ}P\dot{I}C-C\dot{I} PSP\mu C^{\circ} PrPsC\dot{I}C-P\gg CHPSPsC\dot{H}$.

$P\ddot{L}P^{\circ}PSPPr\ddot{P}PrPsP\cdot PSP\ddot{E}PN_{\ddot{e}} P\pm P^{\circ}P\gg P^{\circ}PSC-C,, PePsP\gg P\ddot{e} PjC-C\dot{I}C\dot{I}P\mu PIP^{\circ} C, P\mu C\dot{H}P^{\circ}P\dot{I}C-C\dot{I} PSP\mu$
 $C^{\circ} PrPsC\dot{I}C-P\gg CHPSPsC\dot{H}$.

$P\mu C\dot{H}PsC, P\ddot{e}PiPsPeP^{\circ}P\cdot P^{\circ}PSPSC\dot{I}$.

– $P^{\circ}C-P\ddot{I}P\mu C\dot{H}C\dot{I}C\dot{r}C, P\gg P\ddot{E}PIC-C\dot{I}C, CH PrPs C,, P\gg C\dot{r}PePsPSP^{\circ}P\cdot PsP\gg C\dot{r}$, $PrPs C-PSC\ddot{E}P\ddot{e}C...$

P°P·PsP»CHBSPSëC... CḡPμC†PsPIPëPS P°P±Ps PrPs P±C†PrCHB-CḡPePsC— P·
PrPsP̄PsPjC-PḡPSPëC... CḡPμC†PsPIPëPS P»C-PeP°CḡC†CHBPePsPiPs P·P°C†PsP±C†;

– PsPrPSPsC†P°C†PSPμ P·P°C†C,PsC†C†PIP°PSPSCḡ C,,P»C†PePsPSP°P·PsP»C† P·
C,PμCḡC,,PμPSP°PrPëPSPsPj P̄CḡPsC,PëP̄PsPeP°P·P°PSPμ P̄P°C†C-C”PSC,P°Pj, CḡPeC-
P̄CḡPëP̄N̄PjP°CḡC,CHB C,,P»C†PePsPSP°P·PsP» P±P°PiP°C,PsCḡP°P·PsPIPs C† PrPsP·P°C... 400
PjPi PSP° PrPsP±C† P°P±Ps PIPëC%Pμ (PSP° P̄C-PrC†C,P°PIC- CḡPμP·C†P»CHB,C,P°C,C-PI
PrPsC†P»C-PrPḡPμPSCḡ PIP·P°C”PjPsPrC-C— P̄CḡPë P±P°PiP°C,PsCḡP°P·PsPIPsPjC†
P·P°C†C,PsC†C†PIP°PSPSC-);

– PsPrPSPsC†P°C†PSPμ P·P°C†C,PsC†C†PIP°PSPSCḡ C,,P»C†PePsPSP°P·PsP»C† P·
C-PSCëPëPjPë P»C-PeP°CḡC†CHBPePëPjPë P·P°C†PsP±P°PjPë, C%Ps P̄PsPrPsPIPḡC†CḡC,CHB
C-PSC,PμCḡPIP°P» QT C,P° PjPμC,P°P±PsP»C-P·C†CḡC,CHBḡCḡ P·P° PrPsP̄PsPjPsPiPsCḡ
C,,PμCḡPjPμPSC,C† CYP3Pḡ4 (PSP°P̄CḡPëPeP»P°Pr C†PëP·P°P̄CḡPëPrC†, P°C†C,PμPjC-P·PsP»C†,
P̄C-PjPsP·PëPrC†, C...C-PSC-PrPëPSC† C,P° PμCḡPëC,CḡPsPjC-C†PëPSC†), PrPëPI. C,P°PePsPḡ
CḡPsP·PrC-P»Pë B«PhC†PsP±P»PëPIPsC†C,C- P·P°C†C,PsC†C†PIP°PSPSCḡB» C,P°
B«P’P·P°C”PjPsPrC-Cḡ P· C-PSCëPëPjPë P»C-PeP°CḡC†CHBPePëPjPë P·P°C†PsP±P°PjPë C,P°
C-PSCëC- PIPëPrPë PIP·P°C”PjPsPrC-PN̄B».

***P’P·P°C”PjPsPrC-Cḡ P· C-PSCëPëPjPë P»C-PeP°CḡC†CHBPePëPjPë P·P°C†PsP±P°PjPë C,P°
C-PSCëC- PIPëPrPë PIP·P°C”PjPsPrC-PN̄.***

PμCḡPsC,PëP̄PsPeP°P·P°PSPμ C†C†PjC-C†PSPμ P·P°C†C,PsC†C†PIP°PSPSCḡ P·
PSPëPḡC†PμP·P°P·PSP°C†PμPSPëPjPë P»C-PeP°CḡC†CHBPePëPjPë P·P°C†PsP±P°PjPë

P̄PëP·P°P̄CḡPëPr. PμPsPIC-PrPsPjP»CḡP»Pë P̄CḡPs C,P°PeC- CḡPIPëC%P° P· P±PsPeC†
C†PμCḡC†Cḡ CḡPe P̄P°CḡPsPeC†PëP·PjP°P»CHBSPS° CëP»C†PSPsC†PePsPIP°
C,P°C...C-PeP°CḡPrC-Cḡ C,PëP̄C† B«P̄C-CḡC†PμC,B» C† P̄P°C†C-C”PSC,C-PI, CḡPeC-
PsPrPSPsC†P°C†PSPs P̄CḡPëP̄N̄PjP°P»Pë C,,P»C†PePsPSP°P·PsP» C,P° C†PëP·P°P̄CḡPëPr. PμC-Pr
C†P°C† PePsPSC,CḡPsP»CHBPsPIP°PSPsPiPs PrPsC†P»C-PrPḡPμPSPSCḡ P±C†P»Ps
PIPëCḡPIP»PμPSPs, C%Ps PsPrPSPsC†P°C†PSPμ P·P°C†C,PsC†C†PIP°PSPSCḡ
C,,P»C†PePsPSP°P·PsP»C† PI PrPsP·C- 200 PjPi 1 CḡP°P· PSP° PrPsP±C† C,P°
C†PëP·P°P̄CḡPëPrC† C† PrPsP·C- 20 PjPi 4 CḡP°P·Pë PSP° PrPsP±C† C†P̄CḡPëC†PëPSCḡP»Ps
P·PSP°C†PSPμ P̄C-PrPIPëC%PμPSPSCḡ CḡC-PIPSCḡ C†PëP·P°P̄CḡPëPrC† C† P̄P»P°P·PjC-
PeCḡPsPIC- C,P° P̄PsPrPsPIPḡPμPSPSCḡ C-PSC,PμCḡPIP°P»C† QTC†. P»C-PeC†PIP°PSPSCḡ P·
PsPrPSPsC†P°C†PSPëPj P·P°C†C,PsC†C†PIP°PSPSCḡPj C,,P»C†PePsPSP°P·PsP»C† C,P°
C†PëP·P°P̄CḡPëPrC† P̄CḡPsC,PëP̄PsPeP°P·P°PSPμ (PrPëPI. CḡPsP·PrC-P»
B«PμCḡPsC,PëP̄PsPeP°P·P°PSPSCḡB»).

P̄PμCḡC,,PμPSP°PrPëPS. Pj P·PI’CḡP·PeC† P· PIPëP̄P°PrPeP°PjPë C†PμCḡPN̄PsP·PSPëC...
C†PμCḡC†PμPIPëC... P°CḡPëC,PjC-PN̄, C†P̄CḡPëC†PëPSPμPSPëC... P̄PsPrPsPIPḡPμPSPSCḡPj
C-PSC,PμCḡPIP°P»C† QTc, C† P̄P°C†C-C”PSC,C-PI, CḡPeC- P̄CḡPëP̄N̄PjP°P»Pë P°P·PsP»CHBPS-
P̄CḡPsC,PëP̄CḡPëP±PePsPIC- P·P°C†PsP±Pë PsPrPSPsC†P°C†PSPs P·
C,PμCḡC,,PμPSP°PrPëPSPsPj, P±C†P»Pë P̄CḡPsPIPμPrPμPSC- PrPsC†P»C-PrPḡPμPSPSCḡ
PIP·P°C”PjPsPrC-C— C†PëC... P»C-PeP°CḡC†CHBPePëC... P·P°C†PsP±C-PI. Pj
PrPsC†P»C-PrPḡPμPSPSC- P· P̄CḡPëP̄N̄PsPjPsPj C,,P»C†PePsPSP°P·PsP»C† 200 PjPi PSP°
PrPsP±C† PSPμ P±C†P»Ps P̄CḡPsPrPμPjPsPSC†C,CḡPsPIP°PSPs P̄PsPrPsPIPḡPμPSPSCḡ
C-PSC,PμCḡPIP°P»C† QTc. P†PSCëPμ PrPsC†P»C-PrPḡPμPSPSCḡ P· P̄CḡPëP̄N̄PsPjPsPj
C,,P»C†PePsPSP°P·PsP»C† 400 PjPi C,P° 800 PjPi PSP° PrPsP±C† PIPëCḡPIPëP»Ps, C%Ps
C,,P»C†PePsPSP°P·PsP», P̄CḡPë P·P°C†C,PsC†C†PIP°PSPSC- C† PrPsP·C- 400 PjPi PSP° PrPsP±C†

P°P±Ps PIPëC%Pµ, P·PSP°C±PSPs P·P±C-P»CHC€CfC” CḡC-PIPµPSCḡ
C,PµCḡC,,PµPSP°PrPëPSCf Cf PīP»P°P·PjC- PeCḡPsPIC- PI CḡP°P·C- PsPrPSPsC±P°CfPSPsPiPs
PīCḡPëPNëPsPjCf. PŸCfPjC-CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf PI
PrPsP·P°C... 400 PjPi P°P±Ps PIPëC%Pµ C-P· C,PµCḡC,,PµPSP°PrPëPSPsPj
PīCḡPsC,PëPiPsPeP°P·P°PSPµ (PrPëPI. CḡPsP·PrC-P»B B«PµCḡPsC,PëPiPsPeP°P·P°PSPSCḡB»).

Pj CḡP°P·C- PsPrPSPsC±P°CfPSPsPiPs P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf Cf
PrPsP·P°C... PSPëP¶C±Pµ 400 PjPi PSP° PrPsP±Cf C-P· C,PµCḡC,,PµPSP°PrPëPSPsPj CfP»C-Pr
PīCḡPsPiPsPrPëC,Pë CḡPµC,PµP»CHPSPëPNë PjPsPSC-C,PsCḡPëPSPi CfC,P°PSCf
PīP°CfC-C”PSC,P°.

PḡCfC,PµPjC-P·PsP». PŸCfPjC-CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf P·
P°CfC,PµPjC-P·PsP»PsPj PjPsP¶Pµ P·PjPµPSC€PëC,Pë PeP»C-CḡPµPSCf P°CfC,PµPjC-P·PsP»Cf.
PŸPīCḡPëC±PëPSPµPSP° C±PëPj PīC-PrPIPëC%PµPSP° PePsPSC±PµPSC,CḡP°CfC-Cḡ
P°CfC,PµPjC-P·PsP»Cf Cf PīP»P°P·PjC- PeCḡPsPIC- PjPsP¶Pµ PīCḡPëP·PIPµCfC,Pë PrPs
PīPsPrPsPIP¶PµPSPSCḡ C-PSC,PµCḡPIP°P»Cf QT C,P° PI CḡC-PrPeC-CfPSPëC...
PIPëPīP°PrPeP°C... PrPs PīP°CḡPsPeCfPëP·PjP°P»CHPSPsC— C€P»CfPSPsC±PePsPiPsC—
C,P°C...C-PeP°CḡPrC-C— C,PëPīCf B«PīC-CḡCfPµC,B». PhPrPSPsC±P°CfPSPµ
P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf C,P° P°CfC,PµPjC-P·PsP»Cf
PīCḡPsC,PëPiPsPeP°P·P°PSPµ (PrPëPI. CḡPsP·PrC-P» B«PµCḡPsC,PëPiPsPeP°P·P°PSPSCḡB»).

PµC-PjPsP·PëPr. PhPrPSPsC±P°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf P·
PīC-PjPsP·PëPrPsPj PjPsP¶Pµ PīCḡPëP·PIPµCfC,Pë PrPs C-PSPiC-P±CfPIP°PSPSCḡ
PjPµC,P°P±PsP»C-P·PjCf PīC-PjPsP·PëPrCf, C...PsC±P° PIC-PrPīPsPIC-PrPSPëC...
PrPsCfP»C-PrP¶PµPSCḡ *in vitro* C,P° *in vivo* PSPµ PīCḡPsPiPsPrPëP»Pë. PµC-PrPIPëC%PµPSP°
PePsPSC±PµPSC,CḡP°CfC-Cḡ PīC-PjPsP·PëPrCf Cf PīP»P°P·PjC- PeCḡPsPIC- PjPsP¶Pµ
PīCḡPëP·PIPµCfC,Pë PrPs PīPsPrPsPIP¶PµPSPSCḡ C-PSC,PµCḡPIP°P»Cf QT C,P°, PI
CḡC-PrPeC-CfPSPëC... PIPëPīP°PrPeP°C..., PrPs PīP°CḡPsPeCfPëP·PjP°P»CHPSPsC—
C€P»CfPSPsC±PePsPiPsC— C,P°C...C-PeP°CḡPrC-C— C,PëPīCf B«PīC-CḡCfPµC,B». PhPrPSPsC±P°CfPSPµ
P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf P·
PīC-PjPsP·PëPrPsPj PīCḡPsC,PëPiPsPeP°P·P°PSPµ (PrPëPI. CḡPsP·PrC-P»
B«PµCḡPsC,PëPiPsPeP°P·P°PSPSCḡB»).

PfC-PSC-PrPëPS. PhPrPSPsC±P°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf
C,P° C...C-PSC-PrPëPSCf PjPsP¶Pµ PīCḡPëP·PiPsPrPëC,Pë PrPs C-PSPiC-P±CfPIP°PSPSCḡ
PjPµC,P°P±PsP»C-P·PjCf C...C-PSC-PrPëPSCf, C...PsC±P° PIC-PrPīPsPIC-PrPSPëC...
PrPsCfP»C-PrP¶PµPSCḡ *in vitro* C,P° *in vivo* PSPµ PīCḡPsPiPsPrPëP»Pë.
P—P°CfC,PsCfCfPIP°PSPSCḡ C...C-PSC-PrPëPSCf P±CfP»Ps PīPsPīCḡP·P°PSPµ P·
PīPsPrPsPIP¶PµPSPSCḡPj C-PSC,PµCḡPIP°P»Cf QT C,P° PI CḡC-PrPeC-CfPSPëC...
PIPëPīP°PrPeP°C... Bḡ” PīP°CḡPsPeCfPëP·PjP°P»CHPSPsCḡ C€P»CfPSPsC±PePsPiPsCḡ
C,P°C...C-PeP°CḡPrC-C”Cḡ C,PëPīCf B«PīC-CḡCfPµC,B». PhPrPSPsC±P°CfPSPµ
P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf P· C...C-PSC-PrPëPSPsPj
PīCḡPsC,PëPiPsPeP°P·P°PSPµ (PrPëPI. CḡPsP·PrC-P» B«PµCḡPsC,PëPiPsPeP°P·P°PSPSCḡB»).

P·CḡPëC,CḡPsPjC-CfPëPS. PhPrPSPsC±P°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCḡ
C,,P»CfPePsPSP°P·PsP»Cf P· PµCḡPëC,CḡPsPjC-CfPëPSPsPj PjPsP¶Pµ PīCḡPëP·PiPsPrPëC,Pë PrPs
PīC-PrPIPëC%PµPSPSCḡ CḡPëP·PëPeCf PeP°CḡPrC-PsC,PsPeCfPëC±PSPsCfC,C-
(PīPsPrPsPIP¶PµPSPSCḡ C-PSC,PµCḡPIP°P»Cf QT C,P° PīP°CḡPsPeCfPëP·PjP°P»CHPSPsC—
C€P»CfPSPsC±PePsPiPsC— C,P°C...C-PeP°CḡPrC-C— C,PëPīCf B«PīC-CḡCfPµC,B»), C,P°, CḡPe
PSP°CfP»C-PrPsPe, PrPs CḡP°PīC,PsPiPsC— PePsCḡPsPSP°CḡPSPsC— CfPjPµCḡC,C-.
PhPrPSPsC±P°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf C,P°
PµCḡPëC,CḡPsPjC-CfPëPSCf PīCḡPsC,PëPiPsPeP°P·P°PSPµ (PrPëPI. CḡPsP·PrC-P»
B«PµCḡPsC,PëPiPsPeP°P·P°PSPSCḡB»).

$P''C-PrC\bar{H}PsC...P \gg PsC\bar{H}PsC, C-P^{\circ}P \cdot P\bar{e}Pr$. PJ PrPsCÍP»C-PrP¶PµPSPSC-
C,,P°C $\bar{H}$ PjP°PePsPeC-PSpµC,PëC‡PSPsC— PIP·P°C''PjPsPrC— PsPrPSPsC‡P°CÍPSPµ
P±P°PiP°C,PsPeC $\bar{H}$ P°C,PSpµ P·P°CÍC,PsCÍCÍPIP°PSPSC¶
PiC-PrC $\bar{H}$ PsC...P»PsC $\bar{H}$ PsC,C-P°P·PëPrCÍ P·PrPsC $\bar{H}$ PsPIPëPj PrPsP±C $\bar{H}$ PsPIPsP»CHbC‡C¶Pj,
C¶PeC- PsC,C $\bar{H}$ PëPjCÍPIP°P»Pë C,,P»CÍPePsPSP°P·PsP», PiC-PrPIPëC%oCÍPIP°P»Ps

$$P\hbar PSC, P\ddot{e}PePsP^{\circ}PiC\acute{a}P \gg C\grave{L}PSC, P\ddot{e}. P_{\text{H}}C - P_{\text{T}} C_{\text{H}}P^{\circ}C_{\text{T}} P_{\text{H}}PsC_{\text{T}}C, P_{\text{H}}P^{\circ}C_{\text{H}}PeP_{\text{H}}C, P\ddot{e}PSPiPsPiPsPiPs$$

PīPμCḡC-PsPrCf, CḡPe C- PīCḡPē P·P°CfC,PsCfCfPIP°PSPSC- C-PSCēPēC...
 P°P·PsP»CHBPSPēC... PīCḡPsC,PēPiCḡPēP±PePsPIPēC... P·P°CfPsP±C-PI,
 PīPsPIC-PrPsPjP»CḡP»Pē PīCḡPs PμPīC-P·PsPrPē PeCḡPsPIPsC,PμC‡ (CfPēPSC†C-,
 PSPScfPsPIC- PeCḡPsPIPsC,PμC‡C-, CēP»CfPSPePsPIPs-PePēCēPePsPIC- PeCḡPsPIPsC,PμC‡C-,
 PiPμPjP°C,CfCḡC-Cḡ C,P° PjPμP»PμPSP°), PīPsPI'CḡP·P°PSC- P·C- P·P±C-P»CHCēPμPSPSCḡPj
 PīCḡPsC,CḡPsPjP±C-PSPsPIPsPiPs C‡P°CfCf Cf PīP°C†C-C"PSC,C-PI, CḡPeC-
 PīCḡPēPNēPjP°P»Pē C,,P»CfPePsPSP°P·PsP» PsPrPSPsC‡P°CfPSPs P· PIP°CḡC,,P°CḡPēPSPsPj.
 PμCḡPē PsPrPSPsC‡P°CfPSPsPjCf P·P°CfC,PsCfCfPIP°PSPSC- C,,P»CfPePsPSP°P·PsP»Cf C,P°
 PIP°CḡC,,P°CḡPēPSCf CfPiPsCfC,PμCḡC-PiP°P»PsCfCḡ PrPIPsPeCḡP°C,PSPμ
 PīPsPrPsPIP¶PμPSPSCḡ PīCḡPsC,CḡPsPjP±C-PSPsPIPsPiPs C‡P°CfCf, PjPsP¶P»PēPIPs,
 PIPSP°CfP»C-PrPsPe C-PSPiC-P±CfPIP°PSPSCḡ PjPμC,P°P±PsP»C-P·PjCf PIP°CḡC,,P°CḡPēPSCf
 C‡PμCḡPμP· CYP2C9. PμP°C†C-C"PSC,P°Pj, CḡPeC- PīCḡPēPNēPjP°CḡC,CH
 P°PSC,PēPePsP°PiCfP»CḡPSC,Pē PeCfPjP°CḡPēPSPsPIPsPiPs C,PēPīCf P°P±Ps
 C-PSPrP°PSPrC-PsPS PsPrPSPsC‡P°CfPSPs P· C,,P»CfPePsPSP°P·PsP»PsPj,
 PSPμPsP±C...C-PrPSPs PīCḡPsPIPsPrPēC,Pē CḡPμC,PμP»CHBPSPēPNē PePsPSC,CḡPsP»CH
 PīCḡPsC,CḡPsPjP±C-PSPsPIPsPiPs C‡P°CfCf. PμPsP¶P»PēPIPs, P·PSP°PrPsP±PēC,CHCfCḡ
 PePsCḡPēPiCfPIP°PSPSCḡ PrPsP·Pē P°PSC,PēPePsP°PiCfP»CḡPSC,Cf.

P'PμPSP·PsPrC-P°P·PμPīC-PSPē PePsCḡPsC,PePsC— PrC-C—, PSP°PīCḡPēPeP»P°Pr
PjC-PrP°P·PsP»P°Pj, C,CḡPēP°P·PsP»P°Pj. PμCḡPēP·PSP°C‡PμPSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf
PīC-CfP»Cḡ PīPμCḡPsCḡP°P»CHBPSPsPiPs P·P°CfC,PsCfCfPIP°PSPSCḡ PjC-PrP°P·PsP»P°PjCf
PīCḡPēP·PIPsPrPēP»Ps PrPs P·PSP°C‡PSPsPiPs PīC-PrPIPēC%PμPSPSCḡ
PePsPSC†PμPSC,CḡP°C†C-C— PjC-PrP°P·PsP»P°PjCf C,P° PrPs PīPsCfPēP»PμPSPSCḡ
PīCfPēC...PsPjPsC,PsCḡPSPēC... PμC,,PμPeC,C-PI. PhPrPSPsC‡P°CfPSPμ
P·P°CfC,PsCfCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»Cf Cf PrPsP·C- 200 PjPi C,P°
PjC-PrP°P·PsP»P°PjCf Cf PrPsP·C- 7,5 PjPi PīPμCḡPsCḡP°P»CHBPSPs PīCḡPēP·PIPsPrPēP»Ps PrPs
PīC-PrPIPēC%PμPSPSCḡ AUC C,P° PīPμCḡC-PsPrCf PSP°PīC-PIPIPēPIPμPrPμPSPSCḡ Cf 3,7
C,P° 2,2 CḡP°P·P° PIC-PrPīPsPIC-PrPSPs. P—P°CfC,PsCfCfPIP°PSPSCḡ
C,,P»CfPePsPSP°P·PsP»Cf Cf PrPsP·C- 200 PjPi/PrPsP±Cf C,P° 0,25 PjPi C,CḡPēP°P·PsP»P°PjCf
PīPμCḡPsCḡP°P»CHBPSPs PīCḡPēP·PIPsPrPēP»Ps PrPs PīC-PrPIPēC%PμPSPSCḡ AUC C,P°
PīPμCḡC-PsPrCf PSP°PīC-PIPIPēPIPμPrPμPSPSCḡ C,CḡPēP°P·PsP»P°PjCf Cf 4,4 C,P°
2,3 CḡP°P·P° PIC-PrPīPsPIC-PrPSPs. PμCḡPē PsPrPSPsC‡P°CfPSPsPjCf
P·P°CfC,PsCfCfPIP°PSPSC- C,,P»CfPePsPSP°P·PsP»Cf C,P° C,CḡPēP°P·PsP»P°PjCf
CfPiPsCfC,PμCḡC-PiP°P»PsCfCḡ PiPsC,PμPSC†C-CḡPIP°PSPSCḡ C,P°
PīCḡPsP»PsPSPiP°C†C-Cḡ PμC,,PμPeC,C-PI C,CḡPēP°P·PsP»P°PjCf.

PīPeC%Ps PīP°C†C-C"PSC,Cf, CḡPePēPNē PīCḡPsC...PsPrPēC,CH PeCfCḡCf
 P»C-PeCfPIP°PSPSCḡ C,,P»CfPePsPSP°P·PsP»PsPj, CfP»C-Pr PsPrPSPsC‡P°CfPSPs
 PīCḡPēP·PSP°C‡PēC,Pē C,PμCḡP°PiC-Cḡ P±PμPSP·PsPrC-P°P·PμPīC-PSP°PjPē, PrPsP·Cf
 PsCfC,P°PSPSC-C... CfP»C-Pr P·PjPμPSCēPēC,Pē C,P° PICfC,P°PSPsPIPēC,Pē
 PSP°P»PμP¶PSPēPNē PSP°PiP»CḡPr P·P° CfC,P°PSPsPj PīP°C†C-C"PSC,P°.

PμP°CḡP±P°PjP°P·PμPīC-PS. PμP»CfPePsPSP°P·PsP» PīCḡPēPiPSC-C‡CfC"
PjPμC,P°P±PsP»C-P·Pj PeP°CḡP±P°PjP°P·PμPīC-PSCf C,P° CfPīCḡPēC‡PēPSCḡC"
PīC-PrPIPēC%PμPSPSCḡ CḡC-PIPSCḡ PeP°CḡP±P°PjP°P·PμPīC-PSCf PI CfPēCḡPsPIP°C,C†C-
PeCḡPsPIC- PSP° 30 %. P†CfPSCfC" CḡPēP·PēPe CḡPsP·PIPēC,PeCf PīCḡPsCḡPIC-PI
C,PsPeCfPēC‡PSPsCfC,C- P· P±PsPeCf PeP°CḡP±P°PjP°P·PμPīC-PSCf. PμPsP¶Pμ P±CfC,Pē
PSPμPsP±C...C-PrPSPēPj PePsCḡPēPiCfPIP°PSPSCḡ PrPsP·Pē PeP°CḡP±P°PjP°P·PμPīC-PSCf
P·P°P»PμP¶PSPs PIC-Pr CḡC-PIPSCḡ PNēPsPiPs PePsPSC†PμPSC,CḡP°C†C-C— C,P° PrC-C—
PīCḡPμPīP°CḡP°C,Cf.

P'P»PsPeP°C,PsCḡPē PeP°P»CHC†C-C"PIPēC... PeP°PSP°P»C-PI. P" PμCḡPeC-

P°PSC,P°PiPsPSC-ClC,Pë PeP°P»CHCtC-Cñ (PSC-C,,PµPrPëPïC-PS, C-ClCñP°PrPëPïC-PS, P°PjP»PsPrPëPïC-PS, PIPµCñP°PïP°PjC-P» C,P° C,,PµP»PsPrPëPïC-PS) PjPµC,P°P±PsP»C-P·CfCñC,CHCfCñ C,,PµCñPjPµPSC,PsPj CYP3A4. PαP»CfPePsPSP°P·PsP» PïPsC,PµPSCtC-PNëPSPs PjPsP¶Pµ PïC-PrPIPëC%oCfPIP°C,Pë ClPëClC,PµPjPSCf PµPeClPïPsP·PëCtC-Cñ P±P»PsPeP°C,PsCñC-PI PeP°P»CHCtC-C”PIPëC... PeP°PSP°P»C-PI. P PµPePsPjPµPSPPrPsPIP°PSPëPNë CñPµC,PµP»CHPSPëPNë PjPsPSC-C,PsCñPëPSPi C%oPsPrPs CñPsP·PIPëC,PeCf PïPsP±C-C±PSPëC... CñPµP°PeCtC-PNë.

PiPµP»PµPePsPeClPëP±. PµCñPë PsPrPSPsC±P°ClPSPsPjCf P·P°ClC,PsClCfPIP°PSPSC- C,,P»CfPePsPSP°P·PsP»Cf (200 PjPi PSP° PrPsP±Cf) C,P° CtPµP»PµPePsPeClPëP±Cf (200 PjPi) C_{max} C,P° AUC CtPµP»PµPePsPeClPëP±Cf PïC-PrPIPëC%oCfPIP°P»PëClCñ PSP° 68 % C,P° 134 % PIC-PrPïPsPIC-PrPSPs. PµCñPë PsPrPSPsC±P°ClPSPsPjCf P·P°ClC,PsClCfPIP°PSPSC- CtPµP»PµPePsPeClPëP±Cf C,P° C,,P»CfPePsPSP°P·PsP»Cf PjPsP¶Pµ P±CfC,Pë PSPµPsP±C...C-PrPSPëPj P·PjPµPSC¶PµPSPSCñ PrPsP·Pë CtPµP»PµPePsPeClPëP±Cf PIPrPIC-C±C-.

PiPëPeP»PsC,,PsClC,,P°PjC-Pr. PhPrPSPsC±P°ClPSPµ P·P°ClC,PsClCfPIP°PSPSCñ CtPëPeP»PsC,,PsClC,,P°PjC-PrCf C,P° C,,P»CfPePsPSP°P·PsP»Cf PïCñPëP·PIPsPrPëC,CH PrPs PïC-PrPIPëC%oPµPSPSCñ CñC-PIPSCñ P±C-P»C-CñCfP±C-PSCf C,P° PeCñPµP°C,PëPSC-PSCf PI ClPëCñPsPIP°C,CtC- PeCñPsPIC-. PïC- PïCñPµPïP°CñP°C,Pë PjPsP¶PSP° P·P°ClC,PsClCfPsPICfPIP°C,Pë PsPrPSPsC±P°ClPSPs, P·PIP°P¶P°CñC±Pë PSP° CñPëP·PëPe PïC-PrPIPëC%oPµPSPSCñ PePsPSCtPµPSC,CñP°CtC-C— P±C-P»C-CñCfP±C-PSCf C,P° PeCñPµP°C,PëPSC-PSCf PI ClPëCñPsPIP°C,CtC- PeCñPsPIC-.

PαPµPSC,P°PSC-P». PµPsPIC-PrPsPjP»CñP»Pë PïCñPs PsPrPëPS P»PµC,P°P»CHPSPëPNë PIPëPïP°PrPsPe C-PSC,PsPeClPëPeP°CtC-C— C,,PµPSC,P°PSC-P»PsPj PIPSP°ClP»C-PrPsPe PjPsP¶P»PëPIPsC— PIP·P°C”PjPsPrC-C— C,,PµPSC,P°PSC-P»Cf C,P° C,,P»CfPePsPSP°P·PsP»Cf. P”Ps C,PsPiPs P¶, Cf PrPsClP»C-PrP¶PµPSPSC- P· CfC±P°ClC,Cñ P·PrPsCñPsPIPëC... PrPsP±CñPsPIPsP»CHCtC-PI P±CfP»Ps PïCñPsPrPµPjPsPSCfC,CñPsPIP°PSPs, C%oPs C,,P»CfPePsPSP°P·PsP» P·PSP°C±PSPs CfPïPsPIC-P»CHPSCñPIP°PI PµP»C-PjC-PSP°CtC-Cñ C,,PµPSC,P°PSC-P»Cf. PµC-PrPIPëC%oPµPSPSCñ PePsPSCtPµPSC,CñP°CtC-C— C,,PµPSC,P°PSC-P»Cf PjPsP¶Pµ PïCñPëP·PIPµClC,Pë PrPs PïCñPëPiPSC-C±PµPSPSCñ PrPëC...P°PSPSCñ, C,PsPjCf ClP»C-Pr CñPµC,PµP»CHPSPs PePsPSC,CñPsP»CñPIP°C,Pë ClC,P°PS PïP°CtC-C”PSC,P°. PhPsP¶Pµ P±CfC,Pë PSPµPsP±C...C-PrPSPsCñ PePsCñPµPeCtC-Cñ PrPsP·Pë C,,PµPSC,P°PSC-P»Cf.

PtPSPiC-P±C-C,PsCñPë P”PhP”-PµPsPh-CñPµPrCzPeC,P°P·Pë. PŸCfPjC-ClPSPµ P·P°ClC,PsClCfPIP°PSPSCñ C,,P»CfPePsPSP°P·PsP»Cf C,P° C-PSPiC-P±C-C,PsCñC-PI P”PhP”-PµoA-CñPµPrCfPeC,P°P·Pë, C%oPs PjPµC,P°P±PsP»C-P·CfCñC,CHCfCñ CYP3A4 (P°C,PsCñPIP°ClC,P°C,PëPS C,P° ClPëPjPIP°ClC,P°C,PëPS), P°P±Ps C-PSPiC-P±C-C,PsCñC-PI P”PhP”-PµoA-CñPµPrCfPeC,P°P·Pë, C%oPs PjPµC,P°P±PsP»C-P·CfCñC,CHCfCñ CYP2C9 (C,,P»CfPIP°ClC,P°C,PëPS), PïC-PrPIPëC%oCfC” CñPëP·PëPe CñPsP·PIPëC,PeCf PjC-PsPïP°C,C-C— C,P° CñP°P±PrPsPjC-PsP»C-P·Cf. Pj CñP°P·C- PSPµPsP±C...C-PrPSPsClC,C- PsPrPSPsC±P°ClPSPsPiPs P·P°ClC,PsClCfPIP°PSPSCñ CtPëC... PïCñPµPïP°CñP°C,C-PI ClP»C-Pr CñPµC,PµP»CHPSPs ClPïPsClC,PµCñC-PiP°C,Pë P·P° PïP°CtC-C”PSC,PsPj C%oPsPrPs PIPëPSPëPePSPµPSPSCñ ClPëPjPïC,PsPjC-PI PjC-PsPïP°C,C-C— C,P° CñP°P±PrPsPjC-PsP»C-P·Cf C- PïCñPsPIPsPrPëC,Pë PjPsPSC-C,PsCñPëPSPi CñC-PIPSCñ PeCñPµP°C,PëPSPeC-PSP°P·Pë. Pj PIPëPïP°PrPeCf P·PSP°C±PSPsPiPs PïC-PrPIPëC%oPµPSPSCñ CñC-PIPSCñ PeCñPµP°C,PëPSPeC-PSP°P·Pë, P° C,P°PePsP¶ PïCñPë PrC-P°PiPSPsClC,CfPIP°PSPSC- P°P±Ps PïC-PrPsP·CñC- PSP° PjC-PsPïP°C,C-Cñ/CñP°P±PrPsPjC-PsP»C-P· P·P°ClC,PsClCfPIP°PSPSCñ C-PSPiC-P±C-C,PsCñC-PI P”PhP”-PµoA-CñPµPrCfPeC,P°P·Pë ClP»C-Pr PïCñPëPïPëPSPëC,Pë.

P†P±CḡPëC,PëPSC-P±. PḡPsPjC-CḡPSC- C-PSPiC-P±C-C,PSCḡPë CYP3A4, C,P°PeC- CḡPe C,,P»C†PePsPSP°P·PsP», PiC-PrPIPëC%oC†CḡC,Ch PePsPSC†PḡPSC,CḡP°C†C-Cḡ C-P±CḡPëC,PëPSC-P±C† C† PiP»P°P·PjC- PeCḡPsPIC- C,P° PjPsPḡC†C,Ch PiC-PrPIPëC%oC†PIP°C,Pë CḡPëP·PëPe C,PsPeC†PëC†PSPsC†C,C-. P†PeC%oPs PSPḡPjPsPḡP»PëPIPs C†PSPëPePSC†C,Pë PePsPjP±C-PSP°C†C-C— PiCḡPḡPiP°CḡP°C,C-PI, P†PsC,CḡC-P±PSPs P·PjPḡPSCëPëC,Pë PrPsP·C† C-P±CḡPëC,PëPSC-P±C† PrPs 280 PjPi PsPrPëPS CḡP°P· PSP° PrPsP±C† (2 PeP°PiC†C†P»Pë) P· PjPḡC,PsCḡ PiCḡPsPrPsPIPḡPḡPSPSCḡ P·P°C†C,PsC†C†PIP°PSPSCḡ C-PSPiC-P±C-C,PSCḡC† C,P° P·P°P±PḡP·PiPḡC†PëC,Pë PiPsC†C,C-PNḡPSPëPNḡ PeP»C-PSC-C†PSPëPNḡ PjPsPSC-C,PsCḡPëPSPi.

P†PIP°PeP°C,,C,PsCḡ. PhPrPSPsC†P°C†PSPḡ P·P°C†C,PsC†C†PIP°PSPSCḡ C-PIP°PeP°C,,C,PsCḡC†, CḡPḡPiC†P»CḡC,PsCḡP° C,CḡP°PSC†PjPḡPjP±CḡP°PSPSPsC— PiCḡPsPIC-PrPSPsC†C,C- PiCḡPë PjC†PePsPIC-C†C†PëPrPsP·C- (CFTR), P·P±C-P»ChCëPëP»Ps PḡPeC†PiPsP·PëC†C-Cḡ C-PIP°PeP°C,,C,PsCḡC† PI 3 CḡP°P·Pë C,P° PḡPeC†PiPsP·PëC†C-Cḡ PiC-PrCḡPsPeC†PëPjPḡC,PëP»C-PIP°PeP°C,,C,PsCḡC† (Pḡ1) PI 1,9 CḡP°P·P°. PḡP°C†C-C”PSC,P°Pj, CḡPeC- PsPrPSPsC†P°C†PSPs PiCḡPëPNḡPjP°CḡC,Ch PiPsPjC-CḡPSC- C-PSPiC-P±C-C,PSCḡPë CYP3A, C,P°PeC- CḡPe C,,P»C†PePsPSP°P·PsP» C,P° PḡCḡPëC,CḡPsPjC-C†PëPS, CḡPḡPePsPjPḡPSPPrPsPIP°PSPs P·PjPḡPSCëPëC,Pë PrPsP·C† C-PIP°PeP°C,,C,PsCḡC† PrPs 150 PjPi PsPrPëPS CḡP°P· PSP° PrPsP±C†.

PhP»P°PiP°CḡPëP±. PḡPsPjC-CḡPSC- C-PSPiC-P±C-C,PSCḡPë CYP3A4, C,P°PeC- CḡPe C,,P»C†PePsPSP°P·PsP», P·P±C-P»ChCëC†CḡC,Ch PiP»P°P·PjPsPIC- PePsPSC†PḡPSC,CḡP°C†C-C— PsP»P°PiP°CḡPëP±C†; C—C... PsPrPSPsC†P°C†PSPḡ P·P°C†C,PsC†C†PIP°PSPSCḡ PSPḡ CḡPḡPePsPjPḡPSPPrC†C”C,ChC†Cḡ. P†PeC%oPs C,P°PePsC— PePsPjP±C-PSP°C†C-C— PSPḡ PjPsPḡPSP° C†PSPëPePSC†C,Pë, PiCḡPëPNḡPsPj PsP»P°PiP°CḡPëP±C† C†P»C-Pr PsP±PjPḡPḡC†PIP°C,Pë PrPsP·P°PjPë 200 PjPi PrPIC-C†C- PSP° PrPsP±C†.

P†PjC¿PSPsC†C¿PiCḡPḡC†PSCḡPë (PSP°PiCḡPëPeP»P°Pr C†PëPeP»PsC†PiPsCḡPëPS, PḡPIPḡCḡPsP»C-PjC¿C†, C†PëCḡPsP»C-PjC¿C† C- C,P°PeCḡPsP»C-PjC¿C†)

P†PëPeP»PsC†PiPsCḡPëPS. PḡP»C†PePsPSP°P·PsP» P·PSP°C†PSPs PiC-PrPIPëC%oC†C” PePsPSC†PḡPSC,CḡP°C†C-Cḡ C,P° AUC C†PëPeP»PsC†PiPsCḡPëPSC†. PḡCḡPë PsPrPSPsC†P°C†PSPsPjC† P·P°C†C,PsC†C†PIP°PSPSC- C,,P»C†PePsPSP°P·PsP»C† C† PrPsP·C- 200 PjPi/PrPsP±C† C,P° C†PëPeP»PsC†PiPsCḡPëPSC† C† PrPsP·C- 2,7 PjPi/PePi/PrPsP±C† C†PiPsC†C,PḡCḡ-PiP°P»PsC†Cḡ P·P±C-P»ChCëPḡPSPSCḡ AUC C†PëPeP»PsC†PiPsCḡPëPSC† PI 1,8 CḡP°P·P°. P†C- PiCḡPḡPiP°CḡP°C,Pë PjPsPḡPSP° P·P°C†C,PsC†PsPIC†PIP°C,Pë PsPrPSPsC†P°C†PSPs P·P° C†PjPsPIPë P·PjPḡPSCëPḡPSPSCḡ PrPsP·Pë C†PëPeP»PsC†PiPsCḡPëPSC† P·P°P»PḡPḡPSPs PIC-Pr PNḡPsPiPs PePsPSC†PḡPSC,CḡP°C†C-C—.

P·PIPḡCḡPsP»C-PjC¿C†. P†PsC†P° PrPsC†P»C-PrPḡPḡPSCḡ in vitro C,P° in vivo PSPḡ PiCḡPsIPsPrPëP»Pë, C,,P»C†PePsPSP°P·PsP» PjPsPḡPḡ PiC-PrPIPëC%oC†PIP°C,Pë PePsPSC†PḡPSC,CḡP°C†C-Cḡ PḡPIPḡCḡPsP»C-PjC†C†C† PI C†PëCḡPsPIP°C,C†C- PeCḡPsPIC- C†PḡCḡPḡP· PiCḡPëPiPSC-C†PḡPSPSCḡ CYP3Pḡ4.

PŸPëCḡPsP»C-PjC¿C†. PḡP»C†PePsPSP°P·PsP» PiC-PrPIPëC%oC†C” PePsPSC†PḡPSC,CḡP°C†C-Cḡ C†PëCḡPsP»C-PjC†C†C† C† PiP»P°P·PjC- PeCḡPsPIC-, C-PjPsPIC-CḡPSPs, CëP»CḡC...PsPj PiCḡPëPiPSC-C†PḡPSPSCḡ PjPḡC,P°P±PsP»C-P·PjC† C†PëCḡPsP»C-PjC†C†C† C,,PḡCḡPjPḡPSC,PsPj CYP3A4 C,P° P·PiP»C-PePsPiCḡPsC,PḡC—PSPsPj. P†C- PiCḡPḡPiP°CḡP°C,Pë PjPsPḡPSP° P·P°C†C,PsC†PsPIC†PIP°C,Pë PsPrPSPsC†P°C†PSPs P·P° C†PjPsPIPë PePsCḡPëPiC†PIP°PSPSCḡ PrPsP·Pë C†PëCḡPsP»C-PjC†C†C† P·P°P»PḡPḡPSPs PIC-Pr CḡC-PIPSCḡ PePsPSC†PḡPSC,CḡP°C†C-C— C,P° PḡC,,PḡPeC,C-PI PiCḡPḡPiP°CḡP°C,C†.

$P_j P^\circ P_e C_{\bar{H}} P_s P \gg C - P_j C \acute{z} C \acute{I}$. $P \propto P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg P_j P_s P \parallel P_\mu P \acute{I} C - P r P I P \ddot{e} C \% C r P I P^\circ C, P \ddot{e}$
 $P_e P_s P S C \dagger P_\mu P S C, C_{\bar{H}} P^\circ C \dagger C - C - C, P^\circ P_e C_{\bar{H}} P_s P \gg C - P_j C r C \acute{I} C r P I C \acute{I} P \ddot{e} C_{\bar{H}} P_s P I P^\circ C, C \dagger C - P_e C_{\bar{H}} P_s P I C -$
 $P r P_s 5 C_{\bar{H}} P^\circ P \cdot C - P I P \acute{I} C_{\bar{H}} P \ddot{e} P N_e P_s P_i P_s P_i P_\mu C_{\bar{H}} P_s C_{\bar{H}} P^\circ P \gg C H P S P_s P_j C r P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C -$
 $C \dagger P_\mu C_{\bar{H}} P_\mu P \cdot P \acute{I} C_{\bar{H}} P \ddot{e} P I P S C - C \dagger P_\mu P S P S C \parallel P_j P_\mu C, P^\circ P \pm P_s P \gg C - P \cdot P_j C r C, P^\circ P_e C_{\bar{H}} P_s P \gg C - P_j C r C \acute{I} C r$
 $C, P_\mu C_{\bar{H}} P_j P_\mu P S C, P_s P_j C Y P 3 A 4 C r P_e P \ddot{e} C \epsilon P_\mu C \dagger P S P \ddot{e} P_e C r. P_\mu C_{\bar{H}} P \ddot{e}$
 $P I P S C r C, C_{\bar{H}} C - C \epsilon P S C H P_s P I P_\mu P S P S P_s P_j C r P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C - C, P^\circ P_e C_{\bar{H}} P_s P \gg C - P_j C r C \acute{I} C r$
 $P S P_\mu C \acute{I} P_i P_s C \acute{I} C, P_\mu C_{\bar{H}} C - P_i P^\circ P \gg P_s C \acute{I} C \parallel P \cdot P S P^\circ C \dagger P S P \ddot{e} C \dots P \cdot P_j C - P S$
 $C, P^\circ C_{\bar{H}} P_j P^\circ P_e P_s P_e C - P S P_\mu C, P \ddot{e} P_e P \ddot{e}. P_\mu C - P r P I P \ddot{e} C \% P_\mu P S C - C_{\bar{H}} C - P I P S C -$
 $C, P^\circ P_e C_{\bar{H}} P_s P \gg C - P_j C r C \acute{I} C r P^\circ C \acute{I} P_s C \dagger C - C H C H C, C H C \acute{I} C \parallel P \cdot$
 $P S P_\mu C, C_{\bar{H}} P_s C, P_s P_e C \acute{I} P \ddot{e} C \dagger P S C - C \acute{I} C, C H. P'' P_s P \cdot C r C, P^\circ P_e C_{\bar{H}} P_s P \gg C - P_j C r C \acute{I} C r P r P \gg C \parallel$
 $P_i P_\mu C_{\bar{H}} P_s C_{\bar{H}} P^\circ P \gg C H P S P_s P_i P_s P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C \parallel C \acute{I} P \gg C - P r P \cdot P_j P_\mu P S C \epsilon C r P I P^\circ C, P \ddot{e}$
 $P \cdot P^\circ P \gg P_\mu P \parallel P S P_s P I C - P r P_e P_s P S C \dagger P_\mu P S C, C_{\bar{H}} P^\circ C \dagger C - C - C, P^\circ P_e C_{\bar{H}} P_s P \gg C - P_j C r C \acute{I} C r.$

$P \gg P_s P \cdot P^\circ C_{\bar{H}} C, P^\circ P S. P \propto P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg P \acute{I} C_{\bar{H}} P \ddot{e} P_i P S C - C \dagger C r C'' P_j P_\mu C, P^\circ P \pm P_s P \gg C - P \cdot P_j$
 $P \gg P_s P \cdot P^\circ C_{\bar{H}} C, P^\circ P S C r P r P_s P N_e P_s P_i P_s P^\circ P_e C, P \ddot{e} P I P S P_s P_i P_s P_j P_\mu C, P^\circ P \pm P_s P \gg C - C, C r$
 $(E - 31 \ 74), C \% P_s P \cdot C r P_j P_s P I P \gg C H C'' P \pm C - P \gg C H C \epsilon C r C \dagger P^\circ C \acute{I} C, P \ddot{e} P S C r P^\circ P S C, P^\circ P_i P_s P S C - P \cdot P_j C r$
 $P r P_s C_{\bar{H}} P_\mu C \dagger P_\mu P \acute{I} C, P_s C_{\bar{H}} C - P I P^\circ P S P_i C - P_s C, P_\mu P S P \cdot P \ddot{e} P S C r I I P \acute{I} C - P r C \dagger P^\circ C \acute{I}$
 $P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C \parallel P \gg P_s P \cdot P^\circ C_{\bar{H}} C, P^\circ P S C r. P P_\mu P_e P_s P_j P_\mu P S P r P_s P I P^\circ P S P_s$
 $P \cdot P r C - P N_e C \acute{I} P S C H P I P^\circ C, P \ddot{e} P_i P_s C \acute{I} C, C - P N_e P S P \ddot{e} P N_e P_j P_s P S C - C, P_s C_{\bar{H}} P \ddot{e} P S P_i$
 $P^\circ C_{\bar{H}} C, P_\mu C_{\bar{H}} C - P^\circ P \gg C H P S P_s P_i P_s C, P \ddot{e} C \acute{I} P_e C r C r P_i P^\circ C \dagger C - C'' P S C, C - P I.$

$P_h P_\mu C, P^\circ P r P_s P S. P \propto P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg P_j P_s P \parallel P_\mu P \acute{I} C - P r P I P \ddot{e} C \% C r P I P^\circ C, P \ddot{e}$
 $P_e P_s P S C \dagger P_\mu P S C, C_{\bar{H}} P^\circ C \dagger C - C H P_j P_\mu C, P^\circ P r P_s P S C r C r C \acute{I} P \ddot{e} C_{\bar{H}} P_s P I P^\circ C, C \dagger C - P_e C_{\bar{H}} P_s P I C -. P_\mu C_{\bar{H}} P \ddot{e}$
 $P_s P r P S P_s C \dagger P^\circ C \acute{I} P S P_s P_j C r P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C - P_j P_\mu C, P^\circ P r P_s P S C r C, P^\circ$
 $C, P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg C r P_j P_s P \parallel P_\mu P \pm C r C, P \ddot{e} P S P_\mu P_s P \pm C \dots C - P r P S P \ddot{e} P_j$
 $P_e P_s C_{\bar{H}} P \ddot{e} P_i C r P I P^\circ P S P S C \parallel P r P_s P \cdot P \ddot{e} P_j P_\mu C, P^\circ P r P_s P S C r.$

$P \acute{k} P_\mu C \acute{I} C, P_\mu C_{\bar{H}} P_s C - P r P S C - P \acute{I} C_{\bar{H}} P_s C, P \ddot{e} P \cdot P^\circ P_i P^\circ P \gg C H P S C - P \cdot P^\circ C \acute{I} P_s P \pm P \ddot{e} (P \acute{k} P_\mu P - P -). P_\mu C_{\bar{H}} P \ddot{e}$
 $P_s P r P S P_s C \dagger P^\circ C \acute{I} P S P_s P_j C r P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C - P \cdot C, P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg P_s P_j C_{\max} C, P^\circ$
 $A U C C, P \gg C r C_{\bar{H}} P \pm C - P \acute{I} C_{\bar{H}} P_s C, P_\mu P S C r P \acute{I} C - P r P I P \ddot{e} C \% C r P I P^\circ P \gg P \ddot{e} C \acute{I} C \parallel P S P^\circ 23 \% C, P^\circ 81 \%$
 $P I C - P r P_i P_s P I C - P r P S P_s P_i P_s C_{\bar{H}} C - P I P S C \parallel P S P_s P \cdot P_i P_s P_e P^\circ P \cdot P S P \ddot{e} P_e P^\circ P_j P \ddot{e} P \acute{I} C_{\bar{H}} P \ddot{e}$
 $P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C - C, C - P \gg C H P_e P \ddot{e} C, P \gg C r C_{\bar{H}} P \pm C - P \acute{I} C_{\bar{H}} P_s C, P_\mu P S C r.$
 $P_h P S P^\circ P \gg P_s P_i C - C \dagger P S P_s P_i C_{\bar{H}} P \ddot{e} P_s P r P S P_s C \dagger P^\circ C \acute{I} P S P_s P_j C r P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C -$
 $C, P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg C r P \cdot C_{\bar{H}} P^\circ C \dagger P_\mu P_j C - C \dagger P S P \ddot{e} P_j C - P \pm C r P \acute{I} C_{\bar{H}} P_s C, P_\mu P S P_s P_j (400 P_j P_i) C_{\max}$
 $C, P^\circ A U C C, P^\circ C_{\bar{H}} P_j P^\circ P_e P_s P \gg P_s P_i C - C \dagger P S P_s P^\circ P_e C, P \ddot{e} P I P S P_s P_i P_s C - P \cdot P_s P_j P_\mu C_{\bar{H}} C r S (-) -$
 $C - P \pm C r P \acute{I} C_{\bar{H}} P_s C, P_\mu P S C r P \acute{I} C - P r P I P \ddot{e} C \% C r P I P^\circ P \gg P \ddot{e} C \acute{I} C \parallel P S P^\circ 15 \% C, P^\circ 82 \%$
 $P I C - P r P_i P_s P I C - P r P S P_s P_i P_s C_{\bar{H}} C - P I P S C \parallel P S P_s P \cdot C, P^\circ P_e P \ddot{e} P_j P \ddot{e} P_i P_s P_e P^\circ P \cdot P S P \ddot{e} P_e P^\circ P_j P \ddot{e} P \acute{I} C_{\bar{H}} P \ddot{e}$
 $P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C - C, C - P \gg C H P_e P \ddot{e} C_{\bar{H}} P^\circ C \dagger P_\mu P_j C - C \dagger P S P_s P_i P_s C - P \pm C r P \acute{I} C_{\bar{H}} P_s C, P_\mu P S C r.$

$P \acute{I} P_s C \dagger P^\circ C \acute{I} P_i P_\mu C \dagger C - P^\circ P \gg C H P S P \ddot{e} C \dots P r P_s C \acute{I} P \gg C - P r P \parallel P_\mu P S C H P S P_\mu P \acute{I} C_{\bar{H}} P_s P I P_s P r P \ddot{e} P \gg P \ddot{e},$
 $C, P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg P_i P_s C, P_\mu P S C \dagger C - P N_e P S P_s P \cdot P r P^\circ C, P S P \ddot{e} P N_e P \acute{I} C - P r P I P \ddot{e} C \% C r P I P^\circ C, P \ddot{e}$
 $C \acute{I} P \ddot{e} C \acute{I} C, P_\mu P_j P S C r P_\mu P_e C \acute{I} P_i P_s P \cdot P \ddot{e} C \dagger C - C H C - P S C \epsilon P \ddot{e} C \dots P \acute{k} P_\mu P - P -, C \% P_s$
 $P_j P_\mu C, P^\circ P \pm P_s P \gg C - P \cdot C r C H C, C H C \acute{I} C \parallel C Y P 2 C 9 (P S P^\circ P \acute{I} C_{\bar{H}} P \ddot{e} P_e P \gg P^\circ P r P S P^\circ P \acute{I} C_{\bar{H}} P_s P_e C \acute{I} P_\mu P S C r,$
 $P \gg P_s C_{\bar{H}} P S P_s P_e C \acute{I} P \ddot{e} P_e P^\circ P_j C r, P_j P_\mu P \gg P_s P_e C \acute{I} P \ddot{e} P_e P^\circ P_j C r, P r P \ddot{e} P_e P \gg P_s C, P_\mu P S P^\circ P_e C r).$
 $P P_\mu P_e P_s P_j P_\mu P S P r P_s P I P^\circ P S P_s P_i P_\mu C_{\bar{H}} C - P_s P r P \ddot{e} C \dagger P S P_s P \cdot P r C - P N_e C \acute{I} P S C H P I P^\circ C, P \ddot{e}$
 $P_j P_s P S C - C, P_s C_{\bar{H}} P \ddot{e} P S P_i P_i P_s P \pm C - C \dagger P S P \ddot{e} C \dots C_{\bar{H}} P_\mu P^\circ P_e C \dagger C - P N_e C, P^\circ C, P_s P_e C \acute{I} P \ddot{e} C \dagger P S P \ddot{e} C \dots$
 $P \acute{I} C_{\bar{H}} P_s C \parallel P I C - P I, P_i P_s P \acute{I} C \parallel P \cdot P^\circ P S P \ddot{e} C \dots C - P \cdot P \acute{k} P_\mu P - P -. P_h P_s P \parallel P_\mu P \cdot P S P^\circ P r P_s P \pm P \ddot{e} C, P \ddot{e} C \acute{I} C \parallel$
 $P_e P_s C_{\bar{H}} P \ddot{e} P_i C r P I P^\circ P S P S C \parallel P r P_s P \cdot P \ddot{e} P \acute{k} P_\mu P - P -.$

$P \propto P_\mu P S C - C, P_s C - P S. P \propto P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg P \acute{I} C_{\bar{H}} P \ddot{e} P_i P S C - C \dagger C r C'' P_j P_\mu C, P^\circ P \pm P_s P \gg C - P \cdot P_j$
 $C, P_\mu P S C - C, P_s C - P S C r P I P_i P_\mu C \dagger C - P S C \dagger C -. P_h P r P S P_s C \dagger P^\circ C \acute{I} P S P_\mu P \pm P^\circ P_i P^\circ C, P_s C_{\bar{H}} P^\circ P \cdot P_s P I P_\mu$
 $P \cdot P^\circ C \acute{I} C, P_s C \acute{I} C r P I P^\circ P S P S C \parallel 200 P_j P_i C, P \gg C r P_e P_s P S P^\circ P \cdot P_s P \gg C r C, P^\circ 250 P_j P_i$

C,,PμPSC-C,PSC—PSCr PIPSCrC,CḡC-C€PSCḡPsPIPμPSPSPs PīCḡPēP·PIPsPrPēC,Cḡ PrPs PīC-PrPIPēC%PμPSPSCl AUC₂₄ C,,PμPSC-C,PSC—PSCr PSP° 75 % C,P° PŸ_{min} PSP° 128 %. PμCḡPē PsPrPSPsC†P°CḡPSPsPjCḡ P·P°CḡC,PSCḡCḡPIP°PSPSC- C†PēC... P»C-PeP°CḡCḡCḡPePēC... P·P°CḡPsP±C-PI CḡP»C-Pr PīCḡPsPIPsPrPēC,Pē PjPsPSC-C,PSCḡPēPSPi PePsPSC†PμPSC,CḡP°C†C-C— C,,PμPSC-C,PSC—PSCr Cḡ CḡPēCḡPsPIP°C,C†C- PeCḡPsPIC- PrP»Cḡ CḡPSPēPePSPμPSPSCl CḡPsP·PIPēC,PeCḡ C,PSPeCḡPēC†PSPsC— PrC-C— C,,PμPSC-C,PSC—PSCr.

PμCḡPμPrPSC-P·PsPS. PμPsPIC-PrPsPjP»CḡP»Pē PīCḡPs PIPēPīP°PrPsPe, PePsP»Pē Cḡ PīP°C†C-C" PSC,P° PīC-CḡP»Cḡ C,CḡP°PSCḡPīP»P°PSC,P°C†C-C— PīPμC†C-PSPePē PSP° C,P»C- P·P°CḡC,PSCḡCḡPIP°PSPSCl PīCḡPμPrPSC-P·PsPSCr CḡPsP·PIPēPSCḡP»P°CḡCḡ PīPsCḡC,CḡP° PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ PePsCḡPē PSP°PrPSPēCḡPePsPIPēC... P·P°P»PsP·, C%Ps PIPēPSPēPeP»P° PīC-CḡP»Cḡ PīCḡPēPīPēPSPμPSPSCl C,CḡPēPjC-CḡCḡC†PSPsPiPs PeCḡCḡCḡCḡ C,PμCḡP°PīC-C— C,,P»CḡPePsPSP°P·PsP»PsPj. PμCḡPēPīPēPSPμPSPSCl P·P°CḡC,PSCḡCḡPIP°PSPSCl C,,P»CḡPePsPSP°P·PsP»Cḡ, PNePjPsPIC-CḡPSPs, CḡPīCḡPēC†PēPSPēP»Ps PīPsCḡPēP»PμPSPSCl P°PeC,PēPIPSsCḡC,C- CYP3A4, C%Ps PīCḡPēP·PIPμP»Ps PrPs PīCḡPēCḡPePsCḡPμPSPSCl PjPμC,P°P±PsP»C-P·PjCḡ PīCḡPμPrPSC-P·PsPSCr. PŸP»C-Pr CḡPμC,PμP»CḡPSPs CḡC,PμPḡPēC,Pē P·P° PīP°C†C-C" PSC,P°PjPē, CḡPeC- PīCḡPsC,CḡPiPsPj C,CḡPēPIP°P»PsPiPs C†P°CḡCḡ P·P°CḡC,PSCḡPsPICḡCḡC,Cḡ PsPrPSPsC†P°CḡPSPs C,,P»CḡPePsPSP°P·PsP»C,P° PīCḡPμPrPSC-P·PsPS, P· PjPμC,PSCḡ PīPsPīPμCḡPμPrPḡPμPSPSCl CḡPsP·PIPēC,PeCḡ PSPμPrPsCḡC,P°C,PSPsCḡC,C- PePsCḡPē PSP°PrPSPēCḡPePsPIPēC... P·P°P»PsP· PīC-CḡP»Cḡ PīCḡPēPīPēPSPμPSPSCl P·P°CḡC,PSCḡCḡPIP°PSPSCl C,,P»CḡPePsPSP°P·PsP»Cḡ.

P PēC,,P°P±CḡC,PēPS. PαP»CḡPePsPSP°P·PsP» PīC-PrPIPēC%CḡC" PePsPSC†PμPSC,CḡP°C†C-Cḡ CḡPēC,,P°P±CḡC,PēPSCr PI CḡPēCḡPsPIP°C,C†C- PeCḡPsPIC-, C%Ps PīCḡPēP·PIPsPrPēC,Cḡ PrPs P·P±C-P»CḡC€PμPSPSCl AUPŸ CḡPēC,,P°P±CḡC,PēPSCr PrPs 80 %. PμCḡPē PsPrPSPsC†P°CḡPSPsPjCḡ P·P°CḡC,PSCḡCḡPIP°PSPSC- C,,P»CḡPePsPSP°P·PsP»Cḡ C,P° CḡPēC,,P°P±CḡC,PēPSCr PīPsPIC-PrPsPjP»CḡP»Pē PīCḡPs PIPēPīP°PrPePē CḡPsP·PIPēC,PeCḡ CḡPIPμC—C,Cḡ. PμCḡPē P·P°CḡC,PSCḡCḡPIP°PSPSC- C,P°PePsC— PePsPjP±C-PSP°C†C-C— P»C-PeP°CḡCḡCḡPePēC... P·P°CḡPsP±C-PI CḡP»C-Pr P±CḡP°C,Pē PrPs CḡPIP°PīPē CḡPēPjPīC,PSPjPē C,PSPeCḡPēC†PSPsC— PrC-C— CḡPēC,,P°P±CḡC,PēPSCr.

PŸP°PePIC-PSP°PIC-Cḡ. PαP»CḡPePsPSP°P·PsP» PīC-PrPIPēC%CḡC" AUC C,P° C_{max} CḡP°PePIC-PSP°PIC-CḡCḡ PīCḡPēP±P»PēP·PSPs PSP° 50 % C,P° 55 % PIC-PrPīPsPIC-PrPSPs C†PμCḡPμP· PīCḡPēPīPSC-C†PμPSPSCl PjPμC,P°P±PsP»C-P·PjCḡ CḡP°PePIC-PSP°PIC-CḡCḡ Cḡ PīPμC†C-PSC†C- C,,PμCḡPjPμPSC,PSPj CYP3A4 C,P° C†PμCḡPμP· C-PSPiC-P±CḡPIP°PSPSCl P-PiP»C-PePsPīCḡPsC,PμC—PSCr. P·P·P°C" PjPsPrC-C— PjC-Pḡ C,,P»CḡPePsPSP°P·PsP»PsPj C,P° CḡP°PePIC-PSP°PIC-CḡPsPj/CḡPēC,PSP°PIC-CḡPsPj PSPμ PrPsCḡP»C-PrPḡCḡPIP°P»Pē, C,PSPjCḡ PIPsPSPē PjPsPḡCḡC,Cḡ P±CḡC,Pē P±C-P»CḡC€ PIPēCḡP°PḡPμPSPēPjPē. PḡPsPḡPμ PIPēPSPēPePSCrC,Pē PSPμPsP±C...C-PrPSC-CḡC,Cḡ PePsCḡPēPīCḡPIP°PSPSCl PrPsP·Pē CḡP°PePIC-PSP°PIC-CḡCḡ.

PμPsC...C-PrPSC- CḡCḡP»CḡC,,PsPSC-P»CḡPμC†PsPIPēPSPē. PμCḡPē PsPrPSPsC†P°CḡPSPsPjCḡ P·P°CḡC,PSCḡCḡPIP°PSPSC- C,,P»CḡPePsPSP°P·PsP»Cḡ PīCḡPsP»PsPSPiCḡC"C,CḡCḡCḡ PīPμCḡC-PsPr PSP°PīC-PIPIPēPIPμPrPμPSPSCl PīPμCḡPsCḡP°P»CḡPSPēC... PīPsC...C-PrPSPēC... CḡCḡP»CḡC,,PsPSC-P»CḡPμC†PsPIPēPSPē (C...P»PsCḡPīCḡPsPīP°PjC-PrCḡ, PīP»C-P±PμPSPeP»P°PjC-PrCḡ, PīP»C-PīC-P·PēPrCḡ C,P° C,PSP»P±CḡC,P°PjC-PrCḡ) PīCḡPē C—C... P·P°CḡC,PSCḡCḡPIP°PSPSC- P·PrPsCḡPsPIPēPj PrPsP±CḡPsPIP»CḡC†CḡPj. P PμPePsPjPμPSPrCḡC"C,CḡCḡCḡ PīCḡPsPIPsPrPēC,Pē C†P°CḡC,PēPNe PePsPSC,CḡPsP»Cḡ CḡC-PIPScl PīP»CḡPePsP·Pē PI PeCḡPsPIC- C,P° PIC-PrPīPsPIC-PrPSPēPj C†PēPSPsPj P·PSPēPḡCḡPIP°C,Pē PrPsP·Cḡ PīPsC...C-PrPSPēC... CḡCḡP»CḡC,,PsPSC-P»CḡPμC†PsPIPēPSPē

ΠiCηPē PsPrPSPsC±P°CΓPSPsPjCř P·P°CΓC,PsCΓCřPIP°PSPSC- P·C,,P»CřPePsPSP°P·PsP»PsPj.

PŷPμPsC,,C-P»C-PS. PJ ΠiP»P°C†PμP±Ps-PePsPSC,CηPsP»CHPsPIP°PSPsPjCř
PrPsCΓP»C-PrP¶PμPSPSC- P·PIPēPIC±PμPSPSCΠ PIP·P°C”PjPsPrC-C— C,,P»CřPePsPSP°P·PsP»Cř
C,P° C,PμPsC,,C-P»C-PSCř P±CřP»Ps PIPēCΠIPIP»PμPSPs, C°Ps P·P°CΓC,PsCΓCřPIP°PSPSCΠ
C,,P»CřPePsPSP°P·PsP»Cř ΠiPs 200 PjPi ΠiCηPsC,CΠPiPsPj 14 PrPSC-PI ΠiCηPēP·PIPsPrPēP»Ps
PrPs P·PSPēP¶PμPSPSCΠ CΓPμCηPμPrPSCHsPiPs PeP»C-CηPμPSCΓCř C,PμPsC,,C-P»C-PSCř Cř
ΠiP»P°P·PjC- PeCηPsPIC- PSP° 18 %. P—P° ΠiP°C†C-C”PSC,P°PjPē, CΠPeC-
P·P°CΓC,PsCΓPsPICřCηC,CH C,PμPsC,,C-P»C-PS Cř PIPēCΓPsPePēC... PrPsP·P°C... P°P±Ps
CΠPeC- PjP°CηC,CH ΠiC-PrPIPēC°PμPSPēPNē CηPēP·PēPe CηPsP·PIPēC,PeCř
C,PsPeCΓPēC±PSPēC... ΠiCηPsCΠPIC-PI C,PμPsC,,C-P»C-PSCř P·C-PSCēPēC... ΠiCηPēC±PēPS,
CΓP»C-Pr PICΓC,P°PSPsPIPēC,Pē PSP°PiP»CΠPr C°PsPrPs PIPēCΠIPIP»PμPSPSCΠ PsP·PSP°Pe
CηPsP·PIPēC,PeCř C,PsPeCΓPēC±PSPsC— PrC-C— C,PμPsC,,C-P»C-PSCř. PŷPμCηP°PiC-Cη
CΓP»C-Pr P·PjC-PSPēC,Pē ΠiCηPē ΠiPsCΠPIC- PsP·PSP°Pe C,PsPeCΓPēC±PSPsCΓC,C-.

PŷPsC,,P°C†PēC,PēPSC-P±. P’ΠiP»PēPI C,PsC,,P°C†PēC,PēPSC-P±Cř P·CηPsCΓC,P°C” ΠiCηPē
PsPrPSPsC±P°CΓPSPsPjCř P·P°CΓC,PsCΓCřPIP°PSPSC- P·P»C-PeP°CηCΓCHPePēPjPē
P·P°CΓPsP±P°PjPē, CΠPeC- ΠiCηPēP·PIPsPrCΠC,CH PrPs ΠiPsPjC-CηPSPsPiPs
C-PSPiC-P±CřPIP°PSPSCΠ CYP3A4 C,P° ΠiPsC,CřP¶PSPsPiPs C-PSPiC-P±CřPIP°PSPSCΠ
CYP2C19 (PSP°ΠiCηPēPeP»P°Pr C,,P»CřPePsPSP°P·PsP»). PŷPsPjCř CηPμPePsPjPμPSPrPsPIP°PSPs
P·PjPμPSCēPēC,Pē PrPsP·Cř C,PsC,,P°C†PēC,PēPSC-P±Cř PrPs 5 PjPi PsPrPēPS CηP°P·PSP°
PrPsP±Cř PI PePsPjP±C-PSP°C†C-CΠC... C-P·C†PēPjPē ΠiCηPμPiP°CηP°C,P°PjPē.

PŷPsP»PIP°PiC,P°PS. P·PeCΓPiPsP·PēC†C-CΠ C,PsP»PIP°PiC,P°PSCř P·PSP°C±PSPs
P·P±C-P»CHCēCřC”C,CHCΓCΠ (PSP° 200 % AUC; PSP° 80 % C_{max}) ΠiCηPē
PsPrPSPsC±P°CΓPSPsPjCř P·P°CΓC,PsCΓCřPIP°PSPSC- C,PsP»PIP°PiC,P°PSCř,
CΓCřP±CΓC,CηP°C,Cř CYP3A4, P·C,,P»CřPePsPSP°P·PsP»PsPj, ΠiPsPjC-CηPSPēPj
C-PSPiC-P±C-C,PsCηPsPj CYP3A4, P·CηPsCΓC,P°C” CηPēP·PēPe PIPēPSPēPePSPμPSPSCΠ
ΠiPsP±C-C±PSPēC... CηPμP°PeC†C-PNē, PsCΓPsP±P»PēIPs P·PSP°C±PSPsPiPs PrC-CřCηPμP·Cř,
P·PSPμPIPsPrPSPμPSPSCΠ C- ΠiPsCΓC,CηPsC— PSPēCηPePsPIPsC—
PSPμPrPsCΓC,P°C,PSPsCΓC,C-. PJ CηP°P·C- PsPrPSPsC±P°CΓPSPsPiPs
P·P°CΓC,PsCΓCřPIP°PSPSCΠ PrPsP·Cř C,PsP»PIP°PiC,P°PSCř CΓP»C-Pr P·PjPμPSCēPēC,Pē
PIC-PrΠiPsPIC-PrPSPs PrPs C-PSCΓC,CηCřPeC†C-PNē C°PsPrPs PNēPsPiPs
ΠiCηPēP·PSP°C±PμPSPSCΠ, P° ΠiP°C†C-C”PSC,P° CΓP»C-Pr C±P°CΓC,Ps
PePsPSC,CηPsP»CHPIP°C,Pē CΓC,PsCΓPsIPSPs P±CřPrCH-CΠPePēC... ΠiPsP±C-C±PSPēC...
CηPμP°PeC†C-PNē, ΠiPsPI·CΠP·P°PSPēC... C-P·P·P°CΓC,PsCΓCřPIP°PSPSCΠPj
C,PsP»PIP°PiC,P°PSCř.

PηP»PeP°P»PsC—PrPē P±P°CηPIC-PSPeCž. ΠiPsC±P° PIC-PrΠiPsPIC-PrPSPēC...
PrPsCΓP»C-PrP¶PμPSCH PSPμ ΠiCηPsPIPsPrPēP»Pē, C,,P»CřPePsPSP°P·PsP», C-PjPsPIC-CηPSPs,
C±PμCηPμP·C-PSPiC-P±CřPIP°PSPSCΠ CYP3A4, PjPsP¶Pμ CΓΠiCηPēC±PēPSCΠC,Pē
ΠiC-PrPIPēC°PμPSPSCΠ PePsPSC†PμPSC,CηP°C†C-C— P°P»PeP°P»PsC—PrC-PI
P±P°CηPIC-PSPeCř Cř ΠiP»P°P·PjC- PeCηPsPIC- (PSP°ΠiCηPēPeP»P°Pr
PIC-PSPeCηPēCΓC,PēPSCř C,P° PIC-PSP±P»P°CΓC,PēPSCř), C°Ps ΠiCηPēP·PIPsPrPēC,CH PrPs
CηPsP·PIPēC,PeCř PSPμPNēCηPsC,PsPeCΓPēC±PSPēC... PμC,,PμPeC,C-PI.

P’C-C,P°PjC-PS Pη. PμPsPIC-PrPsPjP»CΠP»Pē, C°Ps Cř ΠiP°C†C-C”PSC,P°, CΠPePēPNē
PsPrPSPsC±P°CΓPSPs P·P°CΓC,PsCΓPsPICřPIP°PI C,CηP°PSCΓCηPμC,PēPSPsC”PICř
PePēCΓP»PsC,Cř (PePēCΓP»PsC,PSP° C,,PsCηPjP° PIC-C,P°PjC-PSCř Pη) C,P°
C,,P»CřPePsPSP°P·PsP», CΓΠiPsCΓC,PμCηC-ΠiP°P»PēCΓCΠ ΠiPsP±C-C±PSC- CηPμP°PeC†C-C— P·
P±PsPeCř P|KPY Cř C,,PsCηPjC- ΠiCΓPμPIPrPsC,CřPjPsCηCř ΠiPsP»PsIPSPsPiPs PjPsP·PeCř;
PrP°PSPēPNē PμC,,PμPeC, P·PSPēPe ΠiC-CΓP»CΠ PIC-PrPjC-PSPē C,,P»CřPePsPSP°P·PsP»Cř. P|C-

P»C-PeP°CĤCÍČĤPeC- P·P°CÍČPsP±Pë PjPsP¶PSP° P·P°CÍČ,PsCÍČPsPICrPIP°C,Pë
PsPrPSPSc±P°CÍČPSPs, P°P»Pµ CÍČP»C-Pr PīP°Pj'CIČC,P°C,Pë PīCĤPs CĤPëP·PëPe
PIPëPSPëPePSPµPSPSCĬ PīPsP±C-C±PSPëC... CĤPµP°PeC†C-PNë P· P±PsPeCÍ PīPíPŸ.

P'PsCĤPëPePsPSP°P·PsP» (C-PSPiC-P±C-C,PsCĤ CYP2PŸ9, CYP2PŸ19 C,P° CYP3Pĥ4).
PhPrPSPSc±P°CÍČPSPµ P·P°CÍČ,PsCÍČrPIP°PSPSCĬ PIPsCĤPëPePsPSP°P·PsP»CÍ
PīPµCĤPsCĤP°P»CHBPSPs (PīPs 400 PjPi PePsP¶PSC- 12 PīPsPrPëPS PīCĤPsC,CĬPīPsPj 1 PrPSCĬ,
PīPsC,C-Pj PīPs 200 PjPi PePsP¶PSC- 12 PīPsPrPëPS PīCĤPsC,CĬPīPsPj 2,5 PrPSC-PI) C,P°
C„P»CÍČPePsPSP°P·PsP»CÍ PīPµCĤPsCĤP°P»CHBPSPs (400 PjPi CÍ PīPµCĤCëPëPNë PrPµPSCĤ,
PīPsC,C-Pj PīPs 200 PjPi PePsP¶PSC- 24 PīPsPrPëPSPë PīCĤPsC,CĬPīPsPj 4 PrPSC-PI) 8
P·PrPsCĤPsPIPëPj PrPsP±CĤPsPIPsP»CHC†CĬPj C±PsP»PsPIC-C±PsC— CÍČ,P°C,C-
PīCĤPëP·PIPµP»Ps PrPs PīC-PrPIPëC%oPµPSPSCĬ PŸ_{max} C,P° AUCτ PIPsCĤPëPePsPSP°P·PsP»CÍ PI
CÍČPµCĤPµPrPSCĤPsPjCÍ PrPs 57 % (90 % P"Pt: 20 %, 107 %) C,P° 79 % (90 % P"Pt: 40 %, 128 %)
PIC-PrPīPsPIC-PrPSPs. PíPµPIC-PrPsPjPs, C±Pë PīCĤPëP·PIPsPrPëC,CH P·PSPëP¶PµPSPSCĬ
PrPsP·Pë C,P°/P°P±Ps C±P°CÍČ,PsC,Pë P·P°CÍČ,PsCÍČrPIP°PSPSCĬ PIPsCĤPëPePsPSP°P·PsP»CÍ
P°P±Ps C„P»CÍČPePsPSP°P·PsP»CÍ PrPs CÍČÍČrPSPµPSPSCĬ C,P°PePsPiPs PµC„PµPeC,CÍ.
PµCĤPë P·P°CÍČ,PsCÍČrPIP°PSPSC- PIPsCĤPëPePsPSP°P·PsP»CÍ PīC-CÍČP»CĬ
C„P»CÍČPePsPSP°P·PsP»CÍ CÍČP»C-Pr PīCĤPsPIPsPrPëC,Pë CÍČPīPsCÍČ,PµCĤPµP¶PµPSPSCĬ
C%oPsPrPs CĤPsP·PIPëC,PeCÍ PīPsP±C-C±PSPëC... PµC„PµPeC,C-PI,
P°CÍČPsC†C-PNëPsPIP°PSPëC... C-P· PIPsCĤPëPePsPSP°P·PsP»PsPj.

P—PëPrPsPICíPrPëPS. P»P»CÍČPePsPSP°P·PsP» PīC-PrPIPëC%oCÍČ" PŸ_{max} C,P° AUC
P·PëPrPsPICrPrPëPSCÍ PSP° 84 % C,P° 74 % PIC-PrPīPsPIC-PrPSPs, C%oPs P·CÍČPjPsPIP»PµPSPs
P·PSPëP¶PµPSPSCĬPj PeP»C-CĤPµPSCÍČr P·PëPrPsPICrPrPëPSCÍ PīCĤPëP±P»PëP·PSPs PSP°
45 % PīCĤPë PNëPsPiPs PīPµCĤPsCĤP°P»CHBPSPsPjCÍ P·P°CÍČ,PsCÍČrPIP°PSPSC-.
PµPµCĤC-PsPr PSP°PīC-PIPIPëPIPµPrPµPSPSCĬ P·PëPrPsPICrPrPëPSCÍ P±CÍPI C,P°PePsP¶
PīPsPrPsPIP¶PµPSPëPNë PīCĤPëP±P»PëP·PSPs PSP° 128 % PīC-CÍČP»CĬ
P·P°CÍČ,PsCÍČrPIP°PSPSCĬ PePsPjP±C-PSP°C†C-C— C„P»CÍČPePsPSP°P·PsP»CÍ C,P°
P·PëPrPsPICrPrPëPSCÍ. P—P° PīP°C†C-C"PSC,P°PjPë, CĬPeC- P·P°CÍČ,PsCÍČPsPICrCĤC,CH
C,P°PeCÍ PePsPjP±C-PSP°C†C-CĤ P»C-PeP°CĤCÍČĤPePëC... P·P°CÍČPsP±C-PI, CÍČP»C-Pr
CÍČPīPsCÍČ,PµCĤC-PiP°C,Pë C%oPsPrPs CĤPsP·PIPëC,PeCÍ PīPsP±C-C±PSPëC...
CĤPµP°PeC†C-PNë, PīPsPīCĬP·P°PSPëC... C-P· P·P°CÍČ,PsCÍČrPIP°PSPSCĬPj
P·PëPrPsPICrPrPëPSCÍ. P»PsP¶PSP° CĤPsP·PiP»CĬPSCÍČ,Pë PrPsC†C-P»CHBPSC-CÍČ,CH
P·PSPëP¶PµPSPSCĬ PrPsP·Pë P·PëPrPsPICrPrPëPSCÍ.

PĥP·PëC,CĤPsPjC-C†PëPS. Pj C...PsPrC- PIC-PrPeCĤPëC,PsPiPs CĤP°PSPPrPsPjC-P·PsPIP°PSPsPiPs
C,CĤPëCÍČ,PsCĤPsPSPSCĤPsPiPs PīPµCĤPµC...CĤPµCÍČPSPsPiPs PrPsCÍČP»C-PrP¶PµPSPSCĬ, PI
CĬPePsPjCÍ PIP·CĬP»Pë CÍČ±P°CÍČ,CH 18 P·PrPsCĤPsPIPëC... PrPsP±CĤPsPIPsP»CHC†C-PI,
PsC†C-PSCĤPIP°P»Pë PIPiP»PëPI P°P·PëC,CĤPsPjC-C†PëPSCÍ C,P° C„P»CÍČPePsPSP°P·PsP»CÍ
PSP° C„P°CĤPjP°PePsPeC-PSPµC,PëPeCÍ PsPrPëPS PsPrPSPsPiPs PīCĤPë C—C...
PsPrPSPSc±P°CÍČPSPsPjCÍ PīPµCĤPsCĤP°P»CHBPSPsPjCÍ CĤP°P·PsPIPsPjCÍ
P·P°CÍČ,PsCÍČrPIP°PSPSC- CÍ PrPsP·P°C... 1200 PjPi C,P° 800 PjPi PIC-PrPīPsPIC-PrPSPs.
P-PsPrPSPëC... P·PSP°C†CÍČ%oPëC... C„P°CĤPjP°PePsPeC-PSPµC,PëC±PSPëC...
PIP·P°C" PjPsPrC-PNë PIPëCĬPIP»PµPSPs PSPµ P±CÍP»Ps.

PµPµCĤPsCĤP°P»CHBPSC- PePsPSC,CĤP°C†PµPīC,PëPIPë. P— PrP°PSPëC... PrPIPSc...
C„P°CĤPjP°PePsPeC-PSPµC,PëC±PSPëC... PrPsCÍČP»C-PrP¶PµPSCĤ
P±P°PiP°C,PsCĤP°P·PsPIPsPiPs P·P°CÍČ,PsCÍČrPIP°PSPSCĬ C„P»CÍČPePsPSP°P·PsP»CÍ C,P°
PePsPjP±C-PSPsPIP°PSPsPiPs PīPµCĤPsCĤP°P»CHBPSPsPiPs PePsPSC,CĤP°C†PµPīC,PëPIP°
PIC-PrPsPjPs, C%oPs PīCĤPë P·P°CÍČ,PsCÍČrPIP°PSPSC- C„P»CÍČPePsPSP°P·PsP»CÍ CÍ PrPsP·C-
50 PjPi PIPiP»PëPICÍ PSP° CĤC-PIPµPSCĤ PīPsCĤPjPsPSC-PI PSPµ P±CÍP»Ps
PIPëCĬPIP»PµPSPs, C,PsPrC- CĬPe PīCĤPë P·P°CÍČ,PsCÍČrPIP°PSPSC-

C,,P»CfPePsPSP°P·PsP»Cf Cf PrPsP·C- 200 PjPi PSP° PrPsP±Cf CfPİPsCfC,PµCfC-PiP°P»PsCfCf P·P±C-P»CHC€PµPSPSCf PµUPŸ PµC,PëPSC-P»PµCfC,CfP°PrC-PsP»Cf PSP° 40 % C,P° P»PµPIPsPSPsCfPiPµCfC,CfPµP»Cf bŸ" PSP° 24 %. PİPµ CfPIC-PrCfPëC,CH PİCfPs C,Pµ, C°Ps P±P°PiP°C,PsCfP°P·PsPIPµ P·P°CfC,PsCfCfPIP°PSPSCf C,,P»CfPePsPSP°P·PsP»Cf Cf P·P°P·PSP°CfPµPSPëC... PrPsP·P°C... PSP°PICfCfPr CfPë PjPsP¶Pµ PİPiP»PëPIP°C,Pë PSP° PµC,,PµPeC,PëPIPSC-CfC,CH PePsPjP±C-PSPsPIP°PSPsPiPs PİPµCfPsCfP°P»CHPSPsPiPs PePsPSC,CfP°CfPµPiC,PëPIP°.

P>C-PeP°CfC- PİPsPIPëPSPSC- P±CfP°C,Pë PrPs CfPIP°PiPë, C°Ps PrPsCfP»C-PrP¶PµPSPSCf PIP·P°C"PjPsPrC-C— P·C-PSC€PëPjPë P»C-PeP°CfCfCHPePëPjPë P·P°CfPsP±P°PjPë PSPµ PİCfPsPIPsPrPëP»Pë, P°P»Pµ C,P°PeC- PIP·P°C"PjPsPrC-C— PjPsP¶CfC,CH PIPëPSPëPeP°C,Pë.

PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSCf.

P" PµCfPjP°C,PsC,,C-C,C-Cf. P'C-PrPİPsPIC-PrPSPs PrPs CfPµP·CfP»CHC,P°C,C-PI PrPsCfP»C-PrP¶PµPSPSCf C,,P»CfPePsPSP°P·PsP»Cf PrP»Cf P»C-PeCfPIP°PSPSCf PrPµCfPjP°C,PsC,,C-C,C-C— Cf PrC-C,PµPñ, C,,P»CfPePsPSP°P·PsP» PSPµ PİPµCfPµPIPëC°CfC" PİCfPëP·PµPsC,,CfP»CHPIC-PS P·P° PµC,,PµPeC,PëPIPSC-CfC,CH C- P·P°PiP°P»CHPSPëPñ PİPsPeP°P·PSPëPe PµC,,PµPeC,PëPIPSPsCfC,C- CfC,P°PSPsPIPëC,CH PjPµPSC€Pµ 20 %. PŸPsPjCf C,,P»CfPePsPSP°P·PsP» PSPµ CfP»C-Pr P·P°CfC,PsCfPsPICfPIP°C,Pë PrP»Cf P»C-PeCfPIP°PSPSCf PrPµCfPjP°C,PsC,,C-C,C-C—.

PµCfPëPiC,PSPePsPePsP·. P"PsPeP°P·C-PI PµC,,PµPeC,PëPIPSPsCfC,C- C,,P»CfPePsPSP°P·PsP»Cf PrP»Cf P»C-PeCfPIP°PSPSCf PeCfPëPiC,PSPePsPePsP·Cf C-PSC€PëC... P»PsPeP°P»C-P·P°CfC-Pñ (PSP°PİCfPëPeP»P°Pr P»PµPiPµPSPµPIPsPiPs PeCfPëPiC,PSPePsPePsP·Cf C,P° PeCfPëPiC,PSPePsPePsP·Cf C€PeC-CfPë) PSPµPrPsCfC,P°C,PSCHPs, C,PSPjCf CfPµPePsPjPµPSPrP°CfC-Pñ C°PsPrPs PrPsP·PsPIPsPiPs CfPµP¶PëPjCf PrP»Cf P»C-PeCfPIP°PSPSCf C,P°PePëC... P·P°C...PIPsCfCHPIP°PSCH PSPµPjP°C".

P" P»PëP±PsPeC- PµPSPrPµPjC-CfPSC- PjC-PePsP·Pë. P"PsPeP°P·C-PI PµC,,PµPeC,PëPIPSPsCfC,C- C,,P»CfPePsPSP°P·PsP»Cf PrP»Cf P»C-PeCfPIP°PSPSCf C-PSC€PëC... C,,PsCfPj PµPSPrPµPjC-CfPSPëC... PjC-PePsP·C-PI, C,P°PePëC... CfPe PİP°CfP°PePsPeCfPëPriPsC—PrPsPjiPePsP·, PİC-CfC,PSPİP»P°P·PjPsP· C,P° C€PeC-CfPSPs- P»C-PjC,,P°C,PëCfPSPëPñ CfPİPsCfPsC,CfPëC...PsP·, PSPµPrPsCfC,P°C,PSCHPs, C,PSPjCf CfPµPePsPjPµPSPrP°CfC-Pñ C°PsPrPs PrPsP·PsPIPsPiPs CfPµP¶PëPjCf PrP»Cf P»C-PeCfPIP°PSPSCf C,P°PePëC... P·P°C...PIPsCfCHPIP°PSCH PSPµPjP°C".

PµP°PSPrPëPrPsP·. P"PsCfP»C-PrP¶PµPSPSCf PİPsPeP°P·P°P»Pë P·P±C-P»CHC€PµPSPSCf PİPsC€PëCfPµPSPsCfC,C- C-PSC,,PµPeCfC-Pñ, CfPİCfPëCfPëPSPµPSPëC... C-PSC€PëPjPë PIPëPrP°PjPë *Candida*, PeCfC-Pj *C. albicans*. P"PsPSPë CfP°CfC,Ps CfPµP·PëCfC,PµPSC,PSC- P·P° CfPIPsC"CH PİCfPëCfPsPrPsCH (PSP°PİCfPëPeP»P°Pr *C. krusei* C,P° *C. auris*) P°P±Ps PİCfPsCfPIP»CfCfC,CH P·PSPëP¶PµPSCf CfCfC,P»PëPIC-CfC,CH PrPs C,,P»CfPePsPSP°P·PsP»Cf (*C. glabrata*). PŸP°PeC- C-PSC,,PµPeCfC-C— PjPsP¶CfC,CH PIPëPjP°PiP°C,Pë P°P»CHC,PµCfPSP°C,PëPIPSPsC— PİCfPsC,PëPiCfPëP±PePsPIPsC— C,PµCfP°PiC-C—. PŸPsPjCf CfPµPePsPjPµPSPrCfC"CHCfCf PİCfP°C...PsPICfPIP°C,Pë PİPsC€PëCfPµPSC-CfC,CH CfPµP·PëCfC,PµPSC,PSPsCfC,C- CfC-P·PSPëC... PIPëPrC-PI *Candida* PrPs C,,P»CfPePsPSP°P·PsP»Cf.

PkPëCfPePsPIP° CfPëCfC,PµPjP°. PµP°CfC-C"PSC,P°Pj C-P· PİPsCfCfC€PµPSPSCfPj

C,,CfPSPeC†C-PM₂ PSPeC₇PsPe C,,P»CfPePsPSP°P·PsP» CfP»C-Pr P·P°CfC,PsCfPsPICfPIP°C,Pë P·PsP±PμC₇PμP¶PSC-CfC,Ch (PrPëPI. C₇PsP·PrC-P» B«PŸPiPsCfC-P±P·P°CfC,PsCfCfPIP°PSPSC¶ C,P° PrPsP·PëB»).

PkPμPrPsCfC,P°C,PSC-CfC,Ch PSP°PrPSPeC₇PePsPIPëC... P·P°P»PsP·.
PлPμC,PsPePsPSP°P·PsP», C¶Pe PIC-PrPsPjPs, CfPiC₇PëC±PëPSC¶C”
PSPμPrPsCfC,P°C,PSC-CfC,Ch PSP°PrPSPeC₇PePsPIPëC... P·P°P»PsP·, C- C†Pμ C,P°PePsP¶
PjPsP¶Pμ CfC,PsCfCfPIP°C,PëCfC¶ C,,P»CfPePsPSP°P·PsP»Cf, C...PsC±P°
CfPiPsCfC,PμC₇C-PiP°C”C,ChCfC¶ C₇C-PrPePs. PkPμPrPsCfC,P°C,PSC-CfC,Ch
PSP°PrPSPeC₇PePsPIPëC... P·P°P»PsP·, PiPsPiC¶P·P°PSP° P· PsPrPSPsC±P°CfPSPëPj
P»C-PeCfPIP°PSPSC¶Pj PiC₇PμPrPSC-P·PsPSPsPj, PsPiPëCfP°PSP° PI C₇PsP·PrC-P»C-
B«P·P·P°C”PjPsPrC-C¶ P· C-PSC€PëPjPë P»C-PeP°C₇CfChPePëPjPë P·P°CfPsP±P°PjPë C,P°
C-PSC€C- PIPëPrPë PIP·P°C”PjPsPrC-PM₂B».

P”PμPiP°C,PsP±C-P»C-P°C₇PSP° CfPëCfC,PμPjP°. PμP°C†C-C”PSC,P°Pj C-P·
PiPsC₇CfC€PμPSPSC¶Pj C,,CfPSPeC†C-PM₂ PiPμC±C-PSPePë PiC₇PμPiP°C₇P°C, CfP»C-Pr
P·P°CfC,PsCfPsPICfPIP°C,Pë P· PsP±PμC₇PμP¶PSC-CfC,Ch. P—P°CfC,PsCfCfPIP°PSPSC¶
C,,P»CfPePsPSP°P·PsP»Cf P°CfPsC†C-C₇PIP°P»PsCfC¶ P· PIPëPSPëPePSPμPSPSC¶Pj
C₇C-PrPeC-CfPSPëC... PIPëPiP°PrPeC-PI C₇PsP·PIPëC,PeCf C,C¶P¶PePsC—
PiPμPiP°C,PsC,PsPeCfPëC±PSPsCfC,C-, PIPeP»C₇C±P°C₇C±Pë P»PμC,P°P»ChPSC-
PIPëPiP°PrPePë, PiPsP»PsPIPSPëPj C±PëPSPsPj Cf PiP°C†C-C”PSC,C-PI C-P· C,C¶P¶PePëPjPë
PsCfPSPsPIPSPëPjPë P·P°C...PIPSC₇ChPIP°PSPSC¶PjPë. Pj PIPëPiP°PrPeP°C..., PePsP»Pë
C₇PsP·PIPëC,PsPe PiPμPiP°C,PsC,PsPeCfPëC±PSPsCfC,C- P°CfPsC†C-C₇PIP°PICfC¶ C-P·
P·P°CfC,PsCfCfPIP°PSPSC¶Pj C,,P»CfPePsPSP°P·PsP»Cf, PSPμ P±CfP»Ps PIC-PrP·PSP°C±PμPSPs
C—C— C¶IPSPsC— P·P°P»PμP¶PSPsCfC,C- PIC-Pr P·P°PiP°P»ChPSPsC— PrPsP±PsPIPsC—
PrPsP·Pë PiC₇PμPiP°C₇P°C,Cf, C,C₇PëPiP°P»PsCfC,C- C,PμC₇P°PiC-C—, CfC,P°C,C- P°P±Ps
PIC-PeCf PiP°C†C-C”PSC,P°. P—P°P·PIPëC±P°PM₂ PiPμPiP°C,PsC,PsPeCfPëC±PSC-CfC,Ch,
CfPiC₇PëC±PëPSPμPSP° C,,P»CfPePsPSP°P·PsP»PsPj, PsP±PsC₇PsC,PSP°, P° C—C—
PiC₇PsC¶PIPë P·PSPëPeP°C₇C,Ch PiC-CfP»C¶ PiC₇PëPiPëPSPμPSPSC¶ C,PμC₇P°PiC-C—.

P—P° PiP°C†C-C”PSC,P°PjPë, Cf C¶PePëC... PiC₇Pë P·P°CfC,PsCfCfPIP°PSPSC-
C,,P»CfPePsPSP°P·PsP»Cf CfPiPsCfC,PμC₇C-PiP°C₇C,ChCfC¶ PIC-PrC...PëP»PμPSPSC¶
C₇PμP·CfP»ChC,P°C,C-PI C,,CfPSPeC†C-PsPSP°P»ChPSPëC... PiC₇PsP± PiPμC±C-PSPePë,
CfP»C-Pr PICfC,P°PSPsPIPëC,Pë C₇PμC,PμP»ChPSPëPM₂ PSP°PiP»C¶Pr CfC,PsCfPsPIPSPs
PjPsP¶P»PëPIPsPiPs C₇PsP·PIPëC,PeCf P±C-P»ChC€ C,C¶P¶PePsPiPs CfC₇P°P¶PμPSPSC¶
PiPμC±C-PSPePë.

PμP°C†C-C”PSC,C-PI CfP»C-Pr PiC₇PsC-PSC,,PsC₇PjCfPIP°C,Pë PiC₇Ps CfPëPjPiC,PsPjPë,
C%₀Ps PjPsP¶CfC,Ch CfPIC-PrC±PëC,Pë PiC₇Ps CfPμC₇PM₂PsP·PSPëPM₂ PIPiP»PëPI PSP°
PiPμC±C-PSPeCf (PIPëC₇P°P¶PμPSP° P°CfC,PμPSC-C¶, P°PSPsC₇PμPeCfC-C¶,
PiPsCfC,C-PM₂PSP° PSCfPrPsC,P°, P±P»C₇PIP°PSPSC¶ C,P° P¶PsPIC,C¶PSPëC†C¶). Pj
C,P°PePsPjCf PIPëPiP°PrPeCf P·P°CfC,PsCfCfPIP°PSPSC¶ C,,P»CfPePsPSP°P·PsP»Cf CfP»C-Pr
PSPμPiP°PM₂PSPs PiC₇PëPiPëPSPëC,Pë C,P° PiC₇PsPePsPSCfCfP»ChC,CfPIP°C,PëCfC¶ P·
P»C-PeP°C₇PμPj.

PŸPμC₇C†PμPIPs-CfCzPrPëPSPSP° CfPëCfC,PμPjP°. P”PμC¶PeC- P°P·PsP»Pë, Cf C,PsPjCf
C±PëCfP»C- PM₂ C,,P»CfPePsPSP°P·PsP», P°CfPsC†C-C₇ChC,ChCfC¶ C-P·
PiPsPrPsPIP¶PμPSPSC¶Pj C-PSC,PμC₇PIP°P»Cf QPŸ PSP°
PμP»PμPeC,C₇PsPeP°C₇PrC-PsPiC₇P°PjC-. PαP»CfPePsPSP°P·PsP» PiPsPrPsPIP¶CfC”
C-PSC,PμC₇PIP°P» QPŸ C€P»C¶C...PsPj PiC₇PëPiPSC-C±PμPSPSC¶
PIPëPiC₇C¶PjP»C¶ChC±PsPiPs PeP°P»C-C”PIPsPiPs PeP°PSP°P»Cf (I_{kr}). PμPsPrPsPIP¶PμPSPSC¶
C-PSC,PμC₇PIP°P»Cf QPŸ PIPSP°CfP»C-PrPsPe PrC— C-PSC€PëC...

PjPμPrPēPeP°PjPμPSC,PsP·PSCř CĤPμP°PeC†C-CĤ P· PμPsP·PēPSPsC,,C-P»C-C" CĤ C-
C†PēC†C,PμPjPSPēPjPē PīCĤPsCĬPIP°PjPē (DRESS).

P"C-PiPμCĤC†CžC,P»PēPIC-C†C,CĤ. Pj CĤC-PrPeC-C†PSPēC... PIPēPiP°PrPeP°C...
PiPsPIC-PrPsPjP»CĬP»Pē PīCĤPs CĤPsP·PIPēC,PsPe P°PSP°C,,C-P»P°PeC,PēC†PSPēC...
CĤPμP°PeC†C-PNē.

PiPēC,PsC...CĤPsPj P 450. P»P»CřPePsPSP°P·PsP» C" PīPsPjC-CĤPSPēPj
C-PSPiC-P±C-C,PsCĤPsPj C,,PμCĤPjPμPSC,C-PI CYP2C9 C,P° CYP3Pĥ4. PŷP°PePsP¶
C,,P»CřPePsPSP°P·PsP» C" PīPsC,CřP¶PSPēPj C-PSPiC-P±C-C,PsCĤPsPj C,,PμCĤPjPμPSC,Cř
CYP2C19. PŷP»C-Pr C†PiPsC†C,PμCĤC-PiP°C,Pē P·P° C†C,P°PSPsPj PiP°C†C-C"PSC,C-PI, CĬPeC-
PsPrPSPsC†P°C†PSPs P·P°C†C,PsC†PsPICřCĤC,CĤ C,,P»CřPePsPSP°P·PsP» C,P°
PīCĤPμPiP°CĤP°C,Pē P· PICřP·CĤPePēPj C,PμCĤP°PiPμPIC,PēC†PSPēPj PIC-PePSPsPj, C%Ps
PjPμC,P°P±PsP»C-P·CřCĤC,CĤC†CĬ P· CřC†P°C†C,CĤ CYP2C9, CYP2C19 C,P° CYP3A4.

PŷPμCĤC,,PμPSP°PrPēPS. PŷP»C-Pr CĤPμC,PμP»CĤPSPs C†PiPsC†C,PμCĤC-PiP°C,Pē P·P°
C†C,P°PSPsPj PiP°C†C-C"PSC,P° PīCĤPē PsPrPSPsC†P°C†PSPsPjCř P·P°C†C,PsC†CřPIP°PSPSC-
C,PμCĤC,,PμPSP°PrPēPSCř C,P° C,,P»CřPePsPSP°P·PsP»Cř Cř PrPsP·C- PjPμPSC€Pμ 400 PjPi PSP°
PrPsP±Cř.

P"PsPiPsPjC-P¶PSC- CĤPμC†PsPIPēPSPē. PμCĤPμPiP°CĤP°C, PjC-C†C,PēC,CĤ P»P°PeC,PsP·Cř.
PμP°C†C-C"PSC,P°Pj P· CĤC-PrPeC-C†PSPēPjPē C†PiP°PrPePsPIPēPjPē
P·P°C...PIPsCĤCĤPIP°PSPSCĬPjPē, C,P°PePēPjPē CĬPe PSPμPiPμCĤPμPSPsC†PēPjC-C†C,CĤ
PiP°P»P°PeC,PsP·Pē, PSPμPrPsC†C,P°C,PSC-C†C,CĤ P»P°PeC,P°P·Pē P»P°PiPiP° C,P°
C†PēPSPrCĤPsPj PjP°P»CĤP°P±C†PsCĤP±C†C-C— PiP»CĤPePsP·Pē-PiP°P»P°PeC,PsP·Pē, PSPμ
C†P»C-Pr P·P°C†C,PsC†PsPICřPIP°C,Pē C†PμPNē PīCĤPμPiP°CĤP°C,.

PĥPrPSP° PeP°PiC†CřP»P° P»C-PeP°CĤC†CĤPePsPiPs P·P°C†PsP±Cř PjC-C†C,PēC,CĤ
PjPμPSC€Pμ 1 PjPjPsP»CĤ PSP°C,CĤC-CĤ (23 PjPi), P° PsC,P¶Pμ, PīCĤPμPiP°CĤP°C, PjPsP¶PSP°
PIPIP°P¶P°C,Pē C,P°PePēPj, C%Ps PSPμ PjC-C†C,PēC,CĤ PSP°C,CĤC-CĤ.

P—P°C†C,PsC†CřPIP°PSPSCĬ Cř PiPμCĤC-PsPr PIP°PiC-C,PSPsC†C,C- P°P±Ps
PiPsPrCřPIP°PSPSCĬ PiCĤCřPrPrCĤ.

P-C-PSPePē CĤPμPiCĤPsPrCřPeC,PēPIPSPsPiPs PIC-PeCř

PμPμCĤPμPr PiPsC†P°C,PePsPj P»C-PeCřPIP°PSPSCĬ PiP°C†C-C"PSC,PeCř C†P»C-Pr
PiPsC-PSC,,PsCĤPjCřPIP°C,Pē PīCĤPs PiPsC,PμPSC†C-PNēPSPēPNē CĤPēP·PēPe PrP»CĬ
PiP»PsPrP°. PμC-C†P»CĬ P·P°C†C,PsC†CřPIP°PSPSCĬ PsPrPSPsCĤP°P·PsPIPsC— PrPsP·Pē
PiPsC,CĤC-P±PSPs PIPēC,CĤPēPjP°C,Pē PiPμCĤC-PsPr PIPēPIPμPrPμPSPSCĬ
C,,P»CřPePsPSP°P·PsP»Cř, CĬPePēPNē C†C,P°PSPsPIPēC,CĤ 1 C,PēP¶PrPμPSCĤ (C%Ps
PIC-PrPiPsPIC-PrP°C" 5БĤ"6 PiPμCĤC-PsPrP°Pj PSP°PiC-PIPIPēPIPμPrPμPSPSCĬ), PrPs
PSP°C†C,P°PSPSCĬ PIP°PiC-C,PSPsC†C,C-.

PμCĤPē C,CĤPēPIP°P»PēC... PeCřCĤC†P°C... P»C-PeCřPIP°PSPSCĬ P¶C-PSPeP°Pj
CĤPμPiCĤPsPrCřPeC,PēPIPSPsPiPs PIC-PeCř C†P»C-Pr CĤPsP·PiP»CĬPSCřC,Pē
PjPsP¶P»PēPIC-C†C,CĤ P·P°C†C,PsC†CřPIP°PSPSCĬ PePsPSC,CĤP°C†PμPiC†C-C—
PīCĤPsC,CĬPiPsPj CřC†CĤPePsPiPs PiPμCĤC-PsPrCř P»C-PeCřPIP°PSPSCĬ C,P° PīCĤPsC,CĬPiPsPj
1 C,PēP¶PSCĬ PiC-C†P»CĬ PīCĤPēPNēPsPjCř PsC†C,P°PSPSCHsC— PrPsP·Pē.

P'P°PiC-C,PSC-C†C,CĤ

PhP±CΓPμCḡPIP°C†C-PNεPSC- PrPsCΓP»C-PrP¶PμPSPSCḡ CΓPIC-PrC‡P°C,CH PiCḡPs
PiC-PrPIPëC%PμPSPëPNε CḡPëP·PëPe CΓPiPsPSC,P°PSPSPsPiPs P°P±PsCḡC,Cr Cr P¶C-PSPsPe,
CḡPeC- PsC,CḡPëPjCΓPIP°P»Pë C,,P»CΓPePsPSP°P·PsP» PiCḡPsC,CḡPiPsPj PiPμCḡCëPsPiPs
C,P°/P°P±Ps PrCḡCΓPiPsPiPs C,CḡPëPjPμCΓC,CḡCΓ, PiPsCḡC-PIPSCḡPSPs P· P¶C-PSPeP°PjPë,
CḡPeC- PSPμ PiCḡPëPNεPjP°P»Pë C,,P»CΓPePsPSP°P·PsP» P°P±Ps PsC,CḡPëPjCΓPIP°P»Pë
PjC-CΓC†PμPIC- P°P·PsP»Pë PiCḡPsC,CḡPiPsPj C,P°PePsPiPs P¶ PiPμCḡC-PsPrCΓ.

P°P°PSC- PeC-P»CHPePsC... C,PëCΓCḡC‡ PIP°PiC-C,PSPëC... P¶C-PSPsPe, CḡPeC-
PsC,CḡPëPjCΓPIP°P»Pë PeCΓPjCΓP»CḡC,PëPIPSCΓ PrPsP·CΓ ≤ 150 PjPi C,,P»CΓPePsPSP°P·PsP»CΓ,
P·P°CΓC,PsCΓPsPIP°PSCΓ Cr P† C,CḡPëPjPμCΓC,CḡC-, PSPμ CΓPIC-PrC‡P°C,CH PiCḡPs
P·P±C-P»CHCëPμPSPSCḡ P·P°PiP°P»CHPSPsPiPs CḡPëP·PëPeCΓ PIP°Pr CḡPsP·PIPëC,PeCΓ
PiP»PsPrP°. P' PsPrPSPsPjCΓ PIPμP»PëPePsPjCΓ CΓPiPsCΓC,PμCḡPμP¶PSPsPjCΓ
PePsPiPsCḡC,PSPsPjCΓ PrPsCΓP»C-PrP¶PμPSPSC- PiPμCḡPsCḡP°P»CHPSPëPNε PiCḡPëPNεPsPj
C,,P»CΓPePsPSP°P·PsP»CΓ Cr P† C,CḡPëPjPμCΓC,CḡC- P±CΓPI P°CΓPsC†C-PNεPsPIP°PSPëPNε P·
PSPμPIPμP»PëPePëPj PiC-PrPIPëC%PμPSPSCḡPj CḡPëP·PëPeCΓ CḡPsP·PIPëC,PeCΓ PIP°Pr
PsPiPsCḡPSPs-CḡCΓC...PsPiPsPiPs P°PiP°CḡP°C,CΓ, C%Ps PIC-PrPiPsPIC-PrP°C"
PiCḡPëP±P»PëP·PSPs 1 PrPsPrP°C,PePsPiPsPjCΓ PIPëPiP°PrPeCΓ PSP° 1000 P¶C-PSPsPe, CḡPeC-
PsC,CḡPëPjCΓPIP°P»Pë PeCΓPjCΓP»CḡC,PëPIPSC- PrPsP·Pë ≤ 450 PjPi, PiPsCḡC-PIPSCḡPSPs P·
P¶C-PSPeP°PjPë, CḡPeC- PsC,CḡPëPjCΓPIP°P»Pë PjC-CΓC†PμPIC- P°P·PsP»Pë, C-
PiCḡPëP±P»PëP·PSPs 4 PrPsPrP°C,PePsPiPëPj PIPëPiP°PrPeP°Pj PSP° 1000 P¶C-PSPsPe, CḡPeC-
PsC,CḡPëPjCΓPIP°P»Pë PeCΓPjCΓP»CḡC,PëPIPSC- PrPsP·Pë PiPsPSP°Pr 450 PjPi.
PŸPePsCḡPëPiPsPIP°PSPëPNε PIC-PrPSPsCΓPSPëPNε CḡPëP·PëPe CΓC,P°PSPsPiPëPI 1,29
(95 % P°P† 1,05 PrPs 1,58) PrP»Cḡ 150 PjPi PiPμCḡPsCḡP°P»CHPSPsPiPs PiCḡPëPNεPsPjCΓ
C,,P»CΓPePsPSP°P·PsP»CΓ C,P° 1,98 (95 % P°P† 1,23 PrPs 3,17) PrP»Cḡ PrPsP· PiPsPSP°Pr
450 PjPi C,,P»CΓPePsPSP°P·PsP»CΓ.

P°PsCΓC,CΓPiPSC- PμPiC-PrPμPjC-PsP»PsPiC-C‡PSC- PrPsCΓP»C-PrP¶PμPSPSCḡ
CΓC,PsCΓPsPIPSPs CḡPsP·PIPëC,PeCΓ PIP°Pr CΓPμCḡC†Cḡ PiCḡPë P·P°CΓC,PsCΓCΓPIP°PSPSC-
C,,P»CΓPePsPSP°P·PsP»CΓ PiC-Pr C‡P°CΓ PIP°PiC-C,PSPsCΓC,C- PjP°CḡC,CH
CΓCΓPiPμCḡPμC‡P»PëPIC- CḡPμP·CΓP»CHC,P°C,Pë. PμCḡPsC,Pμ PjPμC,P°P°PSP°P»C-P· 5
PsP±CΓPμCḡPIP°C†C-PNεPSPëC... PrPsCΓP»C-PrP¶PμPSCḡ, PiCḡPsPiPμPrPμPSPëC... P·P°
CΓC‡P°CΓC,Cḡ PeC-P»CHPePsC... C,PëCΓCḡC‡ PIP°PiC-C,PSPëC... P¶C-PSPsPe, CḡPeC-
PsC,CḡPëPjCΓPIP°P»Pë C,,P»CΓPePsPSP°P·PsP» PiCḡPsC,CḡPiPsPj PiPμCḡCëPsPiPs
C,CḡPëPjPμCΓC,CḡCΓ, PIPëCḡPIPëPI PiC-PrPIPëC%PμPSPSCḡ CḡPëP·PëPeCΓ CḡPsP·PIPëC,PeCΓ
PIP°Pr CΓPμCḡC†Cḡ Cr PSPμPjPsPiP»CḡC, PI
1,8Bḡ"2 CḡP°P·Pë PiPsCḡC-PIPSCḡPSPs P· C,P°PePëPj Cr PSPμPjPsPiP»CḡC,, PjP°C,PμCḡC-
CḡPePëC... PSPμ P·P°CΓC,PsCΓPsPICΓPIP°P»Pë C,,P»CΓPePsPSP°P·PsP» C,P°/P°P±Ps
PIPëPePsCḡPëCΓC,PsPICΓPIP°P»Pë P°P·PsP»Pë PrP»Cḡ PjC-CΓC†PμPiPsPiPs
P·P°CΓC,PsCΓCΓPIP°PSPSCḡ.

Pj P·PIC-C,P°C... PsPiPëCΓP°PSPs PICḡPsPrP¶PμPSC- PIP°PrPë CḡPsP·PIPëC,PeCΓ Cr
PSPμPjPsPiP»CḡC,, PjP°C,PμCḡC- CḡPePëC... PsC,CḡPëPjCΓPIP°P»Pë PIPëCΓPsPeC- PrPsP·Pë
(400Bḡ"800 PjPi/PrPsP±CΓ) C,,P»CΓPePsPSP°P·PsP»CΓ PiC-Pr C‡P°CΓ PIP°PiC-C,PSPsCΓC,C-
PiCḡPsC,CḡPiPsPj 3 PjC-CΓCḡC†C-PI P°P±Ps P±C-P»CHCëPμ PrP»Cḡ P»C-PeCΓPIP°PSPSCḡ
PePsPeC†PëPrC-PsC-PrPsPjC-PePsP·CΓ. P'CḡPsPrP¶PμPSC- PIP°PrPë, CḡPeC-
CΓPiPsCΓC,PμCḡC-PiP°P»PëCΓCḡ Cr C†PëC... PSPμPjPsPiP»CḡC,, PIPeP»CḡC‡P°CḡC,CH
P±CḡP°C...C-C†PμC,,P°P»C-Cḡ, PrPëCΓPiP»P°P·C-Cḡ PICΓCëPSPëC... CḡP°PePsPiPëPS,
PSP°PrPjC-CḡPSPμ P·P±C-P»CHCëPμPSPSCḡ PiPμCḡPμPrPSCḡPsPiPs C,C-Pj'CḡC‡PeP°,
PIPëPeCḡPëPIP»PμPSPSCḡ CΓC,PμPiPSPsPiPsC- PeC-CΓC,PePë C,P° PiCḡPsPjPμPSPμPiPs-
PiP»PμC‡PsPiPëPNε CΓPëPSPsCΓC,PsP·. PμCḡPëC‡PëPSPSPs-PSP°CΓP»C-PrPePsPiPëPNε
P·Pi'CḡP·PsPe PjC-P¶ P·P°CΓC,PsCΓCΓPIP°PSPSCḡPj C,,P»CΓPePsPSP°P·PsP»CΓ C,P° C†PëPjPë

PICḡPsPrP¶PμPSPëPjPë PIP°PrP°PjPë PSPμ PICḡC,P°PSPsPIP»PμPSPëPNë.

PḡPμ CḡP»C-Pr P·P°CḡC,PsCḡPsPICḡPIP°C,Pë P·PIPëC‡P°PNëPSC- PrPsP·Pë
C,,P»CḡPePsPSP°P·PsP»Cḡ C,P° PePsCḡPsC,PePsC,CḡPëPIP°P»C- PeCḡCḡCḡPḡ
P»C-PeCḡPIP°PSPSCḡ C,,P»CḡPePsPSP°P·PsP»PsPj Cḡ PḡPμCḡC-PsPr PIP°PiC-C,PSPsCḡC,C-, P·P°
PIPëPSCḡC,PePsPj PeCḡP°PNëPSCḡPsC— PSPμPsP±C...C-PrPSPsCḡC,C-.

PḡPμ CḡP»C-Pr P·P°CḡC,PsCḡPsPICḡPIP°C,Pë PIPëCḡPsPeC- PrPsP·Pë C,,P»CḡPePsPSP°P·PsP»Cḡ
C,P°/P°P±Ps C,CḡPëPIP°P»C- PeCḡCḡCḡPḡ P»C-PeCḡPIP°PSPSCḡ C,,P»CḡPePsPSP°P·PsP»PsPj Cḡ
PḡPμCḡC-PsPr PIP°PiC-C,PSPsCḡC,C-, P·P° PIPëPSCḡC,PePsPj P»C-PeCḡPIP°PSPSCḡ
C-PSC,,PμPeC‡C-PNë, C°Ps PḡPsC,PμPSC‡C-PNëPSPs P·P°PiCḡPsP¶CḡCḡC,CH P¶PëC,C,Cḡ.

P°PsPrCḡPIP°PSPSCḡ PiCḡCḡPrPrCḡ

PḡP»CḡPePsPSP°P·PsP» PḡCḡPsPSPëPeP°C” Cḡ PiCḡCḡPrPSPμ PjPsP»PsPePs C,P° PrPsCḡCḡPiP°C”
PePsPSC‡PμPSC,CḡP°C‡C-C— PḡPsPrC-P±PSPsC— PrPs CḡC-PIPSCḡ Cḡ PḡP»P°P·PjC-
PeCḡPsPIC- (PrPëPi. CḡPsP·PrC-P» B«PḡP°CḡPjP°PePsPeC-PSPμC,PëPeP°B»).

P°PsPrCḡPIP°PSPSCḡ PiCḡCḡPrPrCḡ PjPsP¶PSP° PḡCḡPsPrPsPIP¶CḡPIP°C,Pë PiC-CḡP»Cḡ
P·P°CḡC,PsCḡCḡPIP°PSPSCḡ CḡP°P·PsPIPSC— PrPsP·Pë C,,P»CḡPePsPSP°P·PsP»Cḡ, C°Ps
CḡC,P°PSPsPIPëC,CH 150 PjPi. PḡC-CḡP»Cḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ
P±P°PiP°C,PsCḡP°P·PsPIPëC... PrPsP· P°P±Ps PIPëCḡPsPePsC— PrPsP·Pë
C,,P»CḡPePsPSP°P·PsP»Cḡ PḡPsPrCḡPIP°PSPSCḡ PiCḡCḡPrPrCḡ PSPμ
CḡPμPePsPjPμPSPPrPsPIP°PSPμ. PḡP»C-Pr PsC‡C-PSPëC,Pë PePsCḡPëCḡC,CH
PiPsPrCḡPIP°PSPSCḡ PiCḡCḡPrPrCḡ PrP»Cḡ CḡPsP·PIPëC,PeCḡ C- P·PrPsCḡPsPI'Cḡ
PrPëC,PëPSPë, P° C,P°PePsP¶ PeP»C-PSC-C‡PSCḡ PḡPsC,CḡPμP±Cḡ PjP°C,PμCḡC- Cḡ
P»C-PeP°CḡCḡCHPePsPjCḡ P·P°CḡPsP±C- C- P±CḡPrCH-CḡPeC- PḡPsC,PμPSC‡C-PNëPSC-
PḡPsP±C-C‡PSC- PμC,,PμPeC,Pë C,,P»CḡPePsPSP°P·PsP»Cḡ P°P±Ps PsCḡPSPsPIPSPsPiPs
P·P°C...PIPSCḡCḡPIP°PSPSCḡ PjP°C,PμCḡC- PrP»Cḡ PrPëC,PëPSPë, CḡPeP° PsC,CḡPëPjCḡC”
PiCḡCḡPrPSPμ PIPëPiPsPrPsPICḡPIP°PSPSCḡ.

PḡPμCḡC,PëP»CHPSC-CḡC,CH

P— PrPsCḡP»C-PrP¶PμPSCḡ PSP° C,PIP°CḡPëPSP°C... PIC-PrPsPjPs, C°Ps
C,,P»CḡPePsPSP°P·PsP» PSPμ PIPḡP»PëPIP°PI PSP° C,,PμCḡC,PëP»CHPSC-CḡC,CH Cḡ
CḡP°PjC‡C-PI C,P° CḡP°PjPëC‡CH C°CḡCḡC-PI.

P—PrP°C,PSC-CḡC,CH PIPḡP»PëPIP°C,Pë PSP° CḡPIPëPrPeC-CḡC,CH CḡPμP°PeC‡C-C— PḡCḡPë
PePμCḡCḡPIP°PSPSC- P°PIC,PsC,CḡP°PSCḡPiPsCḡC,PsPj P°P±Ps C-PSCḡPëPjPë
PjPμC...P°PSC-P·PjP°PjPë.

P°PsCḡP»C-PrP¶PμPSCḡ P·PrP°C,PSPsCḡC,C- C,,P»CḡPePsPSP°P·PsP»Cḡ PIPḡP»PëPIP°C,Pë PSP°
CḡPIPëPrPeC-CḡC,CH CḡPμP°PeC‡C-C— PḡCḡPë PePμCḡCḡPIP°PSPSC-
P°PIC,PsC,CḡP°PSCḡPiPsCḡC,PsPj P°P±Ps CḡPsP±PsC,C- P· C-PSCḡPëPjPë
PjPμC...P°PSC-P·PjP°PjPë PSPμ PiCḡPsPIPPrPëP»Pë.

PḡP°C‡C-C”PSC,C-PI CḡP»C-Pr PḡPsPḡPμCḡPμPrP¶P°C,Pë PḡCḡPs PjPsP¶P»PëPIC-CḡC,CH
P·P°PiP°PjPsCḡPsC‡PμPSPSCḡ P°P±Ps CḡCḡPrPsPj PiC-Pr C‡P°Cḡ PḡCḡPëPNëPsPjCḡ
C,,P»CḡPePsPSP°P·PsP»Cḡ C,P° CḡPμPePsPjPμPSPPrCḡPIP°C,Pë C—Pj CḡC,CḡPëPjCḡCḡPIP°C,PëCḡCḡ
PIC-Pr PePμCḡCḡPIP°PSPSCḡ P°PIC,PsC,CḡP°PSCḡPiPsCḡC,PsPj P°P±Ps PIC-Pr CḡPsP±PsC,Pë
P· C-PSCḡPëPjPë PjPμC...P°PSC-P·PjP°PjPë PI CḡP°P·C- PIPëPSPëPePSPμPSPSCḡ P±CḡPrCH-
CḡPePsPiPs P· C‡PëC... CḡPëPjPiC,PsPjC-PI.

PŸPĩPsCÍC-P± P·P°CÍC,PsCÍCżPIP°PSPSCİ C,P° PrPsP·Pë.

PŸP°PĩCÍCÍP»Pë CÍP»C-Pr PePsPIC,P°C,Pë C†C-P»PëPjPë. PıCŸPëPNëPsPj PĩCŸPıPĩP°CŸP°C,CÍ PSPı P·P°P»PıP¶PëC,CH PIC-Pr PĩCŸPëPNëPsPjCÍ C—P¶C-.

P°PsCŸPsCÍP»C-.

P>C-PeP°CŸCÍCHPePëPNë P·P°CÍC-P± P·P°CÍC,PsCÍPsPICÍPIP°C,Pë PıPıCŸPsCŸP°P»CHPSPs CÍ PrPsP·C- 150 PjPi PsPrPSPsCŸP°P·PsPIPs.

PıP°C†C-C°PSC,Pë P»C-C,PSCHPsPiPs PIC-PeCż.

PıCŸPë PIC-PrCÍCÍC,PSPsCÍC,C- PsP·PSP°Pe PıPsCŸCÍCıPıPSPSCİ C,,CÍPSPeC†C-PNë PSPëCŸPsPe PrP»Cİ P»C-PeCÍPIP°PSPSCİ C†C-C°C— PeP°C,PıPiPsCŸC-C— PıP°C†C-C°PSC,C-PI P·P°CÍC,PsCÍPsPICÍPIP°C,Pë P·PIPëC†P°PNëPSCÍ PrPsP·CÍ PrP»Cİ PrPsCŸPsCÍP»PëC....

PıPsCŸCżCıPıPSPSCİ C,,CżPSPeC†C-PNë PSPëCŸPsPe.

PıP»CÍPePsPSP°P·PsP» PIPëPIPsPrPëC,CHCÍCİ PI PsCÍPSPsPIPsPjCÍ P· CÍPıC†PıCH CÍ PSPıP·PjC-PSPıPSPsPjCÍ PIPëPiP»CİPrC-. PıCŸPë CŸP°P·PsPIPsPjCÍ P·P°CÍC,PsCÍCÍPIP°PSPSC- PıCŸPıPĩP°CŸP°C,CÍ PePsCŸPëPiCÍPIP°C,Pë PrPsP·CÍ C†C-PNë PeP°C,PıPiPsCŸC-C— PıP°C†C-C°PSC,C-PI PSPı PıPsC,CŸC-P±PSPs.

PıPsCŸCżCıPıPSPSCİ C,,CżPSPeC†C-PNë PıPıC†C-PSPePë.

PıP»CÍPePsPSP°P·PsP» CÍP»C-Pr P·P°CÍC,PsCÍPsPICÍPIP°C,Pë P· PsP±PıCŸPıP¶PSC-CÍC,CH PıP°C†C-C°PSC,P°Pj C-P· PıPsCŸCÍCıPıPSPSCİPjPë C,,CÍPSPeC†C-PNë PıPıC†C-PSPePë, PsCÍPeC-P»CHPePë C-PSC,,PsCŸPjP°C†C-C— C°PsPrPs P·P°CÍC,PsCÍCÍPIP°PSPSCİ C,,P»CÍPePsPSP°P·PsP»CÍ C†C-PNë PeP°C,PıPiPsCŸC-C— PıP°C†C-C°PSC,C-PI PSPıPrPsCÍC,P°C,PSCHPs (PrPëPI. CŸPsP·PrC-P»Pë B«PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCÍPIP°PSPSCİB» C,P° B«PıPsP±C-C†PSC- CŸPıP°PeC†C-C—B»).

P°C-C,Pë.

P·C,,PıPeC,PëPIPsC-CÍC,CH C,P° P±PıP·PıPıPeP° P·P°CÍC,PsCÍCÍPIP°PSPSCİ PıCŸPıPĩP°CŸP°C,CÍ PrP»Cİ P»C-PeCÍPIP°PSPSCİ PıPıPSC-C,P°P»CHPSPëC... PeP°PSPPrPëPrPsP·C-PI CÍ PrC-C,PıPNë PSPı PICÍC,P°PSPsPIP»PıPSC-, PSPıP·PIP°P¶P°CHC†Pë PSP° PIPëC†PıCŸPıPSC- PrP°PSC- C°PsPrPs P·P°CÍC,PsCÍCÍPIP°PSPSCİ C,,P»CÍPePsPSP°P·PsP»CÍ PrC-C,CİPj. PıPeC°Ps C-CÍPSCÍC° PSP°PıP°P»CHPSP° PıPsC,CŸPıP±P° P·P°CÍC,PsCÍCÍPIP°PSPSCİ PıCŸPıPĩP°CŸP°C,CÍ PıC-PrP»C-C,PeP°Pj (PIC-PePsPj PIC-Pr 12 PrPs 17 CŸPsPeC-PI), CÍP»C-Pr P·P°CÍC,PsCÍPsPICÍPIP°C,Pë P·PIPëC†P°PNëPSC- PrPsP·Pë PrP»Cİ PrPsCŸPsCÍP»PëC....

PıPıCŸPıPrPsP·CżPIP°PSPSCİ.

PhC,CŸPëPjP°PSPs PıPsPIC-PrPsPjP»PıPSPSCİ PıCŸPs PıPıCŸPıPrPsP·CÍPIP°PSPSCİ C,,P»CÍPePsPSP°P·PsP»PsPj; PsPrPSPsC†P°CÍPSPs PıPsPIC-PrPsPjP»CİP»Pë PıCŸPs

PIP°P»CĤC†PëPSP°C†C-C— C,P° PİP°CĤP°PSPsC—PrP°P»CHbPSCř PİPsPIPµPrC-PSPeCř.

PµCĤPë PİPµCĤPµPrPsP·CřPIP°PSPSC- PSPµPsP±C...C-PrPSPs PİCĤPsPIPµCĤC,Pë CĤPëPjPİC,PsPjP°C,PëC†PSCř PİC-PrC,CĤPëPjCřPIP°P»CHbPSCř C,PµCĤP°PİC-CĤ C,P° Cř CĤP°P·C- PSPµPsP±C...C-PrPSPsCĤC,C- PİCĤPsPjPëC,Pë C€P»CřPSPsPe.

PαP»CřPePsPSP°P·PsP» P·PSP°C†PSPsCĤ PjC-CĤPsCĤ PµPeCĤPeCĤPµC,CřC”C,CHbCĤCĤ P· CĤPµC†PµCĤ; C,,PsCĤCĤPsPIP°PSPëPµ PrC-CřCĤPµP· PjPsP¶Pµ PİCĤPëCĤPePsCĤPëC,Pë PIPëPIPµPrPµPSPSCĤ PİCĤPµPİP°CĤP°C,Cř. PŸPµP°PSCĤ PİPµPjPsPrC-P°P»C-P·Cř C,CĤPëPIP°P»C-CĤC,CĤ 3 PİPsPrPëPSPë P·PSPëP¶CřC” CĤC-PIPµPSCĤ C,,P»CřPePsPSP°P·PsP»Cř Cř PİP»P°P·PjC- PeCĤPsPIC- PİCĤPëP±P»PëP·PSPs PSP° 50 %.

PµPsP±C-C†PSC- CĤPµP°PeC†C-C—.

PĤP°PµC†P°CĤC,C-C€Pµ (≥ 1/100 PrPs < 1/10) PİPsPIC-PrPsPjP»CĤP»Pë PİCĤPs C,P°PeC- PİPsP±C-C†PSC- CĤPµP°PeC†C-C—: PİPsP»PsPIPSPëPµ P±C-P»CHb, P±C-P»CHb Cř P¶PëPIPsC,C-, PrC-P°CĤPµCĤ, PSCřPrPsC,P°, P±P»CĤPIP°PSPSCĤ, PIPëCĤPëPİP°PSPSCĤ, PİC-PrPIPëC%PµPSPSCĤ CĤC-PIPSCĤ P°P»P°PSC-PSP°PjC-PSPsC,CĤP°PSCĤC,,PµCĤP°P·Pë (PĥP»PŸ), P°CĤPİP°CĤC,P°C,P°PjC-PSPsC,CĤP°PSCĤC,,PµCĤP°P·Pë (PĥPŸPŸ), P»CřP¶PSPsC— C,,PsCĤC,,P°C,P°P·Pë PeCĤPsPIC-. PµPsPIC-PrPsPjP»CĤP»Pë PİCĤPs PjPµPrPëPeP°PjPµPSC,PsP·PSCř CĤPµP°PeC†C-CĤ P· PµPsP·PëPSPsC,,C-P»C-C”CĤ C- CĤPëCĤC,PµPjPSPëPjPë PİCĤPsCĤPIP°PjPë (DRESS), P°CĤPsC†C-PµPsPIP°PSCř C-P· P·P°CĤC,PsCĤCřPIP°PSPSCĤPj C,,P»CřPePsPSP°P·PsP»Cř.

P”P»CĤ PsC†C-PSPePë C†P°CĤC,PsC,Pë PIPëPSPëPePSPµPSPSCĤ PİPsP±C-C†PSPëC... CĤPµP°PeC†C-Pµ PIPëPePsCĤPëCĤC,P°PSP° C,P°PeP° PeP»P°CĤPëC,,C-PeP°C†C-CĤ: PrCřP¶Pµ C†P°CĤC,Ps (≥ 1/10), C†P°CĤC,Ps (≥ 1/100 C- < 1/10), PSPµC†P°CĤC,Ps (≥ 1/1000 C- < 1/100), CĤC-PrPePs (≥ 1/10000 C- < 1/1000), PrCřP¶Pµ CĤC-PrPePs (< 1/10000), C†P°CĤC,PsC,P° PSPµPIC-PrPsPjP° (PSPµPjPsP¶P»PëPIPs PsC†C-PSPëC,Pë PSP° PİC-PrCĤC,P°PIC- PSP°CĤPIPSPëC... PrP°PSPëC...).

P— P±PsPeCž PeCĤPsPIPsPSPsCĤPSPsC— C,P° P»C-PjC,,P°C,PëC†PSPsC— CĤPëCĤC,PµPjPë.

PĤPµC†P°CĤC,Ps: P°PSPµPjC-CĤ.

P C-PrPePs: P°PİCĤP°PSCřP»PsC†PëC,PsP·, P»PµPµPePsPİPµPSC-CĤ, PSPµPµC,CĤPsPİPµPSC-CĤ, C,CĤPsPjP±PsC†PëC,PsPİPµPSC-CĤ.

P— P±PsPeCž C-PjCžPSPSPsC— CĤPëCĤC,PµPjPë.

P C-PrPePs: P°PSP°C,,C-P»P°PeCĤC-CĤ.

P— P±PsPeCž PjPµC,P°P±PsP»C-P·PjCž C,P° C...P°CĤC†CžPIP°PSPSCĤ.

PĤPµC†P°CĤC,Ps: P·PSPëP¶PµPSPSCĤ P°PİPµC,PëC,Cř.

P C-PrPePs: PİC-PİPµCĤC,CĤPëPİP»C-C†PµCĤPëPrPµPjC-CĤ, PİC-PİPµCĤC...PsP»PµCĤC,PµCĤPëPSPµPjC-CĤ, PİC-PİPsPeP°P»C-C”PjC-CĤ.

P— P±PsPeCž PİCĤPëC...C-PePë.

P C-PrPePs: C,PsPeCÍPëC‡PSPëPNë PµPíC-PrPµCĤPjP°P»CHßPSPëPNë PSPµPeCĤPsP»C-P·,
CÍPëPSPPrCĤPsPj PŸC,C-PIPµPSCÍP° бĤ „ P°P¶PsPSCÍPsPSP°, PiPsCÍC,CĤPëPNë
PiPµPSPµCĤP°P»C-P·PsPIP°PSPëPNë PµPeP·P°PSC,PµPjP°C,PsP·PSPëPNë PiCrCÍC,CrP»CHßPsP·,
PµPeCÍC„PsP»C-P°C,PëPIPSPëPNë PrPµCĤPjP°C,PëC,, P°PSPiC-PsPSPµPICĤPsC,PëC‡PSPëPNë
PSP°P±CĤCΠPë, PSP°P±CĤCΠPë PsP±P»PëC‡C‡CΠ, P°P»PsPîPµC‡C-CΠ.

**РѢС-СІС†РμР·PSP°С...PsPrP¶PμPSPSCІІ PIPëCЃPsP±PSPëPeP° С,P° P°PrCЃPμCІP°
PjC-СІС†CІІ PïCЃPsPIP°PrP¶PμPSPSCІІ PN₂PsPiPs PrC-СІP»CḤPSPsCІC,C-.**

P"С-P»CḤPSPëC†CІІ 1; H-4042 P"РμP±CЃPμC†PμPS, PICíP». PıP°P»P»P°PiC- 13,
PJPiPsCЃC‰PëPSP°.